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THE USE OF DIETARY SUPPLEMENTS AND MEDICATION AMONG FINNISH ELITE ATHLETES

by

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To my family

ABSTRACT

Anni Aavikko - The use of dietary supplements and medication among Finnish elite athletes. Department of Health Exercise, University of Turku, Department of Physiology and Paavo Nurmi Centre , University of Turku.

Background: Dietary supplements are widely used among elite athletes but the prevalence of dietary supplement use among Finnish elite athletes is largely not known. The use of asthma medication is common among athletes. In 2009, the World Anti-Doping Agency (WADA) and the International Olympic Committee (IOC) removed the need to document asthma by lung function tests before the use of inhaled β2-agonists. Data about medication use by Paralympic athletes (PA) is limited to a study conducted at the Athens Paralympics.

Aims: To investigate the prevalence of the use of self-reported dietary supplements, the use of physician-prescribed medication and the prevalence of physician-diagnosed asthma and allergies among Finnish Olympic athletes (OA). In addition, the differences in the self-reported physician-prescribed medication use were compared between the Finnish Olympic and the Paralympic athletes.

Subjects and methods: Two cross-sectional studies were conducted in Finnish Olympic athletes receiving financial support from the Finnish Olympic Committee in 2002 (n=446) and in 2009 (n=372) and in Finnish top-level Paralympic athletes (n= 92) receiving financial support from Finnish Paralympic committee in 2006. The results of the Paralympic study were compared with the results of the Olympic study conducted in 2009. Both Olympic and Paralympic athletes filled in a similar semi-structured questionnaires.

Results: Dietary supplements were used by 81% of the athletes in 2002 and by 73% of the athletes in 2009. After adjusting for age-, sex- and type of sport, the odds ratio OR (95% confidence interval, CI) for use of any dietary supplement was significantly less in 2009 as compared with the 2002 situation (OR 0.62; 95% CI 0.43-0.90). Vitamin D was used by 0.7% of the athletes in year 2002 but by 2% in 2009 (ns, p = 0.07). The use of asthma medication increased from 10.4 % in 2002 to 13.7% in 2009 (adjusted OR 1.71; 95% CI 1.08-2.69). For example, fixed combinations of inhaled long-acting β2-agonists (LABA) and inhaled corticosteroids (ICS) were used three times more commonly in 2009 than in 2002 (OR 3.38; 95% CI 1.26-9.12). The use of any physician-prescribed medicines (48.9% vs. 33.3%, adjusted OR 1.99; 95% CI 1.13-3.51), painkilling medicines (adjusted OR 2.61; 95% CI 1.18-5.78), oral antibiotics (adjusted OR 4.10; 95% CI 1.30-12.87) and anti-epileptic medicines (adjusted OR 37.09; 95% CI 5.92-232.31) was more common among the PA than in the OA during the previous seven days.

Conclusions: The use of dietary supplements is on the decline among Finnish Olympic athletes. The intake of some essential micronutrients, such as vitamin D, is suprisingly low and this may even cause harm in those well-trained athletes. The use of asthma medication, especially fixed combinations of LABAs and ICS, is clearly increasing among Finnish Olympic athletes. The use of any physician-prescribed medicine, especially those to treat chronic diseases, seems to be more common among the Paralympians than in the Olympic athletes.

Keywords: Olympic athletes, Paralympic athletes, dietary supplements, asthma, medication

TIIVISTELMÄ

Anni Aavikko - Lääkkeiden ja lisäravinteiden käyttö suomalaisilla huippu-urheilijoilla. Department of Health Exercise, University of Turku, Department of Physiology and Paavo Nurmi Centre , University of Turku.

Tausta: Huippu-urheilijoiden lisäravinteiden käytön tiedetään olevan yleistä. Lisäravinteiden käyttöä suomalaisessa urheilussa ei kuitenkaan ole tutkittu. Urheilijat käyttävät astmalääkkeitä normaaliväestöä enemmän. Vuonna 2009 maailman antidopingkomitea (WADA) sekä kansainvälinen olympiakomitea (KOK) poistivat säädöksen, jonka mukaan urheilijan astma on dokumentoitava keuhkojen toimintatutkimuksin, ennen inhaloitavien β2-agonistien käyttöön ottoa. Paralympiaurheilijoiden lääkkeiden käytöstä on julkaistu ainoastaan yksi tutkimus Ateenan paralympialasten yhteydessä.

Tavoite: Tutkia suomalaisten olympiaurheilijoiden lisäravinteiden ja lääkkeiden käyttöä sekä lääkärin diagnosoiman astman ja allergian esiintymistä suomalaisilla olympiaurheilijoilla. Lisäksi tutkimuksessa selvitettiin lääkkeiden käytön eroja suomalaisilla paralympia- ja olympiaurheilijoilla.

Menetelmät: Tutkimus suoritettiin kahtena poikkileikkaustutkimuksena suomalaisille olympiaurheilijoille vuonna 2002 (n= 446) ja vuonna 2009 (n=372) sekä vuonna 2006 paralympiaurheilijoille (n=92), jotka saivat kyseisinä vuosina rahallista tukea suomen Olympia- ja Paralympiakomiteoilta. Paralympiatutkimuksesta saatuja tuloksia verrattiin vuoden 2009 olympiaurheilijoille tehdyn tutkimuksen tuloksiin. Olympia- ja paralympiaurheilijat vastasivat samanlaiseen puolistruktroituun kyselylomakkeeseen.

Tulokset: Lisäravinteita käytti vuonna 2002 81% urheilijoista ja vuonna 2009 73% urheilijoista. Iän- sukupuolen ja lajiryhmien vakioimisen jälkeen lisäravinteiden käyttö oli merkitsevästi vähäisempää vuonna 2009 kuin vuonna 2002 (vakioitu riskisuhde 0.62; 95% luottamusväli 0.43-0.90). D-vitamiinivalmisteita käytti vuonna 2002 0.7% urheilijoista ja vuonna 2009 2% urheilijoista ($p = 0.07$). Astmalääkkeitä käytti vuonna 2002 10.1% ja vuonna 2009 13.7% urheilijoista (riskisuhde, 1.71, 95% luottamusväli 1.08-2.69). Inhaloitavaa kortisonia ja pitkävaikutteista β2-agonistia sisältävien yhdistelmävalmisteiden käyttö lisääntyi kolminkertaisesti tutkimusvuosien välillä (riskisuhde 3.38; 95% luottamusväli 1.26-9.12). Viimeisten seitsemän päivän aikana paralympiaurheilijat käyttivät olympiaurheilijoita merkitsevästi enemmän mitä tahansa lääkärin määräämiä lääkkeitä (48.9% vs. 33.3% vakioitu riskisuhde, 1.99; 95% luottamusväli 1.13-3.51), kipulääkkeitä (vakioitu riskisuhde 2.61; 95% luottamusväli 1.18-5.78), suun kautta otettavia antibiootteja (vakioitu riskisuhde 4.10; 95% CI 1.30-12.87) sekä epilepsialääkkeitä (vakioitu riskisuhde, 37.09; 95% CI 5.92-232.31).

Johtopäätökset: Suomalaisten olympiaurheilijoiden lisäravinteiden käyttö on vähenemässä. Joidenkin välttämättömien vitamiinien ja hivenaineiden, kuten D-vitamiinin käyttö on kuitenkin huolestuttavan vähäistä. Suomalaisten olympiaurheilijoiden astmalääkkeiden, erityisesti inhaloitavaa kortisonia ja pitkävaikutteista β2-agonistia sisältävien yhdistelmävalmisteiden käyttö on lisääntymässä. Paralympiaurheilijat käyttävät olympiaurheilijoita enemmän kroonisten sairauksien hoitoon käytettäviä lääkkeitä.

Avainsanat: olympiaurheilijat, paralympiaurheilijat, lisäravinteet, astma, lääkehoito

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ABBREVIATIONS

AA= α-linoleic acid

AD= autonomic dysreflexia

BCT= basic combat training

CI= confidence interval

CK= creatine kinase

COX= cyclo-oxygenace

COX-1= cyclo-oxygenace-1

COX-2= cyclo-oxygenace-2

DHA= docosahexanoeic acid

DOMS= delayed-onset muscle soreness

DS= dietary supplement

EIB= exercise-induced bronchoconstriction

EICR= exercise-induced cardiac remodeling

EPA= eicosapentanoeic acid

FDA= food and drug administration

GI= gastrointestinal

HO= heterotrophic ossification

ICS= inhaled corticosteroids

ID= iron defiency

IDA= iron deficiency anemia

IOC= International Olympic Committee

km= kilometers

LABA= long-acting β2-agonists

l= litres

LTRA= leukotriene antagonists

mg= milligrams

min= minutes

NSAIDs= non-steroidal anti-inflammatory drugs

NS= nutritional supplements

ns= non significant

n3-PUFA= omega3- fatty acids

n6-PUFA= omega-6 fatty acids

OR= odds ratio

PGE= prostaglandin E

$PGF_{2\alpha}$= prostaglandin $F_{2\alpha}$

PSE= pseudoephedrine

SCI= spinal cord injury

TUE= Therapeutic Use Excemption

URT=upper respiratory trackt

WADA= World Antidoping Agency

WHO= World Health Organisation

$1,25(OH)_2D$= 1,25-hydroxyvitamin D

$25(OH)_2D$= 25- hydroxyvitamin D

µg= micrograms

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications which are referred to in the text by Roman numbers I-IV.

I **Heikkinen A**, Alaranta A, Helenius I, Vasankari T. Use of dietary supplements in Olympic athletes is decreasing: a follow-up study between 2002 and 2009. J Int Soc Sports Nut 2011: 8:v1.

II **Heikkinen A**, Alaranta A, Helenius I, Vasankari T. Dietary supplementation habits and perceptions of supplement use among elite Finnish athletes. Int J Sport Nutr Exerc Metab 2011: 21: 271-279.

III **Aavikko A**, Alaranta A, Helenius I, Vasankari T, Haahtela T. Asthma medication is increasingly prescribed for Finnish Olympic athletes- For a Reason? J Asthma 2012: 49: 744-749.

IV **Aavikko A**, Helenius I, Vasankari T,Alaranta A. A physician-prescribed medication use by the Finnish Paralympic and Olympic athletes. Submitted.

1. INTRODUCTION

The passion for winning is the force that spurs on athletes to overwhelming performances. As a way of gaining a competitive edge over their opponents, some athletes are not only ready to train intensively but also to use performance-enhancing aids. The history of use of performance-enhancing substances goes back thousands of years, in fact, the use of these kinds of agents was even more common among in ancient athletes. An increase in the use of performance-enhancing drugs in sport occured in the 20th century when medicine was rapidly developing. In the early days, stimulants and alcoholic containing products were the substances most commonly being used. The first list of banned substances in sport was published in 1963 and the first doping tests were conducted at the 1968 Grenoble Olympic Games (Alaranta et al, 2007b). The first fatality attributed to doping was reported in 1886: an English cyclist is said to have overdosed on 'tri-methyl', probably a compound containing either caffeine or ether, during a 600km (373 miles) race between Bordeaux and Paris (Prokop, 1970). Today, theuse of medications by athletes is strictly regulated by the World Anti-Doping Agency (WADA) and the International Olympic Committee (IOC). A list of banned substances in sport is published every year by WADA (World Anti-Doping Agency). Paralympic athletes are required to adhere to the same anti-doping regulations as healthy athletes (Official website of the Paralympic Movement, Anti-Doping).

Nutritional supplements (NS) are frequently used in high- level sport (Maughan and Shirreffs, 2012). Some problems have been encountered with these preparations such as contamination with doping-positive substances (Geyer et al., 2004). Little is known about the positive effect of most of the dietary supplements (DSs) to the athletic performance although some DSs, such as vitamin D, iron, calcium and caffeine may be beneficial for athletes (Maughan and Shirreffs, 2012;McClung, 2012;Nieves et al., 2010).

There is a relatively high prevalence of respiratory diseases such as asthma, chronic cough, recurrent respiratory infections and various upper airways conditions among athletes (Boulet, 2012). In addition, athletes can suffer from musculoskeletal injuries especially in sports that include fast movements, jumps or frequent and powerful body contacts (Kujala et al., 1995). All these conditions increase the need for medication use by athletes. However, all medicines have side effects that may have negative impact on athletes´ performance and health. In addition, many athletes may not use the medicines in the way they are generally recommended to be used (Rankin, 2004).

The International Paralympic Committee (IPC) is responsible for organizing the Paralympic Games that are held every two years immediately after their respective Summer and Winter Olympic Games. The Paralympics have grown from a small gathering of

British World War II veterans in 1948 to become one of the largest international sport events of the early 21st century. In the 2008 Summer Paralympic Games, there were more than 4000 athletes competing in 20 different sports. In 2010, there were a total of 502 disabled athletes competing in five different sports in the Vancouver Winter Olympic Games (Official website of the Paralympic Movement, The IPC).

This study was designed to assess the use of DSs and medication and the prevalence of physician-diagnosed asthma and allergies among a large sample of Finnish Olympic athletes. The results were compared between different sport groups. In addition, the prevalence of medication use among Finnish Paralympic athletes was assessed. The review of the literature deals with the specific physiological and pathophysiological changes in highly-trained athletes. The use of dietary supplements, asthma medicines and non-steroidal anti-inflammatory drugs (NSAIDs) and their effects on both the athletes themselves and exercise performance are described. In addition, the special characteristics of the Paralympic athletes are described

2. REVIEW OF THE LITERATURE

2.1 PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL CHANGES IN ELITE ATHLETES

2.1.1 Cardiovascular changes

Cardiac output, defined as the product of stroke volume and heart rate, may increase 5- to 6- fold during a maximal exercise effort. The repetitive participation in vigorous physical exercise results in significant changes in myocardial structure and function. This process, termed exercise induced cardiac remodeling (EICR), is characterized by structural cardiac changes including left ventricular hypertrophy associated with alterations in both systolic and diastolic function. These changes in cardiac function last a lifetime and are generally seen as beneficial physiology for the individual (Pelliccia et al., 2010).

The hemodynamic changes that occur during exercise are the primary stimulus for EICR but the hemodynamic conditions vary widely across sporting disciplines (Rowell, 1986). Although considerable overlap does exist, exercise activity can be segregated into two principal physiological forms according to their hemodynamic characteristics (Maron and Zipes, 2005).Isotonic exercise, commonly referred to as endurance exercise, involves sustained elevations in cardiac output with normal or reduced peripheral resistance. This form of exercise is the basis for such sporting activities as including long-distance running, cycling, rowing, swimming and cross-country skiing. Isometric exercise, commonly referred to as strength training, is characterized by short but intense bouts of increased peripheral vascular resistance and normal or only slightly elevated cardiac output. Strength training physiology is dominant during activities such as weightlifting and track-and-field throwing events, referred to as “speed and power events”. Many sports, including popular team-based activities such as soccer, basketball and ice-hockey, involve significant elements of both endurance and strength exercise (Weiner and Baggish, 2012).

2.1.2 Changes in respiratory function

During exercise, minute ventilation increases by up to 30- fold from a resting level of 5 l/ min, initially to meet the oxygen demands of the muscles and subsequently in response to the metabolic acidosis that develops during prolonged exercise. This is achieved by increasing tidal volume and respiratory frequency leading to increased minute ventilation. A shift from nasal to mouth breathing occurs when the minute ventilation exceeds 35 to 40 l/ min. In comparison with sedentary conditions when air is inhaled primary through the nose and almost fully conditioned to body temperature and 100% relative humidity before it reaches the lower airways, mouth breathing leads in incomplete conditioning and filtration of the inspired air (Niinimaa et al., 1980;Saibene et al., 1978). During mouth breathing, the task of conditioning the inspired air to body temperature and 100% relative humidity is completed by the lower airways and there is a greater deposition of airborne allergens and other inhaled particles on the mucous membranes of the lower airways (McFadden et al., 1985). These changes in the mechanisms of breathing expose athletes to several lower respiratory trackt symptoms such as asthma and exercise-induced bronchoconstriction (EIB) which is the development of a transient narrowing of the airways after exercise (Anderson and Daviskas, 2000).

The major risk factors for asthma in athletes are type and intensity of training (i.e. endurance or speed and power), atopic disposition (Helenius et al., 1998) and environmental factors. Winter sport athletes train all-year round and are exposed to outdoor pollutants and cold air. Indoor athletes, as well as summer sport athletes training inside during the winter season, are exposed to poor air quality and swimmers may breathe chlorine gas present in the air in swimming halls (Helenius et al., 1998) . The prevalence of asthma and EIB is known to be more common among endurance athletes than in other groups of athletes (Lund et al., 2009;Thomas et al., 2010), and it is especially high among cross-country skiers (Wilber et al., 2000) and swimmers (Helenius et al., 1998). The extensive exposure to cold air during training and competition has been proposed to be one of the main reasons for the high prevalence of asthma encountered in cross-country skiers (Larsson et al., 1998). Exposure to cold air (-23ºC) has been shown to induce an increase in the number of inflammatory cells in the lower airways in healthy adults when compared to the situation when similar exercise is done at normal temperature (+22ºC) (Larsson et al., 1998). A mixed type of airway inflammation, mostly consisting of neutrophils and eosinophils, has been shown to afflict elite swimmers and cross-country skiers (Helenius et al., 2002;Karjalainen et al., 2000). Thus, two different phenotypes of asthma may exist in elite athletes: "Classical asthma" characterized by early onset childhood asthma, metacholine responsiveness, atopy and signs of eosinophilic inflammation; "another" phenotype has the onset of symptoms occurring during the sports career, bronchiolar responsiveness in the eucapnic hyperventilation test and a variable association with atopic disposition and eosinophilic inflammation (Haahtela, Malmberg, and Moreira, 2008).

In addition to asthma and EIB, the exposure to allergens may trigger inflammation in the nasal mucous membranes that leads to allergic rhinitis (Bachert et al., 2002). Nasal obstruction causes impaired sleep which in turn may contribute to daytime fatigue and somnolence and thus interfere with an athlete´s physical performance and quality of life (Katelaris, Carrozzi, and Burke, 2003). Allergic rhinitis is an independent risk factor for asthma (Bachert et al., 2002).

Table 1. Prevalence of asthma among Olympic athletes in winter and summer sports

Prevalence of asthma (%)	Study year, athlete group, number of subjects (N)	Method	Reference
9.7%	1976 Australian Olympic team (N=185)	Physical examination	Fitch 1984
8.5%	1980 Australian Olympic team (N=106)	Physical examination	Fitch 1984
4.4%	1984 US Olympic team (N=597)	Questionnaire, treadmill exercise challenge test in selected athletes	Voy 1986
4.4%	1992 Spanish Olympic team	Questionnaire	Drobnic 1994
15.3%[1]	1996 US Olympic team (N=699)	Questionnaire	Weiler et al. 1998
21.9%[2]	1998 US Olympic team (N=196)	Questionnaire	Weiler et al. 2000
23%	2000 US Olympic team participating 1998 Games (N=170)	Exercise challenge	Wilber et al. 2000
7.0%	2000 Italian Olympic athletes trying for Sydney Olympics (N=1060)	Questionnaire, spirometry	Maiolo et al. 2003
17%	2008 German Olympic athletes trying for Beijing Olympics (N=291)	Questionnaire	Thomas et al. 2010

[1]10% had active asthma defined as the athlete´s use of asthma medication at the time of the 1996 Summer Olympics
[2]17% had active asthma defined as the athlete´s use of asthma medication at the time of the 1998 Winter Olympics

2.1.3 Musculoskeletal injuries

Musculoskeletal injuries account for most sports-related injuries causing significant structural or functional damage in the muscle and chronic or intermittent symptoms depending on the activity being done by the athletes (Almekinders, 1999). There are different types of sports injuries such as acute injuries or overuse traumas. The frequency of injury rates between different sports varies greatly (Parkkari et al., 2004). Kujala et al. (1995) defined the injury profiles of six different sports (judo, karate, ice hockey, soccer, volleyball and basketball). The overall risk of acute injuries was highest in sports entailing frequent and powerful body contacts such as judo, karate and ice hockey. Each sport had its own injury profile. Most injuries were sprains, strains and bruises. Knee injuries were the most common cause of permanent disability (Kujala et al., 1995). Different kinds of injury prevention programs have been developed (Aaltonen et al., 2007). Aaltonen et al. (2007) conducted a systematic review of the effects of randomized controlled interventions to prevent sport injuries. A reduction in the risk of sports injuries was associated with the use of insoles, external joint supports, and multi-intervention training programs.

Overuse traumas, such as stress-fractures and tendinopathies, are seen as a result of repeated microtrauma without any single identifiable event being responsible for the condition (Fuller et al., 2006). Tendon pain is frequently reported in many sports in such as volleyball, basketball, long distance running, and jumping events in track and field (Reinking, 2012). Stress fractures occur most commonly in distance runners, athletes who take part in field sports, gymnasts, dancers and military recruits (Pegrum, Crisp, and Padhiar, 2012). Recently, temporal models have been used to describe the development of load-induced injury associated with overuse injuries (Bahr, 2009). In these models, tissue changes associated with load-induced injury can be illustrated as a continuum; at the early stage, a reduction in the load may allow the injured tissue to return to its previous level of structure and capacity (Bahr, 2009). In the later degenerative stages of this continuum, however, there is little capacity for reversibility of the load-induced changes (Bahr, 2009). Overuse injuries of this latter type have been described as becoming chronic, characterized by periods of pain which can only intermittingly relieved by reduced load or supportive interventions (Bahr, 2009;Edwards, Wright, and Hartman, 2005).

Delayed-onset muscle soreness (DOMS), typically associated with new or repeated unaccustomed exercise, manifests as pain, discomfort and decreased performance 24 to 48 hours after the exercise (Byrnes and Clarkson, 1986). Muscle soreness may begin as a concerted area which is sensitive to passive manipulation and active movement (MacIntyre, Reid, and McKenzie, 1995). This early perception may later be experienced as broad muscle soreness with focal points of tenderness reflecting the active process within the musculotendinous junction (Gibson, Arendt-Nielsen, and Graven-Nielsen, 2006). Independently of the subjects´ previous condition, there will be associated muscle weakness after an episode of acute or delayed muscular soreness (Gibson, Arendt-Nielsen, and Graven-Nielsen, 2006;MacIntyre, Reid, and McKenzie, 1995). This decline in muscular performance is related to the associated cell damage and the subsequent inflammatory response (Ingalls et al., 1998). The restoration of muscle strength from the causative exercise may require up to two weeks to occur (Lieber and Friden, 2002). The most effective preventive measure for DOMS is abstaining from prolonged, intense unfamiliar exercises (Lewis, Ruby, and Bush-Joseph, 2012). For athletes however, this recommendation may be impractical and thus other methods need to be used instead (Lewis, Ruby, and Bush-Joseph, 2012). These include physical preparation such as stretching, the benefit of which however is marginal (Herbert, de Noronha, and Kamper, 2011), and the use of nutritional resources such as carbohydrate and protein supplement drinks after muscle-damaging exercise activity (McBrier et al., 2010). The most effective modality to treat muscle soreness is continued exercise (Cheung, Hume, and Maxwell, 2003). In addition, the NSAID may decrease the feelings of DOMS but these agents do not have any impact on either the length or the degree of muscle weakness (Donnelly et al., 1988).

2.2 THE NEED OF DIETARY SUPPLEMENTS AND DIETARY SUPPLEMENT USE AMONG ELITE ATHLETES

2.2.1 The need of macronutrients and dietary supplements among elite athletes

Recent research developments have substantially changed the understanding of sport and exercise nutrition (Maughan and Shirreffs, 2012); nowadays sports nutrition is concerning with the application of nutrition strategies to modulate training-induced muscle adaptation (Hawley et al., 2011). With regular strenuous training, an increased total energy intake is needed to balance the increased energy expenditure (Maughan and Shirreffs, 2012). The amount of energy needed depends of the type and intensity of sport; this means that total energy consumption is highest in endurance athletes (American Dietetic Association et al., 2009) whereas power athletes require a higher intake of proteins to improve muscle mass growth (Alaranta et al, 2007c).

The daily energy consumption among endurance athletes varies from 2500-5000kcal and 55-65% of the daily intake should consist of carbohydrates and 10-15% of proteins (Alaranta et al, 2007a). This may be achieved with the consumption of a normal, varied diet but sometimes, especially during prolonged exercise, high amounts of carbohydrate containing sports drinks or gels/ bars may be beneficial (Alaranta et al, 2007a). The intake of carbohydrates during the endurance exercise improves performance most clearly during long-lasting exercise but these dietary compounds have been proved beneficial even in performances lasting 45-60 minutes (Murray, 2007). In addition, after the endurance type of activity, to improve glycogen synthesis, the carbohydrates should best be taken 30-60 minutes after exercise (Jentjens and Jeukendrup, 2005).

The need for protein intake in athletes depends on many variables such as total energy intake, the duration and intensity of training, sex, age, the quality of proteins in diet, training history and timing of nutrient intake (Lemon, 2000). Based on the laboratory measures intended for males, when compared with the recommendations for sedentary individuals, daily protein requirements are increased by 50-75% (1.2-1.4 vs. 0.8g/kg) in individuals undertaking endurance types of activity and as much as 100% (1.6-1.8 vs. 0.8 g/kg) in individuals undertaking resistance training (Lemon, 2000). Recently, there has been a significant debate on the timing of protein intake and the quality of protein consumed (Alaranta et al, 2007c). The most common protein preparations used by athletes seem to be whey protein, caseine and soybean, of these, whey protein and caseine seem to be the most effective in increasing protein synthesis (Alaranta et al, 2007c). The most important factor for the increase in muscle mass, however, seems to be the timing of the protein intake i.e. protein containing preparations should be taken during the first two hours after resistance training (Cribb and Hayes, 2006;Esmarck et al., 2001).

A wide range of DSs are on sale for athletes, often with exaggerated claims of efficacy for enhancing performance (Maughan et al., 2007). Many of these are not supported by convincing evidence either of their effect on performance or their safety when taken in high doses for prolonged periods (Maughan et al., 2007). Provided that a reasonably varied diet is consumed, this will usually supply more than an adequate amount of protein, minerals, vitamins and other essential dietary components except for athletes who chronically restrict energy intake to limit body mass and especially fat mass (Maughan and Shirreffs, 2012). According to some studies, these individuals may benefit from vitamin and mineral supplements (Maughan and Shirreffs, 2012). In addition, supplemental iron (McClung, 2012) and calcium (Lappe et al., 2008;Nieves et al., 2010) may be beneficial in physically active women. In a Cochrane database review, the use of vitamin C was found to reduce the incidence of common colds among physically active individuals (Douglas et al., 2007). More recently, there has been a considerable interest of the role of vitamin D beyond its well-recognized effects on bone metabolism (Maughan and Shirreffs, 2012).

2.2.1.1 Vitamin D and calcium

Vitamin D is a steroid hormone produced in the skin under the influence of ultraviolet-B radiation which converts 7-dehydrocolesterol to pre-vitamin D_3 (Holick, 1987). In the dermis, pre-vitamin D_3 is further converted to vitamin D_3 (colecalciferol), before its subsequent conversion to 25-hydroxy vitamin D ($25(OH)_2D$) in the liver (Holick, 2007). Further hydroxylation of 25-hydroxy vitamin D to its active form 1,25-hydroxy vitamin D ($1,25(OH)_2D$) takes place in the kidney (Holick, 2007). Lesser quantities of vitamin D are also found in the diet in the form of vitamin D_2 (ergocalciferol), which undergoes the same hydroxylation process (Holick, 2007). Vitamin D is transported in the blood bound to vitamin D binding protein (Holick, 2007). There is a general agreement that 25(OH)D (including $25(OH)D_2$ and $25(OH)D_3$) concentration is the best indicator of vitamin D status (Holick, 2009;Hollis and Horst, 2007). However, the definitive threshold for vitamin D status is not clear (Working group set up by the Finnish Medical Society Duodecim and the Finnish Endocrinology and Gynecology Society., 2006). Currently, in Finland, there are no official recommendations for 25(OH) D concentration but a plasma concentration of 25(OH)D of 40-80nmol/l is considered sufficient (Working group set up by the Finnish Medical Society Duodecim and the Finnish Endocrinology and Gynegology Society., 2006). The recommendation for the intake of vitamin D preparations has recently been changed in Finland so that daily supplementation with 7.5µg vitamin D is recommended for healthy adults (18-60 years) from October to March if vitamin D containing milk products or fish are not consumed regularly (National Institute of Health and Welfare, 2011).

In addition with being essential for bone health, vitamin D deficiency increases the risk for autoimmune diseases and non-skeletal chronic diseases and furthermore, a deficiency of vitamin D can have profound effect on human immune system and inflammation (Hamilton, 2010;Willis, Peterson, and Larson-Meyer, 2008). Among the general, especially the elderly population, vitamin D deficiency has been observed to cause proximal musculoskeletal weakness (Glerup et al., 2000;Holick, 2009) as well as impaired muscle strength (Bischoff et al., 1999). Ward et al., (2009) however, reported that vitamin D insufucency was associated significantly with muscle power and force in post-menarchal girls. Similarly, Gilsanz et al. (2010) reported increased fat infiltration in muscle indicating lower muscle strength and poorer physical performance in vitamin D insufficient healthy postpubertal young women. Studies of muscle biopsies of severely vitamin D-deficient patients have indicated that vitamin D is able to increase the number of fast, type II muscle fibers (Sato et al., 2005). Some placebo-controlled interventional studies in older adults have also found that vitamin D can improve various parameters of neuromuscular functioning (Bischoff et al., 1999;Sato et al., 2005).

Numerous studies have documented a high prevalence of vitamin D deficiency and insufficiency in the general population worldwide but only a few of studies have focused on athletes (Bergen-Cico and Short, 1992;Halliday et al., 2011;Hamilton, 2010;Lehtonen-Veromaa et al., 1999;Lovell, 2008). Overall, these studies have found that 25(OH)D concentration varies in different populations and is generally higher in summer than winter (Halliday et al., 2011;Lehtonen-Veromaa et al., 1999). The most probable reason for poor vitamin D status of athletes is considered to be inadequate endogenous synthesis due to insufficient UVB exposure (Larson-Meyer and Willis, 2010). Factors that may impair synthesis in athletes include skin pigmentation (Hamilton, 2010), early- or late- day training (Hamilton, 2010), indoor training (Halliday et al., 2011), geographic location (Lehtonen-Veromaa et al., 1999) and sunscreen use (Matsuoka et al., 1987). As a consequence, low concentrations of 25(OH)D have been found among young Finnish competing gymnasts and competing runners (Lehtonen-Veromaa et al., 1999). In the winter, after a sunny summer, severe hypovitaminosis D (25(OH)D<20nmol/l) occurred in 13.4% of the study participants and in 67.7% S-25(OH)D was below 37.5nmol/l (Lehtonen-Veromaa et al., 1999). On the other hand, Hamilton (2010) found no correlation between serum 25(OH)D concentration and sunlight exposure, skin coverage and skin colouring

In addition with vitamin D, calcium is needed to achieve and maintain adequate bone density (Nordin, 1971). Only few prospective studies have been made of the benefits of high calcium intake in athletes. According to these studies, a link has been found between calcium intake and either increased bone density or a reduced risk for stress fractures in physically active women (Lappe et al., 2008;Nieves et al., 2010).

2.2.1.2 Iron

Iron is an essential component of the diet, contributing to physiologically essential functions such as oxygen transport and energy metabolism (Nielsen and Nachtigall, 1998). Iron exerts its biological function through incorporation into proteins and enzymes, such as hemoglobin, myoglobin, and cytochrome c (Nielsen and Nachtigall, 1998). Inadequate dietary iron may result in iron deficiency (ID) or iron deficiency anemia (IDA) (Nielsen and Nachtigall, 1998). Both ID and IDA affect premenopausal women with a greater prevalence than men due to their inadequate dietary iron intake and the losses of iron during menstruation, a strong modulator of iron status (Harvey et al., 2005).

Maintaining iron balance is critical during periods of physical activity, as ID and IDA are known to affect both cognitive and physical function, which are important for athletic performance (McClung et al., 2009). Dietary iron intake is the most important factor affecting iron balance, but there are also other factors that influence iron loss and these may interfere with the iron status in athletes such as gastrointestinal (GI) bleeding, sweating, and iron sequestration in response to inflammation (Brune et al., 1986;Peeling et al., 2008;Robertson, Maughan, and Davidson, 1987). Deteriorations in iron status have been observed following physical activity in women soldiers (McClung et al., 2009).

Consuming a balanced diet that includes enhancers of iron absorption (such as red meat and ascorbic acid) is the most important way for maintaining iron status in female athletes (McClung, 2012). Providing additional iron into the diet through the use of DSs or fortified foods is a secondary means for preventing poor iron status, or for treating ID or IDA (McClung, 2012). McClung et al. (2009) conducted a randomized, placebo-controlled trial to assess the effects of iron supplements, provided as daily capsules containing 100 mg ferrous sulfate on iron status and performance in female soldiers during basic combat training (BCT). In soldiers that began the study with normal iron status, declines in serum ferritin and transferrin receptor numbers were observed over the course of the BCT in those that consumed the placebo capsule, but not in the group receiving the iron supplementation. Furthermore, iron supplementation has resulted in an improvement in the mood state and in faster running time in soldiers with iron deficiency anemia. The use of iron-fortified dietary supplements has also improved iron status in physically active women with IDA (Karl et al., 2010).

Although iron supplementation and fortification are mostly considered as being beneficial among physically active pre- menopausal women, it should also be remembered that there are disadvantages associated with iron supplementation (McClung, 2012). These include the potential of iron overload if provided to individuals with robust iron stores, or disorders of iron metabolism, such as hemochromotosis (McClung, 2012).

2.2.1.3 Omega-3 fatty acids

Omega-3 fatty acids comprise a family of polyunsaturated fatty acids (n3-PUFA) that consist of α-linolenic acid (AA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) (Mickleborough and Rundell, 2005). AA is an essential fatty acid that must be obtained from food because of the inability of humans to synthesize this compound (Simopoulos, 2007). The omega-6 polyunsaturated fatty acids (n6- PUFA) consists of linoleic acid, which is an essential fatty acid, and arachinodic acid (Mickleborough and Rundell, 2005). Human beings evolved consuming a diet that contained about equal amounts of n6-PUFA and n3-PUFA (Simopoulos, 1999). Today, in Western diets, the ratio of n6- and n3- PUFA ranges from approximately 10:1 to 20:1 instead of the traditional ranges of 1:1 to 2:1 (Eaton and Konner, 1985), mostly due to the abundance of dietary linoleic acid, which is present in high concentrations in soy, corn, safflower and sunflower oils (Mickleborough and Rundell, 2005). On the other hand, the dietary intake of oily fish and leafy vegetables, the major sources of n3-PUFA, is low (Mickleborough and Rundell, 2005). This elevated intake of n6-PUFA rather than n3-PUFA is unfavorable since it shifts the physiological state to a condition that is prothrombotic and proaggregatory and characterized by increases in blood viscosity and vasospasm and vasoconstriction (Broughton et al., 1997). On the other hand, n3-PUFA have anti-inflammatory, antithrombotic, antiarrhythmic, hypolipidemic and vasodilatory properties (Simopoulos, 1999).

The increased consumption of proinflammatory diet in Western societies has been postulated to predispose some individuals to inflammatory disorders, including asthma (Mickleborough and Rundell, 2005). Epidemiological studies have found a link between increased oily fish consumption and a decreased prevalence of asthma and allergic rhinitis, both among children (Hodge et al., 1996;Nafstad et al., 2003) and adults (Nagel et al., 2003). In intervention studies, the clinical data on the effects of fish oil supplementation in asthma has been equivocal. While no improvement in asthmatic symptoms has been observed in some intervention studies (Hodge et al., 1998;Stenius-Aarniala et al., 1989), several other trials have demonstrated an improvement in asthmatic status following n3-PUFA supplementation (Arm et al., 1989;Broughton et al., 1997;Mickleborough et al., 2003). Mickleborough et al. (2003) demonstrated that three weeks of pharmaceutical grade of fish oil supplementation (a capsule containing 3.2 g EPA and 2.2 g DHA) could reduce the severity of EIB and this resulted a significant suppression of several proinflammatory mediators in nonatopic elite athletes who exhibited asthma- like symptoms following exercise. Similarly, a diet supplemented with pharmaceutical grade of fish oil reduced the airway inflammation and decreased asthmatic and EIB symptoms in mild atopic asthmatics with EIB (Mickleborough et al., 2006). In addition, n3-PUFA supplementation has been shown improve cardiovascular performance in elite athletes and healthy adults (Buckley et al., 2009;Walser and Stebbins, 2008). Supplemental n3-PUFA has also been shown to reduce the symptoms of DOMS after eccentric exercise in healthy men (Tartibian, Maleki, and Abbasi, 2009).On the other hand, concern has been raised about the possibility that supplementation of n3-PUFA and n6-PUFA might lead to increased lipid peroxidation after heavy physical exercise (McAnulty et al., 2010).

2.2.1.4 Lactobacillus and probiotics

Probiotics are live micro-organisms that transiently alter the intestinal microbial flora, which is the diverse bacterial population that inhabits the GI tract (Kudsk, 2002). A large range of bacteria are used as probiotics, with the most common strains belonging to the *Lactobacilli* and *Bifidobacteria* species (Kudsk, 2002). Probiotics are becoming increasingly popular as nutrition supplements to reduce susceptibility to common infectious illnesses, particularly upper respiratory tract (URT) and (GI) illness (West et al., 2011). For athletes, the possibility to reduce the occurrence of these illnesses is a high priority (West et al., 2011). An increased incidence of URT and GI illness, particularly diarrhoea, has been reported during heavy training and competitions in athletes (Mackinnon, 2000;Pyne and Gleeson, 1998). The increased susceptibility to illness is thought to be related to acute post-exercise immune perturbations and chronic suppression of immune factors due to frequent prolonged exercise (Cox et al., 2007;Gleeson, 2000).

There is increasing evidence that probiotic supplementation, alone or in combination with other preventative agents such as prebiotics, can reduce the number, duration and severity of acute infectious diarrhoea and URT in adults, children (Sazawal et al., 2006) and the elderly (Guillemard et al., 2010). In studies conducted with athletes, probiotic supplementation has been useful in enhancing immunity and reducing the duration of URT and GI illness in endurance-discipline athletes (Cox et al., 2010;Gleeson et al., 2011;Kekkonen et al., 2007), whereas probiotic supplementation by commando cadets during a training and combat course had little effect on the incidence of URT (Tiollier et al., 2007). A recent randomized controlled trial made with competitive cyclists reported a reduced severity of self-reported symptoms and illness load of lower respiratory illness, use of cold and flu medication, and severity of GI symptoms at higher training loads with consumption of Lactobacillus fermentum, in male but not in female athletes (West et al., 2011).

2.2.1.5 Magnesium

Magnesium is an essential mineral that regulates membrane stability and neuromuscular, cardiovascular, immune, and hormonal functions and it is a critical cofactor in many metabolic reactions (Newhouse and Finstad, 2000). The dietary reference intake for magnesium for adults is 310 to 420 mg/day (Bohl and Volpe, 2002). However, the intake of magnesium in humans is often suboptimal (Rayssiguier, Guezennec, and Durlach, 1990). Magnesium deficiency may lead to changes in GI, cardiovascular, and neuromuscular function (Newhouse and Finstad, 2000). Physical exercise may deplete magnesium stores, which, together with a marginal dietary magnesium intake, may impair energy metabolism efficiency and reduce the capacity for physical work (Bohl and Volpe, 2002).

Several studies have shown that magnesium deficiency reduces physical performance (Conn et al., 1988;Lukaski et al., 1983;Rayssiguier, Guezennec, and Durlach, 1990).

Both overuse (Deuster et al., 1986;Fogelholm et al., 1992) and underintake (Moffatt, 1984;Singh et al., 1989) of magnesium has been reported among athletes. The intake of magnesium seems to be most compromised in those athletes attempting to maintain a low body weight (Bohl and Volpe, 2002). In addition to its property to impair energy metabolism, magnesium deficiency may cause muscle cramps and muscle spasms which can be treated with supplemental magnesium-gluconate or magnesium-sulfate (Conn et al., 1988). Organic forms of magnesium, such as magnesium citrate, are better absorbed, utilized and assimilated than inorganic forms such as magnesium oxide and hydroxide, in fact these two latter agents are often used as laxatives (Bohl and Volpe, 2002;Walker et al., 2003) The data concerning positive effects of magnesium supplementation on athletic performance is somewhat controversial (Ahlborg, Ekelund, and Nilsson, 1968;Bohl and Volpe, 2002).

2.2.2 Dietary supplement use among elite athletes

Athletes use DSs in order to increase energy, maintain strength, enhance performance, maintain health and immune system and prevent nutritional deficiencies. There are several studies claiming that supplement use among athletes is common and varies between 59 to 88 % with multivitamins, minerals, proteins and energy drinks the most common products being consumed (Braun et al., 2009;Erdman et al., 2007;Froiland et al., 2004;Huang, Johnson, and Pipe, 2006;Petroczi et al., 2008;Ronsen, Sundgot-Borgen, and Maehlum, 1999). Most supplement users consume more than one product (Braun et al., 2009;Huang, Johnson, and Pipe, 2006;Petroczi et al., 2008;Tscholl et al., 2010) and the numbers of supplements used varies between age groups, gender and different sports (Huang, Johnson, and Pipe, 2006;Petroczi and Naughton, 2008;Ronsen, Sundgot-Borgen, and Maehlum, 1999;Tscholl et al., 2010). Ronsen et al (1999) reported a major difference in the supplement use between different sport groups: power sport athletes had the most frequent use of supplemental creatine, proteins/ amino acids, vitamins and minerals while cross-country skiers had the most frequent intake of iron, vitamin C and fish oils.

Despite the frequent use of DSs, recent findings have shown that athletes suffer several misconceptions about the effectiveness of DSs (Petroczi et al., 2007;Petroczi et al., 2008). Petròczi et al. (2007a, 2007b, 2008) did not observe agreement between athletes´ rationale and behavior in relation to their nutritional supplement use except for creatine, whey protein and energy drinks, which the athletes reported that they were using in order to maintain strength (creatine and protein) and enhance endurance (energy drinks). According to some studies, there is also a large population of athletes who claim that they have received inappropriate information about the supplements they are using (Sundgot-Borgen, Berglund, and Torstveit, 2003).

A study that evaluated nutritional intake among high-performance athletes reported consumption of carbohydrates and energy as being inadequate among both male and female athletes. However, intake of micronutrients exceeded daily recommendations by over 20% when supplements were not considered and even more when supplements were included (Lun, Erdman, and Reimer, 2009). Hinton et al. (2004) reported both protein and carbohydrate intake among college athletes as being inadequate based on the recommendations for athletes. Daily recommendations for micronutrients were exceeded for all nutrients except for vitamin E and magnesium (Hinton et al., 2004). Ronsen et al (1999) reported regular cod liver oil consumption being nearly 50% and its occasional use by over 40% of elite Norwegian cross-country skiers.

2.2.3 The effect of dietary supplements on physical performance

2.2.3.1 Caffeine

Caffeine is a common substance in the diets of most athletes and it is now appearing in many new products, including energy drinks, sport gels, alcoholic beverages and diet aids (Paluska, 2003). Currently its use is not considered to be a doping infraction (World Anti-Doping Agency, Prohibited list) in spite of the fact that caffeine appears to have a performance-enhancing effect in certain types of sport performance (Greer, Friars, and Graham, 2000;MacIntosh and Wright, 1995). The ergogenic effects of caffeine seem to be similar in both non-habitual and habitual caffeine consumers (Van Soeren et al., 1993). Several mechanisms have been proposed to explain caffeine's ergogenic effects but three hypotheses have generated the most discussion and investigation: 1) mobilization of intracellular calcium (Fredholm, 1985); 2) catecholamine augmentation and glycogen sparing (Bell, Jacobs, and Ellerington, 2001); and 3) adenosine receptor antagonism (Fredholm, 1985;Van Soeren and Graham, 1998).The majority of available research supports adenosine receptor antagonism as the primary mode of action for caffeine's ergogenic effects (Paluska, 2003).

Early studies conducted in the late 1970s indicated that caffeine administration (approx. 5 mg/kg) improved endurance cycle performance (Costill, Dalsky, and Fink, 1978;Ivy et al., 1979). Subsequently, many laboratory based studies have shown either a greater power output for a given period of time or a greater time to exhaustion in endurance-types of activities in well-trained individuals (Greer, Friars, and Graham, 2000;MacIntosh and Wright, 1995). The vast majority of these studies have used caffeine doses in the range of 3–6 mg/ kg taken approximately 1 h prior to exercise (Greer, Friars, and Graham, 2000;MacIntosh and Wright, 1995). More recently, studies have reported that much lower doses of caffeine (1–2 mg/kg), especially when taken later during an endurance exercise task can be performance-enhancing (Cox et al., 2002). The evidence for an ergogenic effect of caffeine on high-intensity performance is controversial compared to the data for its use in endurance tasks (Astorino and Roberson, 2010).

2.2.4 Contamination of dietary supplements

For more than a decade it has been known that nutritional supplements (NS) can also contain doping substances (Baume et al., 2006;Geyer et al., 2004). Because of the possible side-effects and non-intentional positive doping results, this topic has been widely discussed and various studies have emphasized the seriousness of the problem (Baume et al., 2006;Lukaski, 2004;Petroczi, Taylor, and Naughton, 2011). Geyer et al. (2004) reported the results of wide international study sponsored by IOC concerning the purity of non-hormonal NS. Of the 634 samples analyzed, 14.8 % contained prohormones not declared on the label. Most of the contaminated supplements (68.1%) contained prohormones of testosterone and contamination was found in all kinds of NS (Geyer et al., 2004). Baume et al. (2006) reported similar results in their studies as three of 103 DSs screened contained metandienone and 18 of the products contained precursors or metabolites of testosterone or nandrolone. Although the amounts of the prohormones in NS are mostly low, excretion studies have shown that the amount of their urinary metabolites can rise high because of the high recommended dosages of the NS and this can lead to positive doping test results (Baume et al., 2006;Geyer et al., 2004)

2.3 PHARMACOLOGICAL TREATMENT OF ELITE ATHLETES

2.3.1 Treatment of asthma and allergies among athletes

The frequency of anti-asthmatic medication use in athletes varies between 2 and 10% (Alaranta et al., 2004;Lund et al., 2009;Thomas et al., 2010). The prevalence of asthma medication use among the general population has been reported to be significantly lower (Alaranta et al., 2004). According to the guidelines of the IOC, the management of asthma in athletes should be similar to the treatment of non-athletes (Fitch et al., 2008).

2.3.1.1 Inhaled corticosteroids

Inhaled corticosteroids (ICS) are the primary treatment for patients who have asthma based on the recognition that asthma is characterized by inflammatory changes in airway mucosa even in mild and newly detected asthma (Haahtela et al., 1991). Inhaled corticosteroids decrease the number of inflammatory cells in bronchial mucosa and improve the clinical physiological indices of asthma (Djukanovic et al., 1992;Laitinen, Laitinen, and Haahtela, 1992). Discontinuation of ICS treatment may be followed by an exacerbation of the disease (Haahtela et al., 1991). Long-term treatment with ICS lowers airway responsiveness to various stimuli, including exercise, so in order to prevent asthma and EIB symptoms, ICS need to be administrated for an adequate time (Smith and LaBotz, 1998;Subbarao et al., 2006).

According to IOC, similar to the situation in non-athletes, ICS are the first drug of choice in the treatment of asthma in athletes (Fitch et al., 2008). However, since a mixed type of airway inflammation has been reported to occur in athletes´ asthma, ICS seem to be less effective in reducing airway inflammation and airway hyperresponsiveness to metacholine and less able to relieve the chronic respiratory symptoms in athletes compared to non-athletes (Helenius et al., 2004;Lumme et al., 2003;Subbarao et al., 2006). Thus, the first-line treatment for athletes´ asthma should be preventive, such as reduction of relevant environmental exposures, treatment of associated comorbid conditions, prevention of exacerbations and regular follow-up (Fitch et al., 2008). Athletes are also recommended to avoid training in conditions where the air quality is impaired and under extreme conditions of temperature and humidity (Fitch et al., 2008). The use of face mask can attenuate EIB in athletes breathing cold air and it can exert a synergistic effect when combined with β2-agonists (Millqvist, Bengtsson, and Lowhagen, 2000).

2.3.1.2 Inhaled β2- agonists

Short-acting inhaled β_2-agonists (salbutamol, terbutaline) are the medications of choice for rapid relief of bronchospasm during acute exacerbations of asthma and for the pretreatment of exercise-induced bronchoconstriction (Bateman et al., 2008). These compounds have a rapid onset of action (within 15 minutes), produce a prolonged effect (up to 6 hours), and are convenient to use (Bateman et al., 2008). When given about 30 minutes before exercise, they prevent asthma symptoms in 90% of patients. Inhaled β2-agonists, however, have little or no beneficial effect on the chronic inflammatory response which underlies airway hyperresponsiveness and chronic asthma and they should not be used alone in the treatment of asthma (Fitch et al., 2008).

Long-acting β2-agonists (LABA; salmeterol, formoterol) are both highly selective and potent β2-adrenergic receptor agonists that achieve bronchial smooth muscle relaxation for up to 12 hours (Sears and Lotvall, 2005). Studies have shown improvements in several asthma control measures with the use of LABA but they have failed to show any anti-inflammatory mechanisms (Overbeek et al., 2005;Roberts et al., 1999). According to current asthma treatment recommendations, LABA can be added to asthma or EIB treatment when it is not controlled with a sufficient dose ICS alone (Fitch et al., 2008). However, a growing concern has been raised of the safety of LABA; soon after becoming available, deaths and asthma exacerbations were documented in association with the use of LABA (Lazarus et al., 2001;Lemanske et al., 2001). Therefore, in April 2011, the US Food and Drug Administration (FDA) issued a requirement for all manufacturers of

LABA to conduct a controlled trial to assess the safety and a regimen of LABAs plus ICS compared with ICS alone (Chowdhury, Seymour, and Levenson, 2011).

According to studies, regular treatment with β2-agonists can increase the sensitivity of the airways to bronchoconstrictive stimuli, including exercise and allergens (Hancox et al., 2002). In addition, both the bronchodilator and the bronchoprotective effects of β2-agonists diminish after a few days of regular use. This means that athletes taking β2-agonists regularly may experience reduced protection against EIB even if they take these drugs immediately after exercise (Simons, Gerstner, and Cheang, 1997). These effects are probably a result of the downregulation of β2 receptors in airway smooth muscle and on the inflammatory cells such as mast cells induced by chronic exposure to agonist (Simons, Gerstner, and Cheang, 1997). Other than avoiding the use of β2-agonists, there are no known ways to avoid tolerance (Fitch, 1984). Tolerance occurs to both long- and short acting β2-agonists and it cannot be prevented by either using inhaled corticosteroids or overcome by taking a higher dose of inhaled β2-agonists (Haney and Hancox, 2007;Simons, Gerstner, and Cheang, 1997).

The response to β2-agonists may be influenced by polymorphisms in the β2-receptor (Basu et al., 2009). Several retrospective analyses have demonstrated that asthmatic patients with the most common homozygous genotype of the β2 adrenergic receptors (Arg/Arg) polymorphism may carry an increased risk of adverse outcomes related to regular use of short-acting b2-agonists (Israel et al., 2000).

2.3.1.3 Leukotriene antagonists

Leukotrienes are inflammatory molecules that are one of several substances released by eosinophiles and mast cells during the immediate response to an inhaled allergen (Wenzel, 1997). These compounds are derived from arachidonic acid, the precursor of the prostaglandins (Wasserman, 1988;Wenzel, 1997). With the recognition that elevated levels of leukotrienes are found in the airways of patients with EIB (O’Byrne, 2000) as well as acute and chronic asthma (Drazen, Israel, and O’Byrne, 1999), the effects of leukotriene antagonists (LTRA) and inhibitors of leukotriene synthesis have been explored.

Montelukast is LTRA that reduced asthmatic inflammation, prevents bronchoconstriction (Villaran et al., 1999) and reduces the extent of eosinophilic inflammation in asthma (Bjermer et al., 2003). There are studies showing that a single dose of 10mg (5mg in children) montelukast may have an effect which can last for 24 hours in adults and children with EIB (Kemp et al., 1998;Leff et al., 1998). Tolerance to repeated dosing of montelukast has not been observed in clinical studies (de Benedictis et al., 2006;Leff et al., 1998). On the other hand, there are clamis that orally administrated LTRA may not to be better than placebo in preventing airway inflammation, bronchial hyperresponsiveness, pulmonary function or daily symptoms in athletes (Helenius et al., 2004). According to the current recommendations (Fitch et al., 2008), if asthma or EIB is not controlled with ICS and short-acting β2-agonists alone, then LTRA, alternatively with LABAs, sodium cromoglycate or nedocromil sodium, should be added to the medication. A current Cochrane database review (Ducharme, Lasserson and Cates, 2011) proposes however, that in asthmatic adults with mild or moderate airway obstruction and who are on low doses of ICS and who demonstrate a significant reversibility to a short-acting bronchodilator, the risk of exacerbations requiring oral corticosteroids was 17% lower in patients treated with LABA than in patients treated with LTRA over 12 to 48 weeks. In addition, compared to LTRA, the addition of LABA to ICS was associated with statistically significant improvements in lung function, symptom-free days, need for rescue β_2-agonists, symptoms, night awakenings, and quality of life (Ducharme, Lasserson, and Cates, 2011).

2.3.1.4 Other asthma medicines

Mast-cell stabilizers, such as cromolyn or nedocromil sodium have anti-inflammatory and anti-allergic effects (Leung et al., 1988). Although the exact mechanism of action of the mast cell stabilizing agents is unknown, they appear to stabilize the mast cell membrane to prevent the release of inflammatory mediators (e.g. leukotrienes, prostaglandins, cytokines) from the cell (DiPiro, 1999). These mediators play an important role in the hyperreactivity response, especially as a result of exposure to allergens and exercise (DiPiro, 1999;Young and Koda-Kimble, 1995). At equipotent doses, cromolyn and nedocromil sodium are equally effective (DiPiro, 1999). These drugs are not as effective as ICS for the prevention of asthma symptoms, but they have fewer potential side effects and virtually no systemic toxicity (Donahue et al., 1997). Mast cell stabilizers exert no bronchodilatory effect and they should not be used to treat acute symptoms of asthma and EIB (Houglum, 2000). However, when given about 20 minutes before exercise, they can prevent asthma symptoms in between 70% to 85% patients with exercise-induced asthma (Smith and LaBotz, 1998). Currently, according to recommendations (Fitch et al., 2008), cromolyn and nedocromil sodium represent an alternative treatment option in athletes´ asthma when it is not controlled with ICS alone.

When asthma or EIB is not controlled with the above mention medicines (ICS, β2-agonists, leukotriene modifiers, mast-cell stabilizers) alone, theophylline or ipratropium may be considered (Fitch et al., 2008). Theophylline has bronchodilatory properties, though they are not as strong as LABA. The benefits of theophylline are that is relatively cheap and can be taken orally, but the major limitations of the drug are its narrow therapeutic index and the wide inter-patient pharmacokinetic variability (Rottier and Duiverman, 2009). As a result, dosing must be individually titrated to reach steady-state serum concentrations to achieve both benefit and safety (Rottier and Duiverman, 2009).

Inhaled ipratropium bromide may be used to prevent EIB, but its effect varies between individuals (Boaventura et al., 2010). The recent study by Boaventura et al. (2010) was a randomized, cross-over study which claimed that the therapeutic response to ipratropium bromide was related to the time of day. A significant bronchodilatory effect was detected in the morning, but not in the evening. Similarly, the bronchoprotective effect on EIB appeared only in the morning (Boaventura et al., 2010).

According to the latest research, there are several distinct phenotypes of severe asthma and these might require different therapeutic approaches (Barnes, 2012). More research is needed to identify effective treatment for different phenotypes of asthma (Barnes, 2012).

2.3.1.5 Pseudoephedrine

Pseudoephedrine (PSE) is a sympathomimetic that is an ingredient of many proprietary medicines and which are frequently used by athletes (Tseng et al., 2003). According to studies, this drug does not seem to enhance performance when ingested at therapeutic doses (<120mg) (Chu et al., 2002;Hodges et al., 2003). On the other hand, PSE significantly decreased the time to completion of 1500 m time trials when taken in amounts greater than therapeutic doses (2,5mg/ weight kg, 170mg) (Hodges et al., 2006). Additionally, PSE (180mg) ingestion 45min before exercise improved lower body strength and power, and lung function in university athletes (Gill et al., 2000). Pritchard-Peschek et.al (2010) found an improved time-trial performance in well-trained cyclists and triathletes after ingestion of 180mg of PSE 60 minutes before high-intensity performance.

2.3.2 Non-steroidal anti-inflammatory drugs (NSAIDs)

Non-steroidal anti-inflammatory drugs are a heterogeneous class of medicines that are chemically unrelated but known to have similar therapeutic effects, i.e. antipyretic, analgesic and anti-inflammatory activity (Vane and Botting, 1998). Their primary therapeutic effect is due to inhibition of prostaglandin synthesis by inhibiting the enzyme cyclo-oxygenase-2 (COX-2) activity (Vane and Botting, 1998). Prostaglandins are localized hormones that, once released into intracellular space, can evoke fever, inflammation and pain (Maroon et al., 2006). COX-2 is an enzyme that utilizes arachidonic acid that is released from cellular membranes as a result of tissue injury, to produce prostaglandins (Feucht and Patel, 2010). Another form of COX- enzymes is COX-1 that is expressed in most normal tissues and cells and is the predominant form within gastric epithelial cells (Maroon et al., 2006). The well-known GI effects of NSAID are predominantly, but not exclusively, due to inhibition of COX-1 (Feucht and Patel, 2010). Traditional NSAIDs inhibit the two isoforms of COXs which effectively reduces the inflammatory response, but also impairs gastric protection and interferes with renal function (Ziltener, Leal, and Fournier, 2010). NSAIDs are mostly administeres orally but they can also be delivered topically or by intramuscular injection (Ziltener, Leal, and Fournier, 2010).

The use of NSAID is known to be more common among athletes, especially among speed and power athletes, than in the general population (Alaranta et al., 2006). Few studies have estimated the prevalence of elite athletes´ NSAID use (Berglund, 2001;Corrigan and Kazlauskas, 2003;Huang, Johnson, and Pipe, 2006;Tsitsimpikou et al., 2009b). The exact percentages of elite athletes´ NSAID use is difficult to estimate, however, because different time intervals and classification of medicine categories have been used. Huang et al. (2006) described the medication use by Canadian athletes in Atlanta and Sydney Olympic games, and found out that prevalence of NSAIDs increased between the study years ranged from 33% to 38% of the athletes and that NSAIDs were used more often than any other medicines.

Athletes use NSAID in order to continue their athletic activities even though they have suffered acute traumatic injuries or overload injuries and to accelerate their return to the playing field after an injury (Ziltener, Leal, and Fournier, 2010). Some athletes take NSAIDs also for preventive measures (Tricker, 2000;Warner et al., 2002). However, there is increasing evidence that the inflammation resulting from injury is necessary for adequate tissue repair and thus the use of NSAID may have a deleterious effect on the regeneration process (Rankin, 2004). Recent studies have shown that the harmful effects of NSAID extend to cell metabolism and the growth of the primary tissues making up the musculoskeletal system (Mackey et al., 2007;Smith and Collina, 2007). Trappe et al. (2002) examined the effect of maximal over-the counter doses of ibuprofen (1200mg/d) and acetaminophen (4000mg/d) compared with placebo on the postexercise muscle protein synthesis in sedentary or recreationally active males after eccentric resistance exercise. Postexercise (24 h) skeletal muscle fractional synthesis rate was increased 76% in placebo group (0.058 %/h) but it was unchanged in ibuprofen (35%; 0.021 %/h) and acetaminophen group (22 %; 0.010 %/h) (Trappe et al., 2002). The same study group (Burd et al., 2010) later reported that ibuprofen and acetaminophen inhibited the postexercise protein synthesis by inhibiting the $PGF_{2\alpha}$ production via the COX- enzyme.

2.3.2.1 The effect of NSAIDs on acute ligament injuries

The repair of acute ligament injuries takes place in three phases: an initial inflammatory phase including the cleaning of injured tissue; a proliferative phase including the formation of collagen fibers; and finally a remodeling phase which can last several months when a controlled mechanical stress is applied to the injury (Ziltener, Leal, and Fournier, 2010). In vitro and animal studies have shown contradictory results regarding the effects on NSAIDs on ligament healing (Dahners et al., 1988;Elder, Dahners, and

Weinhold, 2001). In the short term, joint function is sometimes improved; in the medium term the changes are less clear-cut, the ligaments´ resistance to tension may be increased, decreased or remain the same; finally, in the long term potentially deleterious effects on healing have been observed (Dahners et al., 1988;Elder, Dahners, and Weinhold, 2001). Human studies have more consistently demonstrated that NSAIDs are effective at decreasing pain and allowing faster recovery to activity after ankle or knee sprains (Hertel, 1997;Mazieres et al., 2005;Slatyer, Hensley, and Lopert, 1997). Slatyer et al. (1997) showed, however, that Australian army recruits treated with piroxicam 20mg/day for seven days after an acute ankle sprain had a reduced joint amplitude, increased anterior laxity and a higher recidivism rate (25%) 6 months after their treatment.

2.3.2.2 The effect of NSAIDs on tendinopathies

Tendinopathies are often treated with NSAID even though chronic tendinopathy does not display an inflammatory reaction other than in certain cases of bursitis and associated synovitis (Khan et al., 1999). A meta-analysis (Anders & Murrell, 2008) conducted with 37 randomized clinical studies claimed that in tendinopathies treated with NSAIDs only short-term pain (7 to 10 days) was reduced, particularly in the shoulder. In the long-term, there was no evidence that NSAIDs were effective for treating tendon injuries, but in contrast the risks for adverse effects did increase.

2.3.2.3 The effect of NSAIDs on bone fractures

The prostaglandin E (PGE) family plays an important role in bone homeostasis (Vuolteenaho, Moilanen, and Moilanen, 2008). The members of this family stimulate both bone resorption and bone formation by increasing the number and activity of osteoblasts and by increasing replication and promoting the differentiation of osteoclasts (Vuolteenaho, Moilanen, and Moilanen, 2008). It is thus clear that any substance altering prostaglandin synthesis can have an impact on bone. The inhibitory effects of NSAID on prostaglandin synthesis on bone formation can be used to inhibit heterotrophic ossification following prosthetic surgery (Fransen and Neal, 2004;Gaston and Simpson, 2007). On the other hand, since NSAIDs have delaying effects on bone consolidation (Gaston and Simpson, 2007;Koester and Spindler, 2006), it is recommended to avoid using NSAIDs at least for the first week after a fracture or a stress fracture. For the treatment of pain, other analgesics should be used instead (Ziltener, Leal, and Fournier, 2010).

2.3.2.4 The effect of NSAIDs on muscle injuries

The gravity of muscle injuries depends on the degree of which the muscles´ main constituents, the contractile and supporting tissues, are affected (Jarvinen et al., 2005). Immediately following a rupture of the muscle fibers, there is the appearance of both myofiber necrosis and inflammation, with the dominant presence of macrophages and neutrophils (Jarvinen et al., 2005). It is not yet known, whether the role of these inflammatory cells is positive or negative (Bondesen et al., 2004;Rahusen, Weinhold, and Almekinders, 2004;Thorsson et al., 1998). In the repair process that follows the injury, first, the macrophages ingest the necrotic tissue, a process called macrophage phagocytosis (Jarvinen et al., 2005). Then fibrous tissue is produced (Jarvinen et al., 2005). A remodeling phase then occurs in order to regenerate new muscle fibers and to organize the fibrous tissue (Trappe et al., 2001). COX-2 dependent prostaglandin synthesis is required during muscle regeneration (Bondesen et al., 2004). The administration of COX-2-inhibitors soon after muscle injury, although providing the desired analgesic effects, may adversely affect muscle regeneration. The use of NSAIDs after muscle injuries remains controversial. Piroxicam has been demonstrated to delay inflammatory reaction and muscle regeneration in experimental animal model (Almekinders and Gilbert, 1986). In a randomized, double-blind, placebo-controlled trial the reduction of pain and swelling and the return to normal strength was no better with or without NSAID in acute hamstring injuries (Bondesen et al., 2004). In addition, even though NSAID may decrease the inflammatory response and thereby the pain and swelling (Almekinders, 1999) analgesics without anti-inflammatory effects may have similar effects as the NSAIDs in soft tissue injuries (Dalton and Schweinle, 2006;Rahusen, Weinhold, and Almekinders, 2004).

2.3.2.5 The effect of NSAID on Delayed-Onset Muscle Soreness

According to studies, NSAID and analgesics (paracetamol) seem to have similar effects on delayed muscle soreness when measuring the concentrations of inflammatory cells (neutrophils and macrophages) in the muscles or the rate of creatine kinase (CK), PGE_2 or pain intensity (Trappe et al., 2001;Tricker, 2000). However, O` Grady et al. (2000) reported in a randomized, double-blinded study that compared to placebo, the prolonged administration of diclofenac, beginning 15 days before an unusual strenuous 20min stepping program, significantly reduced quantitative indices (amount of CK, and muscle disuse damage in biopsies) of exercise-induced skeletal muscle damage in human muscle. Thus, taking NSAID regularly may allow sufficient tissue concentrations to be reached to potentially modify the local response resulting in DOMS (O'Grady et al., 2000). On the other hand, this increases the risk of adverse effects and the possibility of exerting a negative effect on recovery.

2.3.2.6 Side effects of NSAID

Since the traditional non-selective NSAIDs are known to have serious adverse effects on the GI tract (Feucht and Patel, 2010), several studies have investigated the effectiveness of the selective COX-2 inhibitors in the treatment of acute soft tissue injuries (Jones and

Lamdin, 2010). In the early 2000s, the COX-2 inhibitors (coxibs) enjoyed widespread use (Mamdani et al., 2002) despite their higher cost as compared with other treatments (Spiegel et al., 2003). However, it was soon found out that COX-2 inhibitors were not without problems of their own and doubts were raised about their cardiovascular side effects (Mukherjee, Nissen, and Topol, 2001). A recent narrative (Hinz, Renner, and Brune, 2007) as well as systematic reviews now indicate that there is no difference in the risk of cardiovascular toxicity between most traditional NSAIDs and coxibs (McGettigan and Henry, 2006;White et al., 2007). A systematic meta-analysis by Jones& Lamdin (2010) evaluated the efficacy and safety of coxibs versus non-selective NSAIDs and tramadol in the treatment of acute (<30 days) soft tissue injuries (sprains, strains and contusions of ligaments, muscles or tendons) in 3060 healthy adults. Coxibs were defined as drugs that inhibit COX-2 more than 5-fold as compared with COX-1. For the treatment of pain, no clinically relevant difference was seen between NSAID and coxibs. The risk of any GI tract adverse effect was 41% lower in patients taking coxibs compared with patients taking other NSAIDs. Only three minor cardiovascular side effects were reported; two associated with coxibs and one with NSAID. However, Jones & Lamdin (2010) suggest that the studies may have underestimated the cardiovascular adverse effects, since the studies were not designed to indentify spesific the cardiovascular risks. The follow-up time was also insufficient to evaluate serious cardiovascular side effects. No difference was found in the time to return to full activity after an acute injury between coxibs and NSAIDs (Jones and Lamdin, 2010).

GI side effects (i.e., dyspepsia, nausea, ulcers and bleeding) appear primarily when NSAIDs are taken frequently (Ziltener, Leal, and Fournier, 2010). A less frequent side effect, renal failure, has been observed not only in elderly subjects but also in dehydrated subjects. Since dehydration happens frequently in athletes when playing sports, this risk should be borne in mind (Ziltener, Leal, and Fournier, 2010).

2.3.3 Oral antibiotics

Heavy training predisposes athletes to viral and possibly also to bacterial infections (Nieman, 2000). The awareness of this possibility and also the pressure to succeed may lead to too liberal use of oral antibiotics among elite athletes (Alaranta et al., 2006). The use of oral antibiotics by elite athletes use has been reported to be 2-fold more common than that in the general population of the same age (Alaranta et al., 2006). Excessive and inappropriate use of oral antibiotics may lead to antibiotic resistance (Alaranta et al., 2006). In addition, oral antibiotics have side effects such as GI upset and diarrhea, which may affect on the performance of the athlete (Ciocca, 2005). In addition, tendon injuries have been reported after treatment with fluoroquinolones (Khaliq and Zhanel, 2003;Williams et al., 2000).

2.4 SPECIAL CHARACTERISTICS OF THE PARALYMPIC ATHLETES AND THEIR MEDICATION USE

2.4.1 Common medical problems in disabled athletes

Disabled athletes encounter many medical problems during their careers (Klenck and Gebke, 2007). To ensure fair competition among these athletes, a functional classification system based on the movements required for a sport is in place. Athletes are divided into ten classes and further, subclasses for the competition (Official website of the Paralympic Movement, Classification) (Table 2). The type and severity of the medical problems of the athlete usually depends on the disability class so that some medical problems are more common in certain groups of disabled athletes than in others (Klenck and Gebke, 2007).

Table 2. Paralympic athlete´s classification (according to the International Paralympic Committee)

Impairment type	Description	Examples of the condition
Impaired muscle power	Reduced force generated by the contraction of a muscle or muscle groups	Para- and quadriplegia, spina bifida, muscular dystrophy,post poliomyelitis
Impaired passive range of movement	Range of movement in one or more joint is reduced in systematical way.	
Limb deficiency	A total or partial absence of the bones or joints as a consequence of trauma, illness or congenital limb deficiency	Traumatic amputation, bone cancer, dysmelia
Leg length difference	Due to congenital deficiency or trauma, bone shortening occurs in one leg.	
Short stature	Standing height is reduced due to aberrant dimensions of bones of upper and lower limbs or trunk	Achondroplasia
Hypertonia	A condition marked by an abnormal increase in muscle tension and a reduced ability of a muscle to stretch.	Cerebral palsy (when the injury occurs in children under two years of age), brain injury, multiple sclerosis
Ataxia	Ataxia is a neurological sign and symptom that consists of a lack of co-ordination of muscle movements.	Cerebral palsy (when the injury occurs in children under two years of age), brain injury, multiple sclerosis
Athetosis	Athetosis can vary from mild to severe motor dysfunction. It is generally characterized by unbalanced, involuntary movements of muscle tone and a difficulty maintaining a symmetrical posture.	Cerebral palsy (when the injury occurs in children under two years of age), brain injury
Vision impairment	Vision is impacted by either an impairment of the eye structure, optical nerves or optical pathways, or visual cortex of the central brain.	
Intellectual impairment	A disability characterized by significant limitation both in intellectual functioning and in adaptive behavior as expressed in conceptual, social and practical adaptive skills. This disability originates before the age of 18 years (American Association on Intellectual and Development Disability, 2010).	

Many Paralympic athletes rely on wheelchairs to compete in a variety of sports (Klenck and Gebke, 2007). The most common cause of disability of wheelchair athletes is spinal cord injury (SCI) that predisposes these athletes to many kinds of medical problems (Curtis and Dillon, 1985;Klenck and Gebke, 2007). The common medical problems experienced by wheelchair athletes are autonomic dysreflexia, weakened thermoregulation, pressure sores, neurogenic bladder, premature osteoporosis, peripheral nerve entrapment syndromes and musculoskeletal injuries (Klenck and Gebke, 2007).

Neurogenic bladder is a common result of SCI that predisposes these individuals to urinary tract infections from incomplete voiding, elevated intravesical pressure and/or catheter use (Klenck and Gebke, 2007). Urinary tract infections are a major cause of death among SCI patients, mostly due urinary sepsis (Whiteneck et al., 1992). The typical signs and symptoms of urinary tract infections may be absent in athletes with SCI, meaning that prevention is crucial (Cardenas and Hooton, 1995). Since among SCI patients there are different patterns of neurogenic bladders according to the neurological level (the anatomic level of the spinal cord injury), the management and treatment of the illness are different (Garcia Leoni and Esclarin De Ruz, 2003). Bacteriuria, however, is common among spinal cord injured individuals and its routine treatment without urinary tract infection symptoms is not recommended (Garcia Leoni and Esclarin De Ruz, 2003).

On the basis of previous epidemiological studies, disabled athletes seem to experience similar injury rates and patterns as their able-bodied counterparts (Ferrara and Peterson, 2000;Reynolds et al., 1994). However, some injuries and illnesses are more common in certain disability types than others (Ferrara et al., 1992;Ferrara and Peterson, 2000). Wheelchair athletes typically have injuries affecting the upper extremities and blind athletes affecting the lower extremities whereas cerebral palsy athletes suffer injuries both types of (Ferrara et al., 1992;Ferrara and Peterson, 2000). Webborn, Willick & Emery (2012) examined the incidence proportion and the characteristics of athlete injuries sustained during the 2010 Vancouver Paralympic Games. According to Injury Sustaining System, the incidence proportion of sport-related musculoskeletal injuries was 24%. The injury risk was significantly higher than during the 2002 (9.4%) and 2006 (8.4%) Winter Paralympic Games. The occurrences of musculoskeletal injuries were highest in athletes competing in sledge hockey and alpine skiing which was consistent with previous studies. A similar injury incidence proportion was enconutered in male and female athletes. Webborn, Willick & Emery (2012) explained the increased injury prevalence was that there was larger research team in place to more vigilantly identify all types of injury, and the inclusion of sports-related muscle pain in their study. However, they also pointed out that the patterns of injuries were slowly emerging in certain winter Paralympic sports and more attention needes to be paid in injury prevention in Paralympic sports (Webborn, Willick, and Emery, 2012).

2.4.2 Paralympic athletes´ medication use

Medication use among elite athletes is known to be more common than among in general population (Alaranta et al., 2006). However, the research data of the use of medication among the Paralympic athletes is largely incomplete. Tsitsimpikou et al. (2009) examined the Paralympic athletes´ medication and DS use during the Athens 2004 Paralympic games and compared the results with a representative sample of Olympic athletes. The Paralympic athletes had a more rational intake pattern of medications and food supplements than Olympic athletes. The medication or food supplement intake by Paralympins was 64% NSAIDs, analgesics and medicines for treating infections being biggest groups consumed (Tsitsimpikou et al., 2009a). This study by Tsitsimpikou et al. (2009a) is the only one to report Paralympic athletes´ medication use. Due their basic illnesses it could be assumed that disabled athletes will use more medications than their able-bodied counterparts. This may predispose disabled athletes to side effects the problems of and multimedication. Paralympic athletes are committed to adhering to the same doping regulations as Olympic athletes (Official website of the Paralympic Movement, Anti-Doping) .

2.5 DOPING REGULATIONS CONCERNING ASTHMA AND ALLERGY MEDICATION AND THEIR CHANGES BETWEEN 2002 AND 2012

In response to the apparent increase in the use of inhaled β2-agonists by athletes from Los Angeles (1984) to Atlanta (1996) Olympic Games and further, from Nagano (1998) to Sydney (2000) Olympic Games (Tsitsimpikou et al., 2009b), in 2001 WADA started to demand evidence of asthma or EIB in those athletes using inhaled β2-agonists (World Anti-Doping Agency, Prohibited List). The reason for this was health-related since significant adverse effects of β2-agonists have been documented (Haney and Hancox, 2006;Martinez, 2006;Simons, Gerstner, and Cheang, 1997). In recent years, the regulations concerning athletes´ asthma medication (ICS and inhaled β2-agonists) as well as the use of stimulants have been changed on several occasions (World Anti-Doping Agency, Prohibited List).

In 2004, WADA introduced international standards concerning situations when an athlete is required to take a medication to treat an illness or condition that happens to fall under the Prohibited List called a Therapeutic Use Exemption (TUE) (World Anti-doping agency, Science& Medicine). Previously, the anti-doping regulation had been the national authority (World Anti-doping agency, Science& Medicine). The major change in Finland was that in order to be granted a TUE for the use of a medication, the athlete needed to provide more detailed documentation of the illness (Suomen antidopingtoimikunta, Erivapaus urheilijan lääkityksessä). Between 2004 and 2012, the details of TUE and the various sub-sections needing to be filled have been changed on several occasions (World Anti-doping agency, Science& Medicine).

In 1.1.2009 WADA remodeled the TUE process (World Anti-doping agency, Science& Medicine). The major change was that now an athlete was able to have TUE also issued retroactively for the use of β2-agonists if the doping test was positive. For the use of ICS, a TUE was no longer needed, but instead, athletes were obliged to make a Declaration of Use by themselves. In 2011, however, WADA removed the Declaration of Use, which liberalized the regulations even more concerning the use of asthma medications.

Table 3. Doping regulations concerning inhaled β2-agonists, ICS and pseudoephedrine

Year	Inhaled β2-agonists[1]	Inhaled corticosteroids	Pseudoephedrine
2001-2002	Allowed in treatment of asthma or EIB with a certificate made by a specialiced physician. Urine concentration of salbutamol greater than 1000ng/l defined as anabolic use.	Allowed	Allowed when in urine concentrations are lower than 25mg/l
2003	No changes	No changes	No changes
2004	Allowed as inhalation in treatment of asthma or EIB with a Simplified Therapeutic Use Exemption (Simplified TUE) application template[2]. Urine concentration of salbutamol greater than 1000ng/l explicated as anabolic use.	No changes	Allowed. WADA started to follow the use of pseudoephedrine
2005	No changes[3].	No changes	
2006	Abbreviated Process (ATUE) can also be given for the treatment of other conditions than asthma or EIB	Abbreviated Process (ATUE) needed	No changes
2007	No changes	No changes	No changes
2008	No changes	No changes	No changes
2009	TUE or retroactive TUE needed	Declaration of Use needed[3]	No changes
2010	Salbutamol and terbutaline allowed in treatment of asthma and other pulmonary diseases with and Declaration of Use. TUE needed for the use of salmeterol and formoterol. Retroactive TUE for the use of salmeterol and formoterol no longer possible.	No changes	Prohibited in competitions when used in greater than therapeutic doses (urine concentrations greater than150mg/l)
2011	Salbutamol allowed in doses lower than 1600µg/d. Salmeterol allowed. Formoterol and terbutaline prohibited.	Allowed	No changes
2012	Formoterol allowed up to a maximum therapeutic dose of 36µg/d.	No changes	No changes

[1]Salbutamol, terbutaline, salmeterol, formoterol when not otherwise mentioned
[2]Terbutaline, salmeterol,formoterol tested only in-competition taken samples. Salbutamol tested in all samples.
[3]All inhaled β-agonists tested in- and out- of competition taken samples.

3. AIMS

The general aim of the present study was to investigate the prevalence of the use of self-reported dietary supplements and physician-prescribed medication among Finnish Olympic athletes. The results of this study were compared with results from a similar study conducted in Finnish Olympic athletes in 2002. All the results were compared between different types of sports. In addition, the differences in the self-reported physician-prescribed medication use between the Finnish Olympic and Paralympic athletes were investigated.

The main hypothesis was that that there would be an increase in the use of dietary supplements and physician-prescribed medication among Finnish Olympic athletes between 2002 and 2009. The main and specific aims of this study were as follows:

1. To describe the prevalence of vitamin, mineral and nutritional supplement use among Finnish Olympic athletes
   a. Athletes´ possibility to consult dietary specialists
2. To describe the prevalence of anti-asthmatic and anti-allergic medication use among Finnish Olympic athletes.
   a. The prevalence of physician-diagnosed asthma and physician-diagnosed allergy among these athletes
3. To describe the differences in physician-prescribed medication use between the Finnish Olympic and the Paralympic athletes in 2009 and 2006 respectively.
   a. Differences in the use of medicines that are taken treat chronic diseases
   b. Differences in the use of NSAIDs

4. SUBJECTS AND METHODS

4.1 STUDY DESIGN AND STUDY POPULATION

A cross-sectional study was conducted among the Finnish Olympic athletes receiving financial support from the Finnish Olympic Committee in 2008 and 2009. The study population for the current study was similar to a study conducted in Finnish Olympic athletes in 2002 (population of 494 athletes, response rate 90.3%) so the results of the current study were comparable with those that obtained in the previous study. In Finland, the National Olympic Committee provides financial support for 1) the Finnish national teams of sport associations that have adequate training organization in order for athletes to acquire Olympic success at the next Olympic Games 2) individual skilled athletes who are not associated with any such sport association 3) future Olympic hopefuls 4) team sports with possible success in the Olympic Games. The population of this study comprised all athletes eligible for financial support from the National Olympic Committee in 2008 and 2009. The details of the Olympic study population are given in Tables 4 and 5.

Table 4. Characteristics of the study groups

	Sex (Men/Women)	Age , years, M (SD)	Duration of active sports career, years, M (SD)	Training amount, hr/week M (SD)[1]	Response rate (%)
Olympic athletes 2002 (n= 446)	261/185	23.0 (4.5)	11.7 (4.3)	15.0 (6.0)	90.3
Olympic athletes 2009 (n= 372)	218/154	21.2 (4.3)	10.2 (4.5)	14.0 (5.0)	91.9
Paralympic athletes (n= 92)	80/12	33.6 (11.3)	12.8 (8.1)	7.1 (4.0)	75.0

[1]Mean, Standard Deviation

Table 5. Participating Olympic athletes by type of sport

Summer events	n= 246	Response rate	Winter events	n= 126	Response rate
Speed and power events	Judo	83.2% (89 of 107)	Speed and power events	Freestyle	100% (23 of 23)
	Track and field (sprinters, hurdles, jumpers, throwers, decathletes)			Speed skating	
	Wrestling			Alpine events	
	Weightlifting				
	Boxing				
	Taekwondo				
Endurance events	Rowing	84.4% (38 of 45)	Endurance events	Biathlon	100% (42 of 42)
	Badminton			Cross-country skiing	
	Swimming			Nordic combined	
	Canoeing				
	Track and field (800m+)				
	Tennis				
Motor skills demanding events	Shooting	91.7% (44 of 48)	Motor skills demanding events	Figure skating	100% (25 of 25)
	Archery			Snowboarding	
	Sailing			Ski-jumping	
	Fencing				
	Horse riding				
	Gymnastics				
Team sport events	Volleyball (men)	97.4% (75 of 77)	Team sport events	Ice hockey (women)	94.7% (36 of 38)
	Volleyball (women U-17)			Ice hockey (men U-20)	
	Volleyball (men U-17)				
	Handball (women U-17)				
	Handball (men U-17)				
	Basketball (women U-17)				
	Basketball (men U-17)				

A cross-sectional study was conducted in the Paralympic athletes in 2006 who answered a similar questionnaire as Olympic athletes. We compared the results of the Paralympic study with the results from the Olympic study conducted in 2009. Top-level Paralympic athletes comprised all national team athletes taking part in international competitions in 2006. The details of the study population are given in Tables 4 and 6.

The ethics committee of the University of Turku granted ethical approval for the study.

Table 6. Participating Paralympic athletes by type of sport

Type of sport	Response rate	Type of sport	Response rate
CP[1] football	90% (9 of 10)	Alpine events	100% (1 of 1)
Goalball	40% (6 of 15)	Archery	100% (6 of 6)
Sitting basketball	88% (15 of 17)	Cross-country skiing	50% (1 of 2)
Sitting volleyball	68% (10 of 15)	Shooting	100% (6 of 6)
Amputee hockey	93% (14 of 15)	Swimming	71% (5 of 7)
Wheelchair rugby	90% (9 of 10)	Table tennis	33% (2 of 6)
		Track and field	80% (8 of 10)
		Weight lifting	0% (0 of 3)

[1]Cerebral palsy

4.2 QUESTIONNAIRE

Both Olympic and Paralympic athletes answered a similar semi-structured questionnaires which was based on a national health survey, Health 2000, which is coordinated by the Finnish National Institute for Health and Welfare. The questionnaire was similar to that used in 2002. The questionnaire for the Paralympic study was piloted in 2002 in a study conducted with Finnish Olympic athletes. The questionnaire for the Olympic study was piloted in 2008 with national-level ice hockey players and track and field athletes (N = 30) who were not included in the final survey. Most athletes filled in the questionnaire in their national team camps. The questionnaire was sent by mail to those absent from their national team camps.

A researcher described the study to the athletes and was available to answer any questions. After providing written informed consent, the athletes filled in a semi-structured questionnaire. The off-site athletes were given the possibility to consult the researcher by phone or e-mail. The questionnaire was filled in anonymously and it was confidentially stored, analyzed and reported.

4.2.1 Questions concerning dietary supplements

Athletes were asked to name all vitamins, minerals, NS and herbal as well as homeopathic preparations they had used during the previous 12 months. Of the supplements used, the athletes were asked if they were using the supplement a) regularly or b) occasionally and further, if the athlete had used the supplement during the previous seven days. We also asked “For what purpose do you use this product?” and “Have you noticed any effect from using this product?” Moreover, we asked if an athlete had the opportunity to use the services of a nutritional specialist and if the athlete had visited a nutritional specialist regularly.

4.2.2 Questions concerning the prevalence of asthma and the use of asthma medication

The questions concerned asthma and allergy, exercise-induced bronchial symptoms and the use of asthma medication. The athletes were asked the following questions: 1) “Do you have asthma diagnosed by a physician?” If the athletes answered positively, they were further asked: 2) “Are you using currently any anti-asthmatic medication to treat your asthma? The athletes were also asked to name all the physician-prescribed preparations they had used during the previous 12 months and whether they used the above mentioned medication (a) regularly or (b) as needed. We also asked 3) “Do you have allergic rhinitis diagnosed by a physician?” The following questions were also asked: 4) “How often do you have cough, shortness of breath, or wheezing in connection to exercise (each question asked separately): (a) daily, (b) weekly, (c) monthly, or (d) in connection to respiratory infections or (e) never?”

4.2.3 Questions concerning the prevalence of allergy and the use of anti-allergic medication

The athletes were asked the following question: "Do you have an allergic disease diagnosed by a physician?" If the athletes answered positively, they were further asked whether the condition was (a) allergic rhinitis, (b) allergic conjunctivitis, (c) atopic eczema, or (d) other. Athletes were further asked: "Are you using currently any anti-allergic medication to treat the symptoms of an allergic disease?"

4.2.4 Questions concerning medication use by Olympic and Paralympic athletes

The questions concerned the use of physician-prescribed medication among athletes during the previous seven days and 12 months. The athletes were asked the following questions: 1) "Have you used any medication prescribed by a physician during the previous 12 months (yes/no)?" If the athletes answered positively to this question, they were asked to name all the medicines they had used during the previous 12 months of the study. Of the above named medicines, the athletes were further asked: 2) "Have you used this medicine during the previous seven days (yes/no)".

4.3 DEFINING OF DIETARY SUPPLEMENTS, MEDICATION AND ASTHMA AND ALLERGY

4.3.1 The definition of dietary supplements

An athlete was defined to be a DS user if they had named at least one DS being used during the previous 12 months. Dietary supplements were categorized into subgroups for further analysis. The categorization was identical to a Canadian study concerning elite athlete´s medication and dietary supplement use in the Atlanta and Sydney Olympic games (Huang, Johnson, and Pipe, 2006). Dietary supplements were defined as vitamins, minerals and NS (including amino acids, proteins, carbohydrates, creatine, caffeine, omega-3 fatty acids, herbal or homeopathic supplements and other supplements). The supplements that were defined as "herbal supplements" were products mainly derived from plant sources such as echinacea, garlic and ginseng. "Other supplements" included products that could not be categorized any other way, such as fibres, beastings and conjugated linoleic acid. "Vitamin supplements" included multivitamins, vitamins A, B, C, D and E, beta-carotenes and antioxidant agents. "Mineral supplements" consisted of iron, calcium, magnesium and other mineral products such as zinc, fluorine, potassium and multi-minerals.

We also categorized the athlete´s open ended answers concerning their experiences with the supplements they used. The most often given reasons for DS use were included in categorization**,** which was devised by our study group. In the vitamin and mineral groups, answers that were included in the analysis were defined as follows: 1. to ensure adequate intake of the named vitamin/ mineral, 2. to avoid sickness 3. to prevent cramps. In the NS group answers that were included in the analysis were defined as following: 1. to increase energy, 2. to recover from physical exercise, 3. to increase muscle mass. When categorizing answers concerning the benefits of an athlete´s DS use, we created three categories: 1. no benefits observed, 2. no apparent benefits observed, 3.benefits observed, which included all other reasons except categories 1.and 2.

4.3.2 The definition of asthma and asthma medication

An athlete was defined to have asthma if they answered positively to the question: “Do you have asthma diagnosed by a physician?” An athlete was defined as being an asthma medication user if they answered positively to the question: “Do you currently use any asthma medication?” Asthma medication was classified as inhaled β2-agonists, ICS, cromones (sodium cromoglycate and nedocromil), LTRA and ipratropium bromide. Inhaled β2-agonists were further classified as short-acting (salbutamol and terbutaline) and long-acting (salmeterol and formoterol) β2-agonists.

4.3.3 The definition of allergy and the use of anti-allergic medication

An athlete was defined as having a physician-diagnosed allergy if they answered positively to the question: “Do you have an allergic disease diagnosed by a physician?” Anti-allergic medication was classified as oral antihistamines, intranasal corticosteroids, anti-allergic eye drops, anti-allergic nasal sprays without corticosteroids and sympathomimetics. Sympathomimetics included products containing phenylpropanolamine or PSE. Anti-allergic nasal sprays without corticosteroids included products containing disodium cromoglycate or levocabastine.

4.3.4 The definition of other medication

The medicines used were categorized using the Anatomical Therapeutical Chemical (ATC) classification (WHO Collaborating Centre for Drug Statistics Methodology). Analgesics were classified as paracetamol, paracetamol-codeine, tramadol, dextropropoxyphene, buprenophine, pregabalin, amitriptyline, nortriptyline. Painkilling medicines were classified as analgesics or as NSAIDs.

4.4 STATISTICAL METHODS

4.4.1 Statistical methods used in studies I and II

The odds ratios (OR) for the presence of study variables and their 95% confidence intervals (95% CI) for different athletic groups were analyzed using a logistic regression model (SPSS 16.0 software). Logistic regression model was used as the study variables were binary. Age, sex, type of sport, and study year (2002 vs. 2009) were included as independent variables in the analyses concerning the use of DS. Chi-square tests were performed to test differences in single supplement use in 2002 and 2009. Statistical significance was reported at a p value of .05 or less (ns).

4.4.2 Statistical methods used in studies III and IV

The ORs for the presence of study variables and their 95% CIs in different athletic groups were analyzed using a logistic regression model (SPSS 16.0 software). Age, sex, type of sport, and study year (2002 vs. 2009) were included as independent variables in the analyses. In study III the analyses using logistic regression model were made in two different ways: after adjusting for age, sex and type of sport (referred as "$adjusted_1$") and after adjusting for age and sex (referred as "$adjusted_2$"). Differences in between the winter and summer athletes were evaluated separately using age, sex, and study year as independent variables.

In study IV, age, sex and type of athlete (Paralympic vs. Olympic athlete) were included as independent variables in the analysis. The statistical significances of the variables were tested with likelihood ratio statistics and expressed as exact P values. Chi-square tests were also performed to test differences in medication use between Paralympic and Olympic athletes. Statistical significance was reported at a p value of .05 or less (ns).

5. RESULTS

5.1 DIETARY SUPPLEMENTS (Studies I and II)

5.1.1 Use of dietary supplements

5.1.1.1 Frequencies of all supplement use in 2002 and 2009

The questionnaire was completed by 446 of 494 (90.3%) athletes in 2002 and 372 of 405 (91.7%) athletes in 2009. Of the 446 athletes, 81% reported supplement use during previous 12 months in 2002 and 73% of the 372 athletes in 2009. Decreased consumption of DSs between the study years was observed for all supplements with the exceptions of amino acids, omega-3 fatty acids, homeopathic supplements, vitamin D, antioxidants, beeta-carotene and magnesium. The differences in supplement use between study years are shown in Table 7. The dietary supplement use subdivided according to the different types of sports in 2002 and 2009 are illustrated in Table 8. The mean numbers of supplements consumed were 3.4 ± 3.1 in 2002 and 2.6 ± 2.7 in 2009. In 2002, the greatest number of different DSs consumed by a single athlete was 18. In 2009, the maximum of different DSs was 14 products.

Table 7. Differences in supplement use between the study years

Table 7A

Study year	Vitamins % (N)	Multivitamin % (N)	Vitamin C % (N)	Vitamin D % (N)	Vitamin B % (N)	Vitamin E % (N)	Betacarotine % (N)	Antioxidants % (N)
2002 (N=446)	67.3 (300)	53.6 (239)	27.8 (124)	0.7 (3)	17.9 (80)	2.9 (13)	0	0.7 (3)
2009 (N=372)	55.4 (206)	44.6 (166)	21.2 (79)	2.0 (8)	4.6 (17)	1.9 (7)	0.8 (3)	1.3 (5)

Table 7B

Study year	Minerals % (N)	Iron % (N)	Calcium % (N)	Magnesium % (N)	Other minerals % (N)	Zinc % (N)
2002 (N=446)	36.5 (136)	20.6 (92)	10.3 (46)	16.4 (73)	12.6 (56)	6.5 (29)
2009 (N=372)	30.1 (112)	11.8 (44)	5.9 (22)	17.2 (64)	6.5 (24)	3.2 (12)

Table 7C

Study year	Nutritional supplements % (N)	Creatine % (N)	Omega-3 fatty acids % (N)	Amino acid % (N)	Herbal supplements % (N)	Carbohydrate % (N)	Protein % (N)	Other % (N)	Homeopathic supplements % (N)
2002 (N=446)	51.6 (230)	15.7 (70)	11.2 (50)	3.8 (17)	9.2 (41)	24.4 (109)	47.1 (210)	7.2 (32)	0.4 (2)
2009 (N=372)	59.9 (223)	8.1 (30)	19.1 (71)	7.3 (27)	5.6 (21)	15.6 (58)	38.4 (143)	4.0 (15)	1.6 (6)

Table 8. Dietary supplement use subdivided according to the different types of sport in 2002 and 2009

	Vitamins % (N)	Minerals % (N)	Nutritional supplements % (N)	All supplements % (N)
Speed and power events 2002 (N=113)	81.4 (92)	43.4 (49)	78.8 (89)	92.0 (104)
2009 (N=112)	67.0 (75)	36.6 (41)	65.2 (73)	83.9 (94)
Endurance events 2002 (N= 108)	86.1 (93)	62.0 (67)	72.2 (78)	91.7 (99)
2009 (N=80)	72.5 (58)	55.0 (44)	70.0 (56)	92.5 (74)
Motor skills demanding events 2002 (N=73)	53.4 (39)	13.7 (10)	26.0 (19)	60.3 (44)
2009 (N=69)	53.6 (37)	17.4 (12)	31.9 (22)	65.2 (45)
Team sport events 2002 (N=152)	50.0 (76)	23.0 (35)	53.3 (81)	77.6 (118)
2009 (N=111)	34.2 (38)	13.5 (15)	36.9 (41)	54.1 (60)

After adjusting for age, sex and type of sport, the OR (95% CI) for use of any DS was significantly less in 2009 sample as compared with the 2002 sample (OR 0.62; 95% CI 0.43-0.90). Athletes in speed and power events and endurance events reported the use of any DS significantly more often than team sport athletes both in 2002 and 2009 (Table 9). In 2002, any DS use among athletes in skill-based sports was significantly less than that of athletes in team sports. Neither in 2002 nor in 2009 was any significant difference observed between females and males in DS use. In the 2002 sample group, there was no significant difference in any DS use between the different age groups (Table 9). However, in the 2009 sample group, athletes over 24 years consumed significantly more DS than athletes aged under 21 years.

Table 9. Logistic regression model on dietary supplement use in 2002 and 2009[1]

Characteristic	Vitamins		Minerals		Nutritional supplements		Any dietary supplements	
	OR[2]	95% CI[3]	OR	95% CI	OR	95% CI	OR	95% CI
Sex								
Men (2002)	1		1		1		1	
Men (2009)	1		1		1		1	
Women (2002)	1.32	0.85-2.06	2.13	1.36-3.33	0.54	0.35-0.83	0.92	0.55-1.55
Women (2009)	2.30	1.42-3.72	2.24	1.36-3.68	0.58	0.37-0.91	1.21	0.72-2.02
Type of sport								
Team sport (2002)	1		1		1		1	
Team sport (2009)	1		1		1		1	
Speed and power (2002)	4.67	2.56-8.52	3.85	1.90-7.82	2.76	1.55-4.91	3.37	1.50-7.57
Speed and power (2009)	3.71	2.02-6.81	2.83	1.60-5.03	2.25	1.25-4.05	3.65	1.89-7.03
Endurance (2002)	6.50	3.40-12.42	6.56	3.03-14.2	2.15	1.25-3.72	3.30	1.48-7.32
Endurance (2009)	3.13	1.54-6.36	5.98	3.38-10.58	2.11	1.06-4.20	6.73	2.60-17.48
Skill-based (2002)	1.26	0.71-2.22	1.25	0.53-2.94	0.29	0.16-0.55	0.46	0.25-0.85
Skill-based (2009)	1.90	0.98-3.69	0.70	0.33-1.46	0.53	0.27-1.06	1.29	0.67-2.47
Age (yr)								
Under 21 (2002)	1		1		1		1	
Under 21 (2009)	1		1		1		1	
21-24 (2002)	1.28	0.76-2.16	1.54	0.91-2.62	1.34	0.80-2.23	1.19	0.63-2.27
21-24 (2009)	1.66	0.95-2.90	1.16	0.63-2.14	2.47	1.40-4.34	1.90	0.97-3.70
Over 24 (2002)	0.86	0.51-1.46	1.63	0.95-2.80	0.92	0.55-1.54	0.70	0.38-1.30
Over 24 (2009)	6.77	3.22-14.23	2.15	1.14-4.07	4.43	2.31-8.50	3.18	1.38-7.33

[1]Each logistic regression included age, sex and type of sport as independent variable in the particular model
[2]odds ratio
[3]95% confidence interval

5.1.1.2 Vitamin use

After adjusting for age-, sex- and sport type, the OR (95% CI) for vitamin use was significantly less in 2009 sample group as compared with the 2002 sample (OR 0.62; 95% CI, 0.45-0.85). Both in 2002 and 2009, vitamin use was significantly more frequent among speed and power athletes and endurance athletes when they were compared with team sport athletes (Table 9). Vitamin use was more frequent among female athletes than male athletes in 2009. In 2009, athletes in the age group over 24 years consumed significantly more vitamins than athletes in age group under 21 years. In 2002, no significant difference was seen in vitamin use between the different age groups.

The most popular vitamins used in both study years were multivitamins and their consumption was slightly decreased between the study years: 54% of all athletes in 2002 and 45% in 2009 ($P = 0.01$) (Table 7a). Between the study years, a diminished use was observed of vitamin B preparations during follow-up period. In 2002, 18% of the athletes consumed vitamin B but in 2009 only 5% of the athletes were taking vitamin B preparations ($P < 0.001$). Vitamin D consumption was low in both study years: 0.7% in 2002 vs. 2% in 2009 (ns, $P= 0.07$). Multivitamin use was most common among speed and power athletes both in 2002 and 2009 (69% and 57% of the speed and power athletes, (ns)) whereas vitamin C consumption was most common among endurance athletes in both study years (55% in 2002 and 38% in 2009, $P = 0.02$). Between the study years, the consumption of multivitamin preparations increased among motor skills demanding athletes (42% vs. 49%, (ns)) but decreased among endurance athletes (63% vs. 51% (ns)) and team sport athletes (41% vs. 24%, $P = 0.004$).

5.1.1.3 Mineral use

There was a trend for less use of minerals in 2009 as compared with the 2002 sample group (adjusted OR 0.77; 95% CI 0.56-1.08). Mineral use was significantly more frequent among speed and power athletes and endurance athletes when compared with team sport athletes, both in 2002 and 2009 (Table 9). Women used significantly more often minerals than men both in 2002 and 2009. In 2009, athletes over 24 years used minerals significantly more often than athletes in the youngest age group.

The most popular mineral supplements in both study years were iron (21% of the athletes in 2002 and 12% of the athletes in 2009, $P = 0.001$), magnesium (16% and 17%, (ns)) (Table 7b). Iron was used by 28% of the females and 16% of the males in 2002 ($P = 0.002$) and 19% of the females and 7% of the males in 2009 ($P < 0.001$). Iron use was most common in endurance athletes in both 2002 and 2009 (48% and 34% of the endurance athletes $P = 0.05$), whereas magnesium use was most popular in endurance athletes in 2002 (25%) but in 2009 it was most popular among speed and power athletes (27%).

5.1.1.4 Nutritional supplement use

No significant difference was found in athletes´ NS use after adjustment for age, sex and sport type when the 2009 sample group was compared with the 2002 sample group (OR 0.77; 95% CI 0.56-1.04). Speed and power athletes as well as endurance athletes consumed significantly more often NS than team sport athletes in both 2002 and 2009 (Table 9). Women consumed significantly less nutritional supplements than men both in 2002 and 2009. Nutritional supplement use was significantly more frequent among athletes in the age groups 21-24 years and over 24 years in 2009 when compared with athletes in age group under 21 years. In 2002, no significant difference was seen in NS use between age groups.

The most popular products consumed in both study years were proteins (47% of the athletes in 2002 and 38% of the athletes in 2009, P = 0.01) and carbohydrates (24% and 16%, P = 0.002) (Table 7c). A total of 11% (50 of 446) athletes in 2002 and 19% (71 of 372) in 2009 reported having used omega-3 fatty acids during the previous 12 months (P = 0.002). In 2002, 8 % of the athletes and in 2009, 15% of the athletes consumed these agents regularly (P= 0.002). The most common omega-3 fatty acid users in both study years were endurance athletes (21% in 2002 and 24% in 2009 (ns)). In the other sport groups, the consumption of omega-3 fatty acids was as follows: speed and power athletes 10% in 2002 vs. 21% in 2009 (P = 0.02), motor skills demanding athletes 10% vs. 19% (ns), team sport athletes 6% vs. 14% (P = 0.04). The most common users of protein (71% in 2002 and 56% in 2009, P = 0.03) as well as creatine (35% and 19% P = 0.007) in both study years were speed and power athletes. Creatine was consumed by 7% of the women in 2002 but only 1% of the women in 2009 (P = 0.01) and by 22% of the men in 2002 and 13% of the men in 2009 (P = 0.01).

5.1.2 Reasons for supplement use and the possibility of supplement users to consult dietary specialists in 2009.

In 2009, of the athletes who answered the questions concerning reasons for their supplement use, 64% of vitamin and mineral users explained their use as “to prevent nutritional deficiencies” (67% of the women and 63% of the men) and 30% “to maintain health” (32% of the women and 29% of the men). A total of 48% of the magnesium supplement users took the mineral in order to “prevent cramps” (50% of the women and 60% of the men) and 58% of all the magnesium users were taking it in order to prevent nutritional deficiencies (40% of the women and 60% of the men). A total of 81% of iron supplement users took the mineral in order to “maintain adequate hemoglobin level of blood” (78% of the women and 82% of the men and 86% of the speed and power athletes, 92% of the endurance athletes, 50% of athletes in motor skills demanding group and 50% of team sport athletes). Of the athletes who reported having used some preparation and answered the question concerning the benefits of its use, 77% of magnesium users considered their use as beneficial and 71% of vitamin C users thought they had benefitted of its consumption.

Of the NS users who answered questions concerning reasons for their supplement use, 80% explained their use as “to recover from physical exercise” (80% of the women and 79% of the men), 22% explained their use as “to increase energy” (17% of the women and 25% of the men) and 14% said that their use was “to increase (muscle)mass” (13% of the women and 14% of the men and 17% of the speed and power athletes, 5% of the endurance athletes, 8% of athletes in motor skills demanding group and 19% of team sport athletes). Omega-3 fatty acid users reported their most popular reason for supplementation (84%) as helping recovery from physical exercise (85% of the women and 84% of the men) and a total of 28% of omega-3 fatty acid users had experienced some benefit of their use. Of the all supplements used, 79% were viewed as beneficial and 12% stated that they conferred no benefits by according to the athletes who answered the question.

When athletes were asked about the possibility to consult dietary specialists, it was found that only 27% (99 of 372 athletes) of athletes in 2009 answered “yes”. Of the athletes in different sport groups, 30% of speed and power athletes, 31% of endurance athletes, 36% of athletes in motor skills demanding group and 14% of team sport athletes had had the possibility to consult a nutritional specialist. Of the supplement users, 30% had had the possibility to consult nutritional specialists occasionally. Only 1% of the athletes had beed provided with the possibility to visit dietary specialist on a regularly basis.

5.2 PREVALENCE OF ASTHMA AND ASTHMA MEDICATION USE (Study III)

5.2.1 Prevalence of asthma and asthma-like symptoms

Physician diagnosed asthma was reported by 13.9% (62/446) of the athletes in 2002 and by 15.9% (59/372) in 2009 (OR 1.33; 95% CI 0.89-1.99, after adjusting for age, sex and type of sport ($adjusted_1$)) (Table 10). There was no significant difference detected in the occurrence of wheezing between the study years (Table 10).

Table 10. Prevalence (%) of physician-diagnosed asthma, the use of anti-asthmatic medication and allergic rhinitis and occurrence of wheezing in the athletes in 2002 and 2009

	All athletes	Motor skills demanding events	Endurance events	Speed and power events	Team sport events
Physician-diagnosed asthma 2002	13.9 (62/446)	8.2 (6/73)	22.2 (24/108)	8.8 (10/113)	14.5 (22/152)
2009	15.9 (59/372)	8.7 (6/69)	28.8 (23/80)	14.3 (16/112)	12.6 (14/111)
P[1]	ns[2]	ns	ns	ns	ns
Use of anti-asthmatic medication 2002	10.1 (45/446)	2.7 (2/73)	16.7 (18/108)	7.1 (8/113)	11.2 (17/152)
2009	13.7 (51/372)	5.8 (4/69)	31.2 (25/80)	9.8 (11/112)	9.9 (11/111)
P[1]	0.02	ns	0.02	ns	ns
Occurrence of wheezing 2002	10.3 (46/446)	2.7 (2/73)	19.4 (21/108)	8.8 (10/113)	8.6 (13/152)
2009	10.2 (38/372)	5.8 (4/69)	16.2 (13/80)	9.8 (11/112)	9.0 (10/111)
P[1]	ns	ns	ns	ns	ns
Physician-diagnosed allergic rhinitis 2002	26.5 (118/446)	27.4 (20/73)	36.1 (39/108)	20.4 (23/113)	23.7 (36/111)
2009	24.2 (90/372)	27.5 (19/69)	35.0 (28/80)	21.4 (24/112)	17.1 (19/372)
P[1]	ns	ns	ns	ns	ns

[1]Represents the difference between prevalence in years 2002 and 2009 derived from logistic regression analyses adjusted for age, sex and type of sport

[2]ns= non-significant

5.2.2 Use of asthma medication

In 2002, a total of 10.1% (45/ 446) of the athletes and in 2009, a total of 13.7% (51/372) of the athletes were using asthma medication (adjusted$_1$OR 1.71; 95% CI 1.08-2.69; p = 0.02) (Table 11). After adjusting for age and sex (adjusted$_2$), the most significant increase in the use of asthma medication occurred among the endurance athletes during the study period (OR 2.39; 95% CI 1.17-4.90). After a similar adjustment, the use of asthma medication tended to increase in both winter (OR 1.84; 95% CI 0.94-3.60) and summer athletes (OR = 1.77, 95% CI 0.95-3.28).

Table 11. Prevalence (%) of asthma medication use in 2002 and 2009

	Any asthma medication % (n)	Inhaled β2-agonists % (n)	Inhaled corticosteroids % (n)	Fixed combinations of LABA[1] and ICS[2] % (n)	Cromones % (n)	Leukotriene antagonists % (n)	Ipratropium bromide % (n)
2002 (446)	10.1 (45)	7.4 (33)	6.3 (28)	1.3 (6)	1.6 (7)	0.7 (3)	0.0 (0)
2009 (372)	13.7 (51)	9.7 (36)	9.4 (35)	3.8 (14)	0.3 (1)	2.4 (9)	3.8 (3)
P[3]	0.02	[4]ns(0.06)	0.01	0.02	ns	<0.01	

[1]Long-acting β2- agonists
[2]Inhaled corticosteroids
[3]Represents the difference between prevalence in years 2002 and 2009 derived from logistic regression analyses adjusted for age, sex and type of sport
[4]ns= non-significant

In 2002, none of the athletes but in 2009, six athletes (11.8% of the asthma medication users) used asthma medication without their asthma having been diagnosed by a physician. The asthma medications that were used without diagnosis were inhaled β2-agonists (N = 1), ICS (N = 4) and fixed combinations of ICS and LABA (N = 1).

In 2002, a total of 1.3% of the athletes and in 2009, a total of 3.8% of the athletes were using fixed combinations of ICS and LABA ($adjusted_1$OR 3.38; 95% CI 1.26-9.12). The use of fixed combinations of ICS and LABA increased significantly between the study years among the endurance athletes ($adjusted_2$OR 5.20; 95% CI 1.02-26.46). A significant difference was observed in the use of fixed combinations of ICS and LABA among the summer athletes between the study years ($adjusted_2$OR 4.14; 95% CI 1.03-16.72).

Inhaled β2-agonists were the most frequently used asthma medications in both study years. In 2002, a total of 7.4% (33/446) of the athletes and in 2009, a total of 9.7% (36/372) of the athletes were using this class of drugs ($adjusted_1$OR; 1.64, 95% CI 0.97-2.76; (ns)) (Table 11). The use of inhaled β2-agonist increased significantly between the study years among the endurance athletes ($adjusted_2$OR 2.57; 95% CI 1.09-6.05). Long-acting β2-agonists (salmeterol, formoterol) were used by 2.7% (12/446) of the athletes in 2002 and by 4.6% (17/372) in 2009 ($adjusted_1$OR 2.20; 95% CI 0.96-4.87). Short-acting β2-agonists (salbutamol, terbutaline) were used by 6.5% (29/446) of the athletes in 2002 and by 7.5% (28/372) of the athletes in 2009 ($adjusted_1$OR 1.36; 95% CI 0.76-2.44). In both study years, two athletes reported having used inhaled β2-agonists regularly without using inhaled corticosteroid medication.

ICS were being used by 6.3% (28/446) of the athletes in 2002 and by 9.4% (35/372) of the athletes in 2009 ($adjusted_1$OR 2.00; 95% CI 1.15-3.46; p = 0.01) (Table 11). ICS being were used regularly by 5.4% (24/446) of the athletes in 2002 and by 6.5% (24/372) of the athletes in 2009 ($adjusted_1$OR 1.53; 95% CI 0.81-2.90) and occasionally by 0.9% (4/446) of the athletes in 2002 and by 3.8% (14/372) of the athletes in 2009 ($adjusted_1$OR 4.90; 95% CI 1.56-15.38). The use of ICS increased most significantly between the study years among the endurance athletes ($adjusted_2$OR 2.83; 95% CI 1.21-6.66). A significant increase was seen in the use of ICS among the summer athletes between the study years ($adjusted_2$OR 2.48; 95% CI 1.18-5.18).

5.3 THE USE OF ANTI-ALLERGIC MEDICATION BY OLYMPIC ATHLETES

5.3.1 Prevalence of allergy

The occurrence of physician-diagnosed disturbing allergy was reported by 32.1% (143/446) athletes in 2002 and 28.5% (106/372) athletes in 2009. After adjusting for age, sex and type of sport, no significant difference could be detected in the occurrence of physician-diagnosed allergy between the study years (OR 0.90; 95% CI 0.65-1.25). The occurrence of physician-diagnosed allergic rhinitis was 26.5% in 2002 and 24.2% in 2009 (Table 10), the occurrence of allergic eczema was 4.3% in 2002 and 4.0% in 2009 (OR 1.0; 95% CI 0.48-2.06) and the occurrence of allergic conjunctivitis was 3.6% in 2002 and 4.3% in 2009 (OR 1.22; 95% CI 0.59-2.52)

5.3.2 Most often used allergy medications

The use of anti-allergic medication was 16.8% (75/446) in 2002 and 16.4% (61/372) in 2009 (OR 1.02; 95% CI 0.68-1.53). The use of anti-allergic medication was significantly more common among endurance athletes than in athletes in the motor skills demanding group in both study years (OR 3.54; 95% CI 1.44-8.65 in 2002 and OR 2.92; 95% CI 1.14-7.49 in 2009). The most often used anti-allergic medicines in all study groups and in both study years were oral antihistamines that were used by 12.3% (55/446) of athletes in 2002 and 10.5% (39/372) of athletes in 2009 (ns). Intranasal corticosteroids were used by 6.1% (27/446) and 5.4% (20/372) of the athletes in 2002 and 2009 respectively (ns). Of the athletes with allergic rhinitis, 53.4% in (63/118) in 2002 and 45.6% (41/90) in 2009 were taking some kind of anti-allergic medication (ns). Between study years, a significant increase was seen in the consumption of sympathomimetics by athletes (OR 4.77; 95% CI 1.68-13.52).

Of the other anti-allergic medicines, anti-allergic eye drops were used by 2.2% (10/446) and 0.3% (1/372) (P= 0.05) and anti-allergic nasal sprays without corticosteroids by 1.3% (6/446) and 0.5% (2/372) (ns) athletes in 2002 and 2009 respectively. In 2002, 1.6% (7/446) of the athletes and in 2009, 4.0% (15/372) athletes used anti-allergic medication without physician-diagnosed allergy (P = 0.04).

5.4 PARALYMPIC AND OLYMPIC ATHLETES´ MEDICATION USE (Study IV)

5.4.1 Any use of a prescribed medicine during the past seven days

After adjusting for age and sex, the use of any prescribed medication by the Paralympic athletes was significantly more common than was the case in the Olympic athletes during the previous seven days (48.9% vs. 33.3% OR 1.99; 95% CI 1.13-3.51) (Table 12). The most commonly used medicines during the previous seven days by the Paralympic and Olympic athletes were NSAID, anti-epileptic medicines (9.8% vs. 0.5%), anti-hypertensive medicines (9.8% vs. 0%), oral antibiotics, asthma medicines and anti-allergic medicines. The Paralympic athletes took significantly more commonly painkilling medicines (21.7% vs. 7.5% adjusted OR 2.61; 95% CI 1.18-5.78), analgesics, oral antibiotics and anti-epileptic medicines (adjusted OR 37.09; 95% CI 5.92-232.31) than the Olympic athletes (Table 12). The Paralympic athletes were significantly less likely to be using asthma medicines than the Olympic athletes during the previous seven days (Table 12). A total of 40.0% (4 out of 10) of the Paralympic and 100% (2 out of 2) of the Olympic athletes who were taking anti-epileptic medicines had a diagnosis of epilepsy. Oral antibiotics that were used to treat urinary tract infections had been used by 6.5% (6 out of 92) of the Paralympic but none of the Olympic athletes during the previous seven days.

There was regular use of anti-epileptic and anti-hypertensive medicines as well as medicines to treat urinary tract infection among all the athletes that reported having used them during the previous seven days.

Table 12. The use of physician-prescribed medicines during the previous seven days by the Paralympic and Olympic athletes

	Any medicine % (n)	NSAIDS[1] % (n)	Analgesics % (n)	Muscle relaxants %(n)	Anti-allergic medicines % (n)	Asthma medicines % (n)	Oral antibiotics % (n)
Paralympic athletes (n=92)	48.9 (45)	16.3 (15)	8.7 (8)	5.4 (5)	5.4 (5)	4.3 (4)	9.8 (9)
Olympic athletes (n=372)	33.3 (124)	6.7 (25)	1.1 (4)	0.3 (1)	8.6 (32)	11.0 (41)	3.5 (13)
OR;95% CI[2]	1.99; 1.13-3.51	1.82; 0.77-4.26	11.23; 2.09-60.21	7.95; 0.79-80.45	0.62; 0.20-1.90	0.30; 0.10-0.96	4.10; 1.30-12.87
P[3]	<0.01	<0.01	0.01	<0.01	[4]ns	0.05	0.01

[1]non-steroidal anti- inflammatory drugs
[2]odds ratio, confidence interval; logistic regression analysis, after adjusting for age and sex
[3]Chi-square test for the difference between Paralympic and Olympic athletes
[4]ns= non-significant

5.4.2 Any use of a prescribed medicine during the previous 12 months

A total of 84.8% of the Paralympic athletes and a total of 73.9% of the Olympic athletes had taken some kind of physician-prescribed medicine during the past 12 months (Table 13). The most commonly used medicines during the previous 12 months by the Paralympic and Olympic athletes were NSAIDs, oral antibiotics, analgesics, anti-epileptic medicines (10.9% vs. 0.5%), anti-allergic medicines and asthma medicines. Oral antibiotics were used to treat urinary tract infections by 8.7% (8 out of 92) of the Paralympic athletes and by 0.5% (2 out of 372) of the Olympic athletes during the previous 12 months (adjusted OR 18.56; 95% CI 2.61-131.82). The Paralympic athletes consumed significantly more anti-epileptic medicines (10.9% vs. 0.5% adjusted OR 37.08; 95% CI 6.06-227.11) and anti-hypertensive medicines (9.8% vs. 0.3% adjusted OR 21.82; 95% CI 1.67-284.87) than the Olympic athletes during the previous 12 months. In contrast, the Paralympic athletes were significantly less likely to be consuming painkilling (42.4% vs. 50.8%

adjusted OR 0.50; 95% CI 0.28-0.87), NSAID, anti-allergic medicines than the Olympic athletes during the previous 12 months.

Table 13. The use of physician- prescribed medicines during the previous 12 months by the Paralympic and Olympic athletes

	Any medicine % (n)	NSAIDS[1] % (n)	Analgesics % (n)	Muscle relaxants %(n)	Anti-allergic medicines % (n)	Asthma medicines % (n)	Oral antibiotics % (n)
Paralympic athletes (n= 92)	84.8 (78)	34.8 (32)	16.3 (15)	6.5 (6)	7.6 (6)	6.5 (6)	29.3 (27)
Olympic athletes (n=372)	73.9 (275)	48.7 (181)	7.8 (29)	5.1 (19)	15.9 (59)	13.7 (51)	28.2 (105)
OR;95% CI[2]	1.04; 0.49-2.22	0.39; 0.22-0.70	1.63; 0.72-3.70	0.56; 0.19-1.65	0.35; 0.14-0.87	0.38; 0.14-1.02	0.69; 0.38-1.27
P[3]	0.03	0.02	0.01	[4]ns	0.04	ns	ns

[1]non-steroidal anti-inflammatory drugs
[2]odds ratio, confidence interval; logistic regression analysis, after adjusting for age and sex
[3]Chi-square test for the difference between Paralympic and Olympic athletes
[4]ns= non-significant

A total of 33 % (7 out of 21) and 56% (59 of 106) of the Paralympic and Olympic athletes who had an allergic disease diagnosed by a physician were taking anti-allergic medicines. Physician-diagnosed asthma was reported by 6.5% of the Paralympic and 15.9% of the Olympic athletes (adjusted OR 0.35; 95% CI 0.13-0.91). A total of 83.3% (5 out of 6) and 88.2% (45 out of 51) of the Paralympic and Olympic athletes who were taking asthma medicines had had asthma diagnosed by a physician.

The most commonly used asthma medicines by the Paralympic and Olympic athletes during the previous 12 months were inhaled β2-agonists (4.3% vs. 9.7% respectively; adjusted OR 0.46; 95% CI 0.14-1.51) and inhaled corticosteroids (4.3% vs. 9.4%; adjusted OR 0.33; 95% CI 0.10-1.05). The most commonly used anti-allergic medicines which had been used during the previous 12 months were oral antihistamines (3.3% vs. 10.5%; adjusted OR 0.31; 95% CI 0.08-1.14), pseudoephedrine (3.3% vs. 4.3%; adjusted OR 0.45; 95% CI 0.11-1.81) and anti-allergic nasal sprays (3.3% vs. 4.8%; adjusted OR 0.46; 95% CI 0.12-1.87).

6. DISCUSSION

The use of dietary supplements among Finnish Olympic athletes is decreasing. The consumption of some micronutrients, such as multivitamins and vitamin C, is high and the recommendations for daily intake may be exceeded. On the other hand, the intake of some essential micronutrients, such as vitamin D, is suprisingly low, even raising the possibility of serious harm in those well-trained athletes. The use of asthma medication, especially fixed combinations of LABA and ICS, is clearly increasing among Finnish Olympic athletes. This trend is not based on an increased occurrence of asthma symptoms, asthma diagnoses or objective lung function measurements. The use of any physician-prescribed medicines, especially those treat chronic diseases, seems to be more common among the Paralympic than the Olympic athletes.

6.1 VALIDITY OF THE DATA

Two cross-sectional studies with a high response rate (92% for Olympic athletes in 2009 and 75% for Paralympic athletes in 2006) involving a large number of Finnish Olympic and Paralympic athletes were conducted. Both Paralympic and Olympic athletes filled out similar, semi-structured questionnaires and had the opportunity to consult the researchers on these occasions. The statistical analyses were made after assuming that there were no Olympic athletes answering to both questionnaires although in theory, there may have been a very limited number of athletes taking part in the study in both in 2002 and 2009. However, due the large study sample this was not relevant. Since athletes filled the questionnaire anonymously, we were not able to trace these possible athletes. Like always in questionnaire studies, there may have been questions that athletes did not answer completely.

6.1.1 Studies on Olympic athletes (Studies I,II,III)

When collecting data for the Olympic study, the main intention was to ensure that the source population was similar to the study population in 2002. However, between the study years, the National Olympic Committee had somewhat raised the criteria for receiving financial support and therefore some smaller sport federations did not obtain support for adult athletes in 2009. This resulted in a slightly smaller study population in 2009 than 2002. However, the subgroup sizes in 2002 and 2009 (speed and power athletes, endurance athletes, athletes in motor skills demanding events and team sport athletes) were rather similar. Raising the criteria for financial support also led to slight changes in the age profile of the study population between the study years: the athletes' mean age was greater in 2002 than in 2009 (23.0 vs. 21.2 years; Table 4). The lower mean age of the athletes may also explain lower mean training hours per week and shorter durations of active sport career of the athletes in 2009. However, all values were calculated using logistic regression models in order to adjust for these possible confounding factors.

6.1.1.1 Dietary supplements

Athletes were asked to name all DSs, all vitamins, minerals and herbal and homeopathic preparations that they had used during the previous 12 months without any examples being supplied. In some of the other studies conducted with elite athletes, there are surveys that have provided examples or listed the supplements they wanted athletes to name in their questionnaire (Braun et al., 2009;Froiland et al., 2004;Scofield and Unruh, 2006). In the comparison with these studies, the absence of examples may have caused some underreporting of supplement use. Similarly, athletes´ reasons and opinions of their supplement use in 2009 were asked with open questions. We did not include any specific laboratory measurements e.g. to further confirm adequate vitamin D plasma level. Due to the large sample size we were able to detect even small changes in DS use, but these may not be clinically relevant.

6.1.1.2 The prevalence of asthma and asthma medication use

Although we adjusted for possible confounding factors in the logistic regression model, physician diagnosed asthma could not be included, as it was strongly associated with use of asthma medication. Thus, a change in the occurrence of asthma would have affected also the frequency of anti-asthmatic treatment.

The inclusion of pulmonary function tests for all athletes would have provided increased information. However, introducing the IOC regulations (including eucapnic hyperventilation test, metacholine challenge test, exercise challenge test and bronchodilatation test) would have required that there were over 3 000 tests performed in the current study.

6.1.1.3 Paralympic and Olympic athletes (Study IV)

The studies were made three years apart during which there were changes in the WADA regulations considering the use of medication, especially asthma medication by athletes (World Anti-Doping Agency, Prohibited List). Due the inclusion criteria of the study, there were differences in the types of sports of the athletes represented so that the total amount of different sports was lower among the Paralympians than the Olympic athletes (14 vs. 40 respectively; Table 4). Among the Paralympic athletes, there were relatively less athletes taking part in endurance and speed and power types of sports and relatively fewer athletes taking part in team sports. These differences in the types of athletes may partly explain the differences in the medication use between the study groups, especially with the respect to asthma medication and NSAID use. The age profiles of the two study groups were also somewhat different so that the mean age of the Paralympic athletes was ten years greater (34 vs. 23 years) than their Olympic colleagues.

6.2 COMPARISON WITH PREVIOUS FINDINGS

6.2.1 Dietary supplements

When comparing the numbers in the study population in this study with other surveys concerning elite athletes´ supplement use, it was noted that there are only two studies (Erdman et al., 2007;Petroczi et al., 2008) that had larger study populations than examined here. The characteristics of participants in this present study were similar to those in other studies with elite athletes (Braun et al., 2009;Erdman et al., 2007;Froiland et al., 2004;Huang, Johnson, and Pipe, 2006;Petroczi et al., 2008;Ronsen, Sundgot-Borgen, and Maehlum, 1999;Tsitsimpikou et al., 2009b). When comparing the present results with a study (Huang, Johnson, and Pipe, 2006) that reported Canadian Olympic athlete´s DS use in Atlanta (69%) and Sydney Olympic Games (74%), it can be seen that rates of supplement use among elite Finnish athletes are still high. No other cross-sectional studies were found which evaluated trends in elite athlete´s DS use. Here, NS use was significantly higher among males than females both in 2002 and 2009 whereas the Canadian study (Huang, Johnson, and Pipe, 2006) reported all DS use as being slightly more common among female athletes both in the Atlanta and Sydney Olympic Games. In 2002, there was a mean of 3.4 DSs per athlete, whereas in 2009 the mean amount had declined to 2.6 DSs per athlete. The maximum amount of different DSs consumed by an individual athlete decreased as well. In the first survey, one athlete was consuming 18 different DSs, whereas in the second study one athlete was consuming 14 different products.

The most frequent vitamin and mineral as well as overall DS users in both study years were endurance athletes and speed and power athletes. Similarly to Huang et al´s report (2006), it seems that athletes competing in sports that involve endurance-type of activity and that can be classified as single sports are more likely to use DSs. This is also supported with the fact that in this present study, team sport athletes consumed less DSs. However, it was interesting to observe that between the study-years athletes in motor skills demanding sports increased their frequency of supplement use. This may be evidence of a spreading culture of supplement use as athletes who have not traditionally used these products start to add supplements into their diet.

The most often products being used by our study population during both study years were multivitamins (54% in 2002 and 45% in 2009), proteins (47% and 38%) and vitamin C

(28% and 21%). These findings are in line with the literature (Braun et al., 2009;Erdman et al., 2007;Froiland et al., 2004;Huang, Johnson, and Pipe, 2006;Petroczi and Naughton, 2008;Ronsen, Sundgot-Borgen, and Maehlum, 1999) except for carbohydrates which were reported rather infrequently by the present study participants. It can be assumed that there was some underreporting of carbohydrate use since many of the athletes may not consider sports drinks with high levels of carbohydrates as NS. This is supported with the fact that an American study (Froiland et al., 2004) of college athletes reported that 33% of the athletes did not consider fluid and caloric replacement products (such as Energy mix, Gatorade, Recovery mix) as DS.

One of the findings in this thesis was the effect of athlete´s age on the DS consumption rate. In 2002, there was no statistical difference between the age groups when examining the frequency of dietary supplementation. In 2009, the consumption of DSs increased significantly in older age groups. Similarly, a Canadian study (Erdman et al., 2007) of high performance elite athletes and a German study (Braun et al., 2009) of young elite athletes as well as a recent international study (Tscholl et al., 2010) conducted with track and field athletes reported higher rate of DS use among older athletes than with younger athletes. A study (Petroczi et al., 2008) with young elite athletes between the ages 12-21 reported that 48.1% were using at least one supplement. Similarly, a study (Scofield and Unruh, 2006) made with adolescent athletes in central Nebraska reported that only 27% of the athletes had used supplements in the past. These rates of consumption are considerably lower than percentages of supplement use in older athletes (Erdman et al., 2007;Huang, Johnson, and Pipe, 2006;Petroczi et al., 2007;Petroczi et al., 2008). In this study, in 2002, athletes in the age group of 21-24 years were the most frequent DS users, whereas in 2009 athletes in the oldest age group (over 24 years) were more likely to be consuming supplements.

Only 30% of the supplement users and 27% of all athletes had had the possibility to consult a dietary specialist when needed. The appropriate intake of macro- and micronutrients is essential for high training elite athletes in order to optimize the results of physical exercise. Planning of a well-balanced diet can be particularly complicated e.g. athletes in sports where a low body weight is considered to benefit performance (e.g. high-jumpers,figure skaters) or for endurance athletes who need to consume large amounts of calories (especially carbohydrates) per day. The intake of micro- and macronutrients may not to be optimal among elite athletes (Hinton et al., 2004;Lun, Erdman, and Reimer, 2009). Thus, coaches, dietitians and other professional working with elite athletes must pay attention to the nutritional habits of their athletes first to ensure that the daily intake of macronutrients is sufficient to allow recovery and still achieve optimal benefit from the exercise, and second to ensure that daily intake of micronutrients does not exceed safe limits

When examining the reasons that they gave for their supplement use, the most common given reasons by athletes in this study were similar to other reports examining elite athletes (Braun et al., 2009;de Silva et al., 2010;Erdman et al., 2007;Froiland et al., 2004). However, there were some differences when comparing the popularity of reasons given. In this present study, only 30% of vitamin and mineral users stated that they were taking thse products in order to maintain health. In other studies (Braun et al., 2009;Froiland et al., 2004) made, 45 to 63%, of the athletes were using supplements in order to maintain health. Recovering from physical exercise was one of the most important reasons that our athletes gave for their supplement use (80%). There is only one study (Erdman et al., 2007) that reported nearly such a high percentage in their study. In our study, 81% of iron users were taking the mineral to maintain adequate hemoglobin level of blood. However the percentage was even slightly higher among in male than female athletes (81% and 78% respectively), which is interesting since in view of the physiological fact that females are more sensitive to anemia than men (Sinclair and Hinton, 2005).

Surprisingly few athletes reported additional vitamin D use in both study years. In 2002, only 0.7% percent of the athletes were taking vitamin D preparations and in 2009 that percentage had only risen to 2.0%. Since vitamin D is known to be essential for bone health and immune system (Hamilton, 2010;Willis, Peterson, and Larson-Meyer, 2008) and also to have an influence on muscle function (Hamilton, 2010;Ward et al., 2009), attention must be taken to the vitamin D status of the Finnish athletes in order to avoid the harmful effects of vitamin D deficiency, especially during the winter months.

Interestingly, there was a significant increase between the study years in the consumption of omega-3 fatty acids. In addition, regular use of those preparations nearly doubled (8% in 2002 and 15% in 2009), the difference between study years being statistically significant. The consumption of omega-3 fatty acids was most frequent among endurance athletes in both study years but when the consumption of those preparations was compared between study years, the increase in consumption was notably high in other subgroups. Ronsen et al (1999) reported that regular cod liver oil consumption being nearly 50% and occasional use of the product in over 40% of Norwegian elite cross-country skiers. It has been claimed that N3-PUFA supplementation may have a positive effect in reducing asthma or EIB symptoms in athletes (Arm et al., 1989;Broughton et al., 1997;Mickleborough, Lindley, and Montgomery, 2008). Thus, it may be useful for athletes to increase the amounts of omega3-fatty acids (EPA and DHA, derived from fish oils) in their diet. According to the present results, it seems that there is increased awareness of the beneficial effects of unsaturated fatty acids among Finnish elite athletes.

On the contrary, a significant decrease was occured vitamin B consumption between study years and the intake was decreased in all subgroups of athletes. Limited research has been conducted whether physical exercise increases the need for vitamin B complexes

(Woolf and Manore, 2006). According to the statement of American Dietetic Association, the intake of vitamin and mineral preparations does not improve performance among individuals consuming nutritionally adequate diets. On the other hand, prolonged folate or vitamin B12 deficiencies may result in anemia and reduced endurance performance (American Dietetic Association et al., 2009).

6.2.2 The occurrence of asthma and asthma medication use

The occurrence of physician-diagnosed asthma in the current study was 14% in 2002 and 16% in 2009. These percentages are in accordance with previous studies (Locke and Marks, 2007;Lumme et al., 2003;Lund et al., 2009;Tanaka et al., 2010;Thomas et al., 2010;Weiler and Ryan, 2000). The frequency of wheezing did not change during the follow-up period.

According to the literature (Corrigan and Kazlauskas, 2003;Locke and Marks, 2007;Thomas et al., 2010;Weiler and Ryan, 2000) , the frequency of asthma medication use in athletes varies between 2 and 10%. In the current survey, the prevalence of asthma medication use was 10% in 2002 and 14% in 2009; these prevalences are rather high compared with other studies. However, in the current study, the athletes were considered to be asthma medication users if they had used asthma medication during the previous 12 months.

None of the athletes in 2002 but six in 2009 were using asthma medication without physician diagnosed asthma (ICS or β2-agonists). This may partly be explained by the changes in the regulations concerning asthma medication made by WADA between the study years (Table 3). Thus, our findings may be evidence of inappropriate use of asthma medication by elite athletes. In all patients, athletes or not, long-term asthma medication should be employed only if there is a rationale for use based on objective lung function measurements.

Similar to other studies (Corrigan and Kazlauskas, 2003;Locke and Marks, 2007;Tsitsimpikou et al., 2009b;Weiler and Ryan, 2000), the prevalence of inhaled β2-agonist use was higher than ICS use in both study years. However, a significant increase was seen in the use of ICS and there was a trend towards increased regular use of these agents. Furthermore, the use of fixed combinations of ICS and LABA increased by three-fold. According to IOC recommendations (Fitch et al., 2008) , the first-line pharmacotherapy for asthma in athletes should be ICS and inhaled β2-agonists should be used only infrequently to avoid the tolerance and other harmful effects associated with these sympathomimetics. In addition, concern has been raised of the safety of LABA (Chowdhury, Seymour, and Levenson, 2011). It does seem that WADA´s decision to remove the requirement for documentation of asthma via pulmonary functions tests before permitting the use of asthma medication seems to have resulted in increased use of inhaled β2-agonists and fixed combinations of LABA and ICS.

6.2.3 The occurrence of allergy and use of anti-allergic medication

In their recent study, Thomas et al. (2010) reported the occurrence of self-reported hay fever as being 25.4% in 291 elite German summer athletes. Helenius et al (1998) reported that clinically evident pollen allergy (positive skin test reaction to pollen and symptoms of rhinoconjunctivitis) affected 29.6% of athletes competing in summer events. A survey conducted in 241 Australian Olympic athletes reported that 56% of the athletes had a symptom history consistent with allergic rhinoconjunctivitis and 29% had actually seasonal allergic rhinoconjunctivitis (a positive history and at least one positive skin prick test to a seasonal allergen (Katelaris, Carrozzi, and Burke, 2003). In the present study, the prevalence of physician-diagnosed allergic rhinoconjunctivitis was 27% in 2002 and 24% in 2009 with the corresponding values for prevalence physician-diagnosed disturbing allergy being 32 and 29%.

The most often used allergy medications in both study years were oral antihistamines and intranasal corticosteroids. A significant increase was seen in anti-allergic medication use without physician-diagnosed allergy. The occurrence of allergic symptoms is common and most of the anti-allergic drugs can be purchased without a prescription. However, it should be noted that other conditions can cause similar symptoms to allergic rhinitis; these include non-allergic rhinitis with eosinophilia syndrome, aspirin sensitivity, idiopathic rhinitis, side effects of systemic drugs, abuse of topical decongestants, hormonal and mechanical factors, for example deviated septum, foreign body, ciliary defects and cerebrospinal rhinorrhoea (Bachert et al., 2002). Furthermore, before treating allergic rhinitis, the presence of benign and malignant tumors as well as diseases such as nasal polyposis should be excluded. Therefore, it is concerning to find that an increasing number of elite athletes in Finland are using anti-allergic medication without any accurate diagnosis.

The use of PSE increased significantly between 2002 and 2009. There were changes in the doping regulations concerning the use of PSE between the study years (Table 3). Thus our finding may be a sign of inappropriate use of this possibly performance-enhancing substance by elite Finnish athletes.

6.2.4 The use of medication by Paralympic and Olympic athletes

Medication use among the Paralympic athletes was more common than the Olympic athletes both during the previous seven days (49% vs. 33%) and in the past 12 months (85% vs. 74%). A significant difference was seen in the seven day use of medications which can be attributed to more common occurrence of chronic illnesses such as epilepsy, different pain conditions and disturbances in the autonomic nervous system of the Paralympians. Tsisimpikou et al. (2009) reported Paralympic athletes´ medication or food supplement intake as being 64% at the Athens Paralympic games.

Oral antibiotic use was more common among the Paralympic than the Olympic athletes during the previous seven days (10% vs. 4%) but equal if assessed over the previous 12 months (29% vs. 28%). Of the antibiotics used by the Paralympic athletes, two thirds were being used to prevent urinary tract infections. The more common use of oral antibiotics during the previous seven days by the Paralympic athletes in the current study can be partly explained by their risk of suffering neurogenic bladder. During the Athens Paralympic Games, only 1.6% of the athletes were taking antibiotics to treat urinary tract infections (Tsitsimpikou et al., 2009a).

Autonomic dysreflexia (AD) is a condition usually seen in individuals with SCI at or above T6 level and it results in an uncontrolled sympathetic response that is precipitated by some noxious stimulus below the SCI level (Bycroft et al., 2005). The common symptoms of AD include headache, hypertension, flushing, diaphoresis and bradycardia and it occurs up in to 90% of individuals with a cervical or high-thoracic SCI (Klenck and Gebke, 2007;Krassioukov, 2012). The initial treatment of AD is non-pharmacological but when this is not sufficient, it can be treated with pharmacological agents such as anti-hypertensive medicines. In the current study, a total of 10% of the Paralympic athletes were regular users of anti-hypertensive medicines. Only one Olympic athlete had anti-hypertensive medication in regular use. There does not seem to be any published data of the use of anti-hypertensive medication by elite athletes.

In the current study, physician-prescribed NSAIDs had been taken by 16% and 7% of the Paralympic and Olympic athletes during the previous seven days and by 35% and 49% during the previous 12 months. The use of NSAIDs by the Paralympic athletes during the previous seven days was relatively high in the current study since Tsitismpikou et al. (2009) reported the prevalence of NSAID use among athletes as being 10% during the Athens Paralympics and 11% in the corresponding Olympic Games. The frequent use of NSAIDs among the Paralympic athletes may partly be due to the fact that these individuals may experience neuropathic pain which is common among the patients with SCI (Finnerup and Baastrup, 2012). The drugs of choice for treating neuropathic pain are NSAIDs and paracetamol. In the current study, the Paralympic athletes were consuming more analgesics (including paracetamol) than the Olympic athletes both during the previous 7 days and 12 months. On the other hand, Olympic athletes consumed significantly more NSAIDs than their Paralympic counterparts during the previous 12 months. One explanation for this may be a higher training volume of the Olympic athletes (7.1 vs. 15 h/wk). The current study, did not inquire whether athletes were under a competitive or training regime when answering the questionnaire, which may also have influenced their reporting on medication use. Medication use by Paralympians has been reported to be higher in the competitive period than during the training season (Tsitsimpikou et al., 2009a).

Athletes use NSAID to suppress inflammation and pain after soft tissue injuries (Weiler, 1992). However, the inflammatory process caused by the injury is known to be necessary to allow adequate tissue repair and thus the long term use of NSAID may have a deleterious effect on the regeneration process (Rankin, 2004). In addition, one major problem when using NSAIDs is the possibility to adverse effects, such as renal and cardiovascular side effects as well as their effects on the liver and the GI system (Ziltener, Leal, and Fournier, 2010). These may be a risk especially for the Paralympic athletes who have a higher intake of other medicines due their illnesses. The long-term use of NSAID may also inhibit the normal hypertrophic response in the skeletal muscle to resistance training by attenuating the normal prostaglandin response ($(PG)F_{2\alpha}$) that stimulates skeletal muscle protein synthesis (Trappe et al., 2001;Trappe et al., 2002).

Heterotrophic ossification (HO), the presence of bone in soft tissues where bone normally does not exist, is one of the most common orthopedic complications encountered after SCI (Banovac et al., 2004). This occurs mostly after two months of SCI below the level of paralysis and may lead to reduced joint mobility in its severe forms (Banovac et al., 2004). HO may also occur after trauma such as bone fracture, total hip arthroplasty or direct muscular trauma (Shehab, Elgazzar, and Collier, 2002). In addition to radiation therapy, both the non-selective and COX-2 selective NSAIDs have been shown to be effective in the prophylaxis and treatment of HO (Banovac et al., 2001;Banovac et al., 2004;Kjaersgaard-Andersen and Ritter, 1992;Thomas and Amstutz, 1985). Thus the use of NSAIDs among the Paralympic athletes may be beneficial in some conditions, especially after sport injuries (Kjaersgaard-Andersen and Ritter, 1992;Thomas and Amstutz, 1985).

There was a striking difference in the use of asthma medication between Paralympic and Olympic athletes (4% vs. 11% during the previous 7 days and 7% vs. 14% during the previous 12 months). The use of anti-asthmatic medication among Olympic athletes is known to be common and there may be overuse of asthma medications in sportsmen/women (Alaranta et al., 2004;Corrigan and Kazlauskas, 2003;Locke and Marks, 2007;Lund et al., 2009;Thomas et al., 2010;Weiler and Ryan, 2000). As Paralympic athletes have increased stress on their cardiopulmonary organs, they would be predicted also to be more susceptible to suffer symptoms of asthma than the general population. This finding may suggest that one factor to explain their relatively low use may be the athletes' own critical evaluation of the need for anti-asthmatic medication. On the other hand, Paralympic athletes suffer from other diseases requiring medication use so that they may not consider treatment of asthma as a primary concern.

7. CONCLUSIONS

The use of dietary supplements is decreasing and the use of asthma medication is increasing among Finnish Olympic athletes.

1. A significant decrease was observed in overall supplement use and vitamin use. The decrease in DS use may be partly explained with athletes´ increased awareness of purity issues and risks of contamination of DSs. The intake of some essential micronutrients, such as vitamin D, is suprisingly low, even raising the possibility of serious harm in those well-trained athletes. In addition, lack of vitamin D intake and synthesis may potentially have an impact on performance abilities in otherwise healthy athletes. On the other hand, the consumption of some micronutrients, such as multivitamins and vitamin C, is high and the recommendations for daily intake may be exceeded.

   a. The nutritional counseling for Finnish Olympic athletes is inadequate

2. The use of asthma medication, especially fixed combinations of LABA and ICS, is clearly increasing among Finnish Olympic athletes. No significant change was seen in the use of anti-allergic medication between the study years.

   a. The trend in asthma medication use is not based on an increased occurrence of asthma symptoms, asthma diagnoses or objective lung function measurements. Attention needs to be paid to asthma diagnosis and its treatment in elite athletes. More data, also from other countries, will be needed before there can be a change to the recommendations or WADA rules.

3. The use of any physician-prescribed medicines, especially those treat chronic diseases, seems to be more common among the Paralympic than the Olympic athletes.

   a. The use of asthma and allergy medication seems to be less common in Paralympians than in Olympic athletes, suggesting that there should be a more critical evaluation on the need of anti-asthmatic medication in Paralympic athletes. In addition, despite the fact that Paralympic athletes are predisposed to urinary tract infections due the SCI, no differences were observed in the prevalence of use of oral antibiotics during the previous 12 months between the study groups.

   b. The use of NSAIDs during the past 12 months seems to be less common among Paralympic than Olympic athletes.

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