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## Original article

## Relation between plasma antioxidant vitamin levels, adiposity and cardio-metabolic profile in adolescents: Effects of a multidisciplinary obesity programme

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## SUMMARY

**Background & aims:** In vivo and in vitro evidence suggests that antioxidant vitamins and carotenoids may be key factors in the treatment and prevention of obesity and obesity-associated disorders. Hence, the objective of the present study was to determine the relationship between plasma lipid-soluble antioxidant vitamin and carotenoid levels and adiposity and cardio-metabolic risk markers in overweight and obese adolescents participating in a multidisciplinary weight loss programme.

**Methods:** A therapeutic programme was conducted with 103 adolescents aged 12–17 years old and diagnosed with overweight or obesity. Plasma concentrations of  $\alpha$ -tocopherol, retinol,  $\beta$ -carotene and lycopene, anthropometric indicators of general and central adiposity, blood pressure and biochemical parameters were analysed at baseline and at 2 and 6 months of treatment.

**Results:** Lipid-corrected retinol ( $P < 0.05$ ),  $\beta$ -carotene ( $P = 0.001$ ) and  $\alpha$ -tocopherol ( $P < 0.001$ ) plasma levels increased significantly, whereas lipid-corrected lycopene levels remained unaltered during the treatment. Anthropometric indicators of adiposity ( $P < 0.001$ ), blood pressure ( $P < 0.01$ ) and biochemical parameters ( $P < 0.05$ ) decreased significantly, whereas fat free mass increased significantly ( $P < 0.001$ ). These clinical and biochemical improvements were related to changes in plasma lipid-corrected antioxidant vitamin and carotenoid levels. The adolescents who experienced the greatest weight loss also showed the largest decrease in anthropometric indicators of adiposity and biochemical parameters and the highest increase in fat free mass. Weight loss in these adolescents was related to an increase in plasma levels of lipid-corrected  $\alpha$ -tocopherol ( $P = 0.001$ ),  $\beta$ -carotene ( $P = 0.034$ ) and lycopene ( $P = 0.019$ ).

**Abbreviations:** ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; BMI, body mass index; CRP, C-reactive protein; CVD, cardiovascular diseases; DBP, diastolic blood pressure; FFM, fat free mass; FMI, fat mass index; HDL, high density lipoprotein; LC, lipid-corrected; LDL, low density lipoprotein; SDS-BMI, BMI standard deviation score; SBP, systolic blood pressure; TAG, triacylglycerols; UHPLC, Ultra High Performance Liquid Chromatography.

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**Conclusions:** Plasma lipid-soluble antioxidant vitamin and carotenoid levels are associated with reduced adiposity, greater weight loss and an improved cardio-metabolic profile in overweight and obese adolescents.

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## 1. Introduction

The prevalence of obesity has increased in recent decades and this disorder is now considered a 21st century epidemic. It is the most common nutritional issue among children and adolescents in developed countries, but has also reached alarming values in developing countries [1].

Obesity is an important risk factor of cardiovascular diseases (CVD) and is strongly related to other cardiovascular risk factors such as hypertension, diabetes, dyslipidemia and inflammation [2], therefore onset of obesity is of particular concern in children and adolescents [3,4]. It has been found that similar to obese adults, obese children present a higher degree of oxidative stress than their normal weight counterparts [5]. Moreover, obesity is linked to decreased plasma antioxidant vitamin levels and antioxidant capacity [6]. Thus, the scientific evidence suggests that antioxidant vitamins and carotenoids may be key factors in the treatment and prevention of obesity and obesity-associated disorders.

Recent studies have indicated that vitamin A [7] and  $\beta$ -carotene [8] are important regulators of body fat reserves. As an example, retinoic acid derived from vitamin A and  $\beta$ -carotene is involved in the expression of lipogenic transcription factors [7,8]. Furthermore, it has been observed that vitamin A and carotenoids present anti-inflammatory properties [9–11] and have an antioxidant action [10–12]. Within the carotenoids, lycopene has the highest antioxidant capacity compared to  $\alpha$ -tocopherol and  $\beta$ -carotene [13]. Numerous epidemiological studies have shown a significant inverse association between plasma or tissue lycopene levels and the incidence of CVD or CVD risk factors (atherosclerosis, hypertension, diabetes, metabolic syndrome, inflammation and oxidative stress) [12]. Also, it has been suggested that lycopene can prevent inflammation [11] by decreasing transcription factor activation and secretion of inflammatory markers in adipose tissue [9].

Vitamin E is another lipid-soluble vitamin that presents a high antioxidant capacity [13,14]. Recently, it was found that vitamin E is involved in the expression of genes associated with glucose and lipid metabolism [15,16]. In addition, some authors have observed a lower incidence of chronic disease and cardiovascular events when dietary intake of vitamin E is increased [14].

The study of changes in anthropometric and metabolic parameters and plasma antioxidant levels in obese children is useful in order to determine their associations and establish dietary regimes aimed at reducing the prevalence of paediatric obesity and associated pathologies. Nonetheless, to our knowledge, few studies have focussed in this issue. Hence, the objective of the present study was to determine the relationship between plasma levels of  $\alpha$ -tocopherol, retinol,  $\beta$ -carotene and lycopene and adiposity and cardio-metabolic risk markers in overweight and obese adolescents participating in a multidisciplinary weight loss programme.

## 2. Materials and methods

### 2.1. Ethics statement

This study was conducted in accordance with the ethical rules of the Helsinki Declaration (Hong Kong revision, September 1989,

Edinburgh revision 2000 and Korea revision 2008), the European Economic Community (EEC) Good Clinical Practice guidelines (document 111/3976/88 of July 1990) and current Spanish law, which regulates clinical research on humans (Royal Decree 561/1993 regarding clinical trials). Written informed consent was obtained from all adolescents and their parents, and the study was approved by the local ethics committees. Data obtained during the intervention was confidential and restricted to the participating investigators.

### 2.2. Participants and study design

The study sample used in the present analysis comprised 103 adolescents aged 12–17 years old and diagnosed with overweight and obesity at four hospitals located in different Spanish cities (Granada, Madrid, Pamplona and Zaragoza). The inclusion criteria were as follows: to be overweight or obese as defined by International Obesity Task Force age- and sex-specific body mass index (BMI) values [17], to be Spanish or to have been educated in Spain, and to be free of any other diagnosed disease. Adolescents receiving pharmacological treatment or diagnosed with anorexia, bulimia or any other eating disorder except binge eating disorder, were excluded. All selected adolescents were treated as part of the EVASYON Study (Development, implementation and evaluation of the efficacy of a therapeutic programme for adolescents with overweight and obesity: comprehensive education on nutrition and physical activity) [18].

The EVASYON project was an intervention study in a cohort of overweight and obese adolescents. It comprised a long-term (approximately 13 months) multidisciplinary treatment programme based on a calorie-restricted diet (10–40%), increased physical activity (at least 60 min/day, 5 days a week), psychological therapy and nutritional education. The maximum energy intake was 1800 kcal/day for females and 2200 kcal/day for males. Macronutrient distribution was 50% of energy from carbohydrates, 30% from fat and 20% from proteins. The adolescents were treated in groups of a maximum of 10 subjects and each group had 20 visits during the intervention. The treatment comprehended two stages, an intensive intervention phase (1st to 9th visits) with weekly checks during the first 2 months, and an extensive intervention phase (10th to 20th visits) where adolescents were monitored monthly until the end of programme. The complete and detailed methodology of the EVASYON Study has been described elsewhere [18].

### 2.3. Dietary intake and physical condition

Dietary intake was assessed by applying 72-h dietary record and a semi-quantitative food-frequency questionnaire, previously validated. Data of food intake by 72-h dietary record were transformed into food volume/weight (in mL or g). The nutrient consumption was determined using the latest available information in food-composition tables from Spain. Vitamins and carotenoids were estimated from the intake of respective food sources.

To evaluate the physical activity, several tests and questionnaire were used, such as Physical Activity Questionnaire for Adolescents

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