Clinical science

Dietary omega-3 polyunsaturated fatty acids as a protective factor of myopia: the Hong Kong Children Eye Study

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ABSTRACT

Purpose To evaluate the associations between omega-3 polyunsaturated fatty acids (ω-3 PUFAs) and other dietary factors with myopia.

Methods A total of 1005 Chinese children, aged from 6 to 8 years, from a population-based Hong Kong Children Eye Study, were included in the analysis. Diet was assessed using a validated food-frequency questionnaire. Cycloplegic spherical equivalent (SE) refraction was assessed with an autorefractometer, and axial length (AL) by an IOL Master.

Results AL was longest in the lowest quartile group of ω-3 PUFAs intake, compared with the highest (adjusted mean (95% CI), 23.29 (23.17 to 23.40) mm vs 23.08 (22.96 to 23.19) mm, p=0.01; p-trend=0.02) after adjusting for age, sex, body mass index, near-work time, outdoor time, and parental myopia history. The corresponding trends were observed in SE (−0.13 (−0.32 to 0.07) D in the lowest and 0.23 (0.03 to 0.42) D in the highest quartile groups, p=0.01; p-trend=0.01). In contrast, AL was longest in the highest quartile group of saturated fatty acids (SFA) intake, compared with the lowest (23.30 (23.17 to 23.42) mm vs 23.13 (23.01 to 23.24) mm, p=0.05; p-trend=0.04). The corresponding trends were observed in SE (−0.12 (−0.33 to 0.09) D in the highest and 0.13 (-0.04 to 0.31) D in the lowest quartile group, p=0.06; p-trend=0.04). A lower intake of ω-3 PUFAs was associated with myopia (p-trend=0.006). None of the other nutrients were associated with SE or AL or myopia.

Conclusions Intake of ω-3 PUFAs is a protective factor against myopia, while higher SFA intake is a risk factor. Our findings indicated a possible effect of diet on myopia, of which ω-3 PUFAs intake may play a protective role against myopia development in children.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Myopia prevalence is rising globally, necessitating identification of modifiable risk factors, such as diet, to inform prevention strategies.

⇒ Previous animal studies suggest omega-3 polyunsaturated fatty acids (ω-3 PUFAs) may suppress myopia progression by modulating choroidal blood flow and scleral hypoxia.

WHAT THIS STUDY ADDS

⇒ This study provides the human evidence that higher dietary ω-3 PUFA intake is associated with shorter axial length and less myopic refraction, highlighting ω-3 PUFAs as a potential protective dietary factor against myopia development.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Public health policies and clinical guidelines could integrate nutritional advice into myopia management.

INTRODUCTION

Myopia is a global threat to public health, with increasing prevalence across many regions in the past decades, especially in East Asia.[1 2] It is predicted that around half and one-tenth of the world's population will have become myopic and highly myopic by 2050.[1] Myopic individuals have excessive globe elongation and higher risks of sight-threatening complications that can lead to poor vision and even blindness.[3] Increased online-viewing time, as well as behavioural changes resulting from prolonged COVID-19 home confinement, may have longlasting impacts on myopia progression in children.[4 5]

The risk factors for developing myopia are multifactorial, involving both genetic and environmental factors. Diet is an important environmental factor that has been studied in many ocular diseases because of its potentially modifiable nature.[6] Nutritional intervention has been evoked as a critical tool for protecting the eyes and vision. However, the relationship between dietary factors and myopia development remains uncertain. The omega-3 polyunsaturated fatty acids (ω-3 PUFAs) are termed 'essential' as they cannot be synthesised in the body and, thus, must be obtained from the diet. ω-3 PUFAs mediate a wide variety of functions in the body. Diets rich in long-chain ω-3 fatty acids have been suggested to provide long-term benefits for several chronic ocular conditions, including dry eye disease and age-related macular degeneration.[7]

The therapeutic effect of dietary supplements containing ω-3 PUFAs on myopia progression has been reported in animal models, and also regarding the decreases in choroidal blood perfusion (ChBP) caused by near work.[8] A daily intake of ω-3 PUFAs significantly reduced the development of form-deprivation myopia in guinea pigs and mice, and lens-induced myopia in guinea pigs.[8] Another study also reported that ω-3 PUFAs could suppress experimental myopia progression in mice.[9] However, up to now, the effect of dietary ω-3 PUFAs on myopia has not been reported in humans. Nutrition early in life is important for the health and development of a child, who, during this period, is more susceptible to myopia and myopia progression. The aim of this study is to examine the relationship between myopia and dietary ω-3 PUFAs and other nutrients intakes in Hong Kong children.

METHODS

Study design and population

Participants in this study were randomly recruited from the Hong Kong Children Eye Study (HKCES), which is an ongoing population-based study of eye conditions among school children across Hong Kong.[2 5] HKCES was designed to document the occurrence and development of eye disorders and the associated factors in children. Sample selection was based on a stratified and clustered randomised sampling frame. The details of the protocol and sample size considerations have been described in our previous studies.[2] The current study excluded children with any systemic diseases (except obesity) and ocular diseases (except refractive errors). The study adhered to the Declaration of Helsinki, and ethical approval was obtained from the institutional review board of the Chinese University of Hong Kong. All children and their parents/guardians signed an informed consent form.

Ocular examinations

Distance best-corrected visual acuity was measured using a logarithm of the minimum angle of resolution chart (Nidek, Gamagori, Japan). Axial length (AL) was measured through non-contact partial-coherence laser interferometry (IOL Master; Carl Zeiss Meditec, Oberkochen, Germany). Refractive status was measured both before and after cycloplegia using an autorefractor (Nidek ARK-510A, Gamagori, Japan) for each child. Three cycles of 1% cyclopentolate (Cyclogyl, Alcon-Convreur, Rijksweg, Belgium) and 1% tropicamide (Santen, Osaka, Japan) were administered to ensure no pupillary light reflex or that the pupil size >6.0 mm. An ophthalmologist made detailed examinations of the anterior segment using a slit-lamp (Haag-Streit, Koeniz, Switzerland) and the retina using a 20 D lens (Volk, Houston, Texas, USA). Cycloplegic spherical equivalent refraction (SE) was calculated as the sum of spherical power plus one-half of cylindrical power using cycloplegic refraction. Myopia was defined as SE of −0.50 D or less.

Dietary assessment

Dietary assessment was conducted using a modified food frequency questionnaire (FFQ) with 280 food items, which has been validated in Chinese adults and developed for use in the Hong Kong population.[10] The 280 items were categorised into 10 groups: bread/cereals/pasta/rice/noodles, vegetables and legumes, fruits, meat, fish, eggs, milk and dairy products, beverages, dim sum/snacks/fats/oils and soups. Children and their families filled out the questionnaire with the face-to-face assistance of trained interviewers. They were asked to report the intake and consumption from the food list as frequency per day, per week, or per month during the past 12 months, as an indicator of long-term habitual diet.[11] To aid the recall, life-size food models, food pictures, and household utensils were used, and the corresponding common portions were adopted as measures of usual serving size in the FFQ to facilitate weight estimation.[12] For seasonally consumed vegetables and fruits, participants were asked about the months of food consumption by the child over the past year. The amount of cooking oil was estimated according to the usual cooking methods of preparing standardised portion of different foods and the usual portion of different foods consumed by the child/family. Energy intake, carbohydrate, proteins, total fat, saturated fatty acids (SFAs), monounsaturated fatty acids, polyunsaturated fatty acids (PUFAs), cholesterol, iron, calcium, vitamins A and C, fibre, starch, and sugar were calculated. Nutritional intakes were computed by a software Food Processor and its ESHA Nutrient Databases, accounting for the weight and frequency of food consumption, and the nutrient composition.

Questionnaires on children's outdoor time and near-work time

The validated questionnaires on lifestyles used in the current study were derived from the Chinese translated versions that had been used in the Sydney Myopia Study[13] and later adopted in the HKCES.[2] Time outdoors was calculated for two categories: leisure (eg, walking, leisure bike riding, playing in the park, and picnicking) and sports activities. Reading and writing time were defined as time for any near visual activities, excluding the time engaged with electronic devices. Screen time was defined as time spent on using a computer and any handheld electronic devices. Total near work was defined as the sum of total reading, writing and screen time, excluding watching television and videos. All the variables were collected separately for weekdays and weekends. Parental myopia was defined as one or both parents having myopia.

Physical examinations

Height and weight were measured using a professional integrated set (Seca, Hamburg, Germany). Body mass index (BMI) was then calculated.

Statistical analysis

The demographic characteristics of participants were summarised using descriptive statistics. Continuous variables were reported as means and standard deviations (SDs), while categorical variables were reported as values and percentages. Group differences in data were tested using Student's t-test for the continuous variables and Pearson's X^2 test for the categorical variables. Multivariable linear regression models were constructed with SE or AL as the dependent variable to assess the association of myopia with each nutrient, with initial adjustments for age and sex (model 1). Multiple logistic regression models were constructed to determine also the association of myopia with each nutrient, with adjustments for age and sex (model 1). Model 2 adjusted for age, sex, BMI, near-work time, outdoor time and parental myopia history. All statistical analyses were performed using SPSS (version 24.0, IBM Corp., Armonk, New York, USA). P values <0.05 were considered statistically significant.

Table 1 Participant demographic characteristics

	Current study (n=1005)	HKCES (n=20 527)	
Characteristics	Mean (SD)	Mean (SD)	P value
Sex, male (%)	524 (52.1%)	10 828 (52.8%)	0.70
Children's age, years	7.64 (0.93)	7.33 (0.89)	<0.001
Children's spherical equivalent, diopter	0.00 (1.61)	0.22 (1.48)	<0.001
Children's axial length, mm	23.22 (1.01)	23.04 (0.91)	<0.001
Children myopia rate (%)	276 (27.5%)	5275 (25.7%)	0.21

Results are mean (SD) unless stated otherwise.
HKCES, Hong Kong Children Eye Study.

RESULTS

Study participants

A total of 1005 Chinese children were included in the analysis, including 524 (52.1%) boys and 481 (47.9%) girls, with mean (SD) age 7.64 (0.93) years. The mean SE and AL were 0.00 (1.61) D and 23.22 (1.01) mm, respectively. Among them, 276 (27.5%) children had myopia. The demographic characteristics in the current cohort and HKCES are shown in table 1.

Association of SE and AL by quartile groups of nutrients intake

AL was longest in the lowest quartile group of ω-3 PUFAs intake, compared with the highest (adjusted mean (95% CI), 23.29 (23.17 to 23.40) mm vs 23.08 (22.96 to 23.19) mm, p=0.01; p-trend=0.02) after adjustment for age, sex, BMI, near-work time, outdoor time and parental myopia history. Correspondingly, SE was the most myopic in the lowest quartile group of ω-3 PUFAs intake, compared with the highest (−0.13 D (-0.32 to 0.07) D vs 0.23 (0.03 to 0.42) D, p=0.01; p-trend=0.01). In contrast, AL was longest in the highest quartile group of saturated fatty acids (SFA) intake, compared with the lowest (23.30 (23.17 to 23.42) mm vs 23.13 (23.01 to 23.24) mm, p=0.05; p-trend=0.04) with the adjustment of these confounders (table 2). None of the other nutrients was associated with SE or AL (online supplemental table 1).

Association of myopia by quartile groups of nutrients intake

A lower intake of ω-3 PUFAs was associated with myopia (overall p-trend=0.006) after adjustment of these confounders (table 3). None of the other nutrients were found to be associated with myopia (online supplemental table 2).

DISCUSSION

In the current study, we found that a lower intake of ω-3 PUFAs was associated with more myopic SE and longer AL at ages 6 to 8 years among Hong Kong children. Numerous studies have shown that ω-3 PUFAs play an important role in many aspects of health.[7] It has been reported that ω-3 PUFAs intake had long-term positive effects on the visual function in school-age children.[14] However, very few investigations reported about ω-3 PUFAs and myopia in children.

Recent animal model studies have yielded strong supporting data for the potential therapeutic benefits of ω-3 PUFAs on myopia.[8] Pan and his colleagues found that daily gavage of ω-3 PUFAs (300 mg docosahexaenoic acid (DHA) plus 60 mg eicosatetraenoic acid) significantly attenuated the formation and development of myopia in guinea pigs and mice. The mechanism of ω-3 PUFAs suppression of myopia may be related to its effect on inhibiting myopic ChBP and attenuated scleral hypoxia.[8] Previous studies have highlighted the significance of the cascade of events wherein the reduction of ChBP induces scleral hypoxia and myopia.[15 16] The scleral hypoxia affected extracellular matrix remodelling, thereby biomechanically weakening and

Table 2 Mean axial length and refractive errors among children in quartiles of nutrients intake

		Spherical equivalent, D		Axial Length, mm	
Omega−3 fatty acids (g/kcal/day)	No.	Model 1*	Model 2†	Model 1	Model 2
First quartile	250	−0.14 (−0.33 to 0.05)	−0.13 (−0.32 to 0.07)	23.28 (23.17 to 23.40)	23.29 (23.17 to 23.40)
Second quartile	251	−0.06 (−0.25 to 0.13)	0.08 (−0.11 to 0.28)	23.23 (23.12 to 23.34)	23.15 (23.04 to 23.27)
Third quartile	252	−0.01 (−0.20 to 0.19)	0.13 (−0.08 to 0.34)	23.23 (23.11 to 23.34)	23.16 (23.04 to 23.28)
Fourth quartile	252	0.15 (−0.04 to 0.35)	0.23 (0.03 to 0.42)	23.12 (23.00 to 23.23)	23.08 (22.96 to 23.19)
P-trend		0.03	0.01	0.04	0.02
P value (fourth vs first)		0.03	0.01	0.04	0.01
SFA (g/kcal/day)	No.				
First quartile	251	0.13 (−0.04 to 0.31)	0.19 (0.02 to 0.36)	23.16 (23.05 to 23.28)	23.13 (23.01 to 23.24)
Second quartile	252	0.06 (−0.13 to 0.25)	0.19 (0.01 to 0.38)	23.17 (23.06 to 23.28)	23.11 (23.00 to 23.23)
Third quartile	249	−0.04 (−0.23 to 0.14)	0.04 (-0.15 to 0.24)	23.20 (23.10 to 23.30)	23.15 (23.04 to 23.25)
Fourth quartile	253	−0.12 (-0.33 to 0.09)	−0.05 (−0.27 to 0.17)	23.32 (23.20 to 23.44)	23.30 (23.17 to 23.42)
P-trend		0.04	0.04	0.04	0.04
P value (fourth vs first)		0.06	0.09	0.06	0.05

*Adjusted for age and sex.
†Adjusted for age, sex, body mass index, near-work, outdoor hours and parental myopia history.
SFA, saturated fatty acids.

Table 3 Myopia among children in quartiles of nutrients intake.

Omega−3 fatty acids (g/kcal/day)	No.	Model 1*	P value	Model 2†	P value
First quartile	250	1.00 (Reference)		1.00 (Reference)	
Second quartile	251	0.95 (0.64, 1.40)	0.78	0.75 (0.49, 1.15)	0.19
Third quartile	252	0.85 (0.56, 1.29)	0.45	0.67 (0.42, 1.05)	0.08
Fourth quartile	252	0.60 (0.39, 0.92)	0.02	0.53 (0.33, 0.84)	0.007
P-trend		0.02		0.006	

*Adjusted for age and sex.
†Adjusted for age, sex, body mass index, near-work, outdoor hours and parental myopia history.

thinning the sclera that led to AL elongation.[17] An untargeted mass spectrometric assay also reported that the levels of serum DHA were significantly lower in the myopic group.[18]

Our study has echoed these laboratory studies and suggested that ω-3 PUFAs can play a protective role in myopia. Our research indicates that ω-3 PUFAs may serve as potential and accessible options for myopia control. Our findings are also supported by a recent Mendelian randomisation analysis that revealed a protective effect of ω-3 and DHA on myopia.[19]

We also found that higher saturated fat was associated with longer AL; although the association is statistically noteworthy, its borderline nature underscores the importance of future studies to validate the finding. The total daily intakes of all the other nutrients and micronutrition analysed were not found to be related to more myopic SE or AL, or to the presence of myopia. The possibility that nutritional variations, protein, fat and cholesterol intakes, may be related to myopia was first proposed by Gardiner in 1956.[20] He revealed that active myopes consumed less protein and more fat and carbohydrate. After that, Cordain and his team were the first to suggest that the intake of refined carbohydrates, through hyperinsulinism, might play a role in the onset of juvenile myopia.[21] He speculated that hyperinsulinaemia might modify scleral growth factors, which he postulated as a possible underlying mechanism.[21] This hypothesis has been supported by subsequent evidence.[22] Studies using animal models of myopia have provided evidence linking insulin with enhanced eye growth.[23] However, our findings showed no association of myopia or AL elongation with the intake of carbohydrate. Further studies are warranted to validate this finding.

Our finding of the association between longer AL and high intake of SFAs was consistent with a previous study in Singapore.[24] Saturated fat is a known antagonist of insulin and a contributor to insulin resistance,[25] so our findings lend some support to the hyperinsulinaemic theory.[21] Previous links between protein intake and myopia were inconsistent and weak. A study in the UK showed that myopic children, when treated with a high animal protein diet, displayed slower progression of myopia than the controls.[26] A study carried out on young adults in India, found a higher prevalence of myopia among vegetarians than non-vegetarians, indicating a potential relationship between myopia and protein.[27] Our findings showed a lack of associations between protein and myopia.

We found no associations of vitamin D intake with myopia. A previous study showed that time spent outdoors is protective against the onset of myopia.[28] There has been interest in whether vitamin D could also protect the sort of myopia which is due to a high relationship between serum vitamin D levels and time spent outdoors. A large cohort study in Korean adolescents found that low serum vitamin D levels were a risk factor for myopia development.[29] However, another study demonstrated that vitamin D serum levels were highly related to time spent outdoors, and that they were not associated with myopia, having been adjusted for the confounding effect of time outdoors.[30] This result is consistent with the observations from a previous genome-wide association study.[31] Our current study, as in a number of other studies, failed to establish a link between a low level of vitamin D and myopia.[32]

A small number of Asian studies have reported lower levels of micronutrients, such as zinc and copper, in myopic children/adolescents, in comparison with controls.[33] In the current study, we did not find any micronutrition to be associated with myopia. Our findings align with previous studies reporting no association between myopia and dietary zinc levels in US children and adolescents[34] and Korean adolescents.[35] However, these results contrast with a study in Poland, which identified significantly lower serum zinc concentrations in myopic patients compared with controls.[33] Micronutrient status is influenced by several factors. Differences in trace element concentration could result from soil, geographical location, food preparation, ethnic differences and genetics. Thus, further studies on the effect of micronutrition on myopia are warranted.

Limitations

The current study administered an age-appropriate, validated Asian FFQ to assess the habitual intake of a comprehensive range of nutrients and food groups in Asian children and assessed myopia with cycloplegia. However, the study had several limitations. First, the cross-sectional study design limits the exploration of the causal and temporal relationships between dietary intakes and myopia. A future longitudinal study providing stronger evidence regarding the relationship between ω-3 PUFAs intake and myopia progression is warranted. Second, the FFQ questionnaire offered only a snapshot of children's food intake through their daily interactions with family members, which may not represent the typical nutrition intakes. In addition, we recognised that dietary shifts could not be determined using a single assessment of habitual intake in the past months. Third, objective and robust evidence of nutrition intakes, such as serum biomarkers, was not collected. Similar to any other dietary assessment methods, the FFQ is more susceptible to recall bias and subject to measurement errors from the lack of capture of certain food items, the inaccurate estimation of portion sizes and the comprehensiveness of the nutrient databases used. Fourth, the unmeasured confounding factors, such as environmental and genetic factors, might have the potential to impact the observed associations. Fifth, our study specifically examines the association between dietary ω-3 PUFAs and myopia, without exploring the impact of ω-3 supplements or additional intake in children. Sixth, the differences observed in AL and SE, although statistically significant, are relatively small. Nevertheless, given the safety profile of ω-3 PUFAs and their potential benefits beyond eye health, including their potential to support eye health by modulating ChBP, a diet rich in ω-3 PUFAs is also suggested, particularly during childhood—a critical period for myopia development. Further research in larger cohorts is needed to fully understand their clinical significance. Finally, this study was on Chinese children in Hong Kong, where the prevalence of myopia is among the highest in the world. Whether intake of ω-3 PUFAs as a protective factor applies to other ethnic groups with different lifestyles and less myopia remains to be verified.

CONCLUSION

Lower ω-3 PUFAs intake in diet was significantly associated with myopia and AL elongation, indicating that ω-3 PUFAs intake may play a protective role in myopia development in children. Higher SFAs intake was associated with higher axial length. Finally, our study has indicated a possible effect of diet on myopia.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee, CREC Ref. No.: 2015.033 Participants gave informed consent to participate in the study before taking part.

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