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Fish Consumption, Fish Atopy and Related Heavy Metals in Childhood Eczema

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ABSTRACT

Due to increasing worldwide water pollution, fish might be a source of excessive zinc, mercury, arsenic or manganese intake. The aim of this study was to evaluate if fish atopy/sensitization and fish consumption behavior are associated with eczema severity and blood levels of the 4 heavy metals.

One-hundred and nineteen patients with eczema and 43 patients with miscellaneous non-eczema skin diseases were studied. There were no differences in average weekly fish consumption and blood levels of the 4 heavy metals between eczema and non-eczema groups.

Blood levels of these metals were generally within the upper limits of local reference ranges in all these patients. In eczema patients, freshwater fish consumption behavior in days-per-week was correlated with blood arsenic and mercury levels (*rho*=0.17, $p<0.01$ for both metals), but not with zinc or manganese. Levels of arsenic and mercury were also correlated with days of seawater fish consumption per week (arsenic: 0.38, mercury: 0.24, $p<0.05$).

Fish sensitization was present in 25% of patients with eczema. Nevertheless, there was no difference in terms of fish consumption behavior, eczema severity, quality of life, and heavy metal levels between eczema patients with or without fish sensitization. We conclude that without exceeding local normal reference ranges, blood arsenic and mercury levels correlated with fish consumption behavior. There is no evidence to suggest that fish sensitization is associated with more severe eczema (bad for eczema), or that patients have milder eczema with more days of fish consumption (good for eczema).

Keywords: Arsenic; Eczema; Fish consumption; Manganese; Mercury; NESS; Quality of life; SCORAD; Severity; Zinc

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INTRODUCTION

Atopic eczema (AE) is a distressing disease associated with pruritus, sleep disturbance and impaired quality of life.[1] The incidence of AE has been increasing in developed countries.[2] Food atopy and environmental pollution with heavy metals have been implicated as possible associated factors. Seafood avoidance in AE, with the exception of fish, is widely practiced among the fish-loving Cantonese Chinese in Hong Kong.[3,4] Fish is believed to be good for children and is commonly consumed in the local diets. Fish might be a source of zinc, mercury, arsenic or manganese intake.[5,6] These metals have been found to be associated with eczema and some skin diseases.[7-10] Zinc is the most widely studied metal in childhood diseases and dermatological conditions, and low zinc level has been reported in children with AE.[11,12] Mercury, arsenic and manganese have been associated with contamination of seawater fish.[5,6] This study was aimed to evaluate if fish atopy/sensitization is associated with fish consumption behavior, eczema severity and blood levels of zinc, mercury, arsenic and manganese.

PATIENTS AND METHODS

We measured the serum levels of zinc, and whole blood levels of mercury, arsenic and manganese in consecutive new patients and selected existing patients who happened to require blood taking at the pediatric dermatology clinic of a university teaching hospital between July 2008 and December 2009. Eligibility criteria included patients > 1 month of age seen at the pediatric dermatology clinic with a skin disease (eczema or non-eczema skin condition) confirmed by the physician and that the patients or the parents were able to give a reliable history of fish consumption. AE is diagnosed according to Hanifin and Rajka's criteria.[13] Correlations between these levels, serum IgE levels as a marker of atopy, eosinophil counts, AE severity (by SCORAD and Nottingham Eczema Severity Score-NESS)[14-17] and quality of life (by Children Dermatology Life Quality Index-CDLQI)[17,18] were also evaluated. SCORAD is a widely used score in eczema research which evaluates eczema severity over a one-week period and NESS is a simple and easy-to-perform score which assesses the symptomatology of eczema over the preceding 12 months.[14-17] A validated Cantonese version of NESS is available.[15-17] NESS was performed on patients older than one year of age and CDLQI on children older than five years of age. These scores (SCORAD, NESS and CDLQI) have encompassed both the symptoms and signs of AE. Average freshwater and seawater fish consumption (in days-per-week over the past 4-8 weeks by recall) were recorded. Skin prick testing (SPT) is routinely offered to patients at the clinic, using diluent (negative control) and histamine solution (10 mg/ml; positive control) and standardized food and aeroallergen extracts, including dust mites, cockroach, cat and dog danders, beef, egg white, egg yolk, cow's milk, soybean, peanut, almond, crab, shrimp, lobster, mixed shellfish, tomato, orange and mixed fish (ALK Abelló, Round Rock, Texas). This panel of common food and aeroallergen extracts was determined and regularly reviewed by the medical and pediatric services to be relevant to the local setting. Reactions were considered positive if the wheal was at least 3 mm greater than that of diluent, and was further classified as 1+ (3-5 mm), 2+ (6-8 mm), 3+ or more (9 mm). Patients discontinued all pharmacotherapy (antihistamines and/or steroids) at least 3 days before SPT. Patients were excluded if they suffered a nonspecific dermatitis, epidermolysis bullosa, acrodermatits enteropathica or if the diagnosis was unclear. Levels of heavy metals were measured by inductively coupled plasma mass spectrometry (ICP-MS). The Clinical Research Ethics Committee of the Chinese University of Hong Kong approved this study. Pearson and Spearman coefficients were used to analyze the correlations between clinical indices and heavy metal levels. *P*-values less than 0.05 were considered to be statistically significant.

RESULTS

Between July 2008 and December 2009, 119 patients with eczema and 43 patients with miscellaneous skin conditions (warts, scabies, onychomycosis, skin hyperpigmentation, psoriasis, alopecia, vitiligo, naevi) were evaluated (Table 1). Blood levels of the four heavy metals were generally within the upper limits of local reference ranges in these patients. There was no difference in average weekly fish consumption and levels of the 4 heavy metals between eczema and non-eczema groups. Fish atopy, determined by skin prick positivity, was present in 25% of patients with eczema.

Table 1. Blood trace element levels in patients with and without eczema

Topics	Eczema (n=119)	Non-eczema (n=43)	p-value
Age, yr	9.9 (4.7)	11.6 (5.0)	0.07
Male, n (%)	63 (52.9)	28 (65.1)	0.06
CDLDI score	8.5 (5.7)	4.1 (4.7)	0.0001
Log (IgE)	3.10 (0.81)	2.15 (0.66)	<0.0001
Eosinophil (%)	8.9 (5.6)	4.4 (3.2)	<0.0001
Blood trace element levels			
Manganese (nmol/L)	214.1 (66.43)	219.6 (76.43)	0.67
Arsenic (nmol/L)	27.90 (17.63-47.31)	30.32 (17.58-52.21)	0.79
Mercury (nmol/L)	11.00 (7.00-19.00)	10.00 (5.75-17.25)	0.32
Zinc (µmol/L)	8.5 (2.7)	9.0 (2.5)	0.24

Results expressed in mean (standard deviation) unless stated otherwise

All *p*-values (except whole blood arsenic and mercury levels) were obtained from Student t test

Whole blood arsenic and mercury levels were expressed as median (interquartile range) and analyzed by Mann Whitney test

Local reference ranges: zinc 9.4-18.4 µmol/l; mercury < 77 nmol/l; arsenic (<310 nmol/l), manganese: 70-280 nmol/l.

Nevertheless, there were no differences in terms of fish consumption behavior, eczema severity, quality of life and heavy metal levels between AE patients with or without fish atopy (Table 2).

In AE patients, freshwater fish consumption behavior in days-per-week correlated with blood arsenic and mercury levels (*rho*=0.17, $p < 0.01$ for both metals; Table 3). Levels of these two heavy metals were also correlated with days of seawater fish consumption per week (arsenic: 0.38, mercury: 0.24, $p < 0.05$)

Table 2. Comparison of clinical parameters and laboratory tests between eczema patients with fish atopy (skin prick positive) and those who had no fish atopy

Topics	No fish atopy (n = 70)	Fish atopy (n = 27)	*p* value
Males (%)	55.7%	55.6%	0.99
Age (years)	10.2±4.2	10. 2±5.3	0.98
Freshwater fish (days/wk)	1.2±1.2	1.1±1.7	0.29
Seawater fish (days/wk)	1.7±1.8	1.7±1.9	0.57
SCORAD	37.77±20.37	46.02±19.95	0.08
Objective SCORAD	28.22±17.48	34.46±18.22	0.12
NESS	11.4±2.6	12.3±2.0	0.13
CDLQI (for 5 -16 years)	8.6±5.0	10.1±6.6	0.23
Eosinophils (%)	8.42±5.10	9.07±4.15	0.55
Log (IgE)	3.06±0.81	3.30±0.64	0.18
Zinc (µmol/L)	8.26±2.80	8.42±3.04	0.81
Mercury (nmol/L)	13.9±9.4	15.7±11.1	0.70
Manganese (nmol/L)	220.1±72.4	231.4±81.9	0.52
Arsenic (nmol/L)	41.8±36.0	34.4±27.6	0.22

Results are in mean ± SD

Table 3. Correlations between blood trace element levels and weekly fish consumption

Metals	Freshwater fish		Seawater fish	
	Corr. Coefficient	*p* value	Corr. Coefficient	*p* value
Zinc (μmol/L)	0.005	0.95	-0.072	0.38
Mercury (nmol/L)	0.17	0.042	0.24	0.004
Manganese (nmol/L)	-0.14	0.085	0.13	0.13
Arsenic (nmol/L)	0.17	0.043	0.38	p<0.001

Fish consumptions were measured in days-per-week. All associations were done by Spearman rho's test.

DISCUSSION

AE is a common and distressing childhood disease associated with chronicity and impaired quality of life. The incidence of eczema has been increasing in developed countries.[2] The incidence in Hong Kong is approximately 10%.[19,20] Environmental and dietary factors have been incriminated.[2,7,21] Westernized life style, air and food pollution with heavy metals have been considered as possible culprits.[7,9,10,22] The Cantonese Chinese have peculiar views on dietary restriction and supplementation[3,4,23] Seafood avoidance, with the exception of fish, is widely practiced in Hong Kong. Locally, some parents believe that freshwater fish might be contaminated by antibiotic usage in fish farming (personal observations). On the contrary, many parents would not consider seawater fish as "seafood". They believe that seawater fish is nutritious and is generally good for children. They prefer its frequent consumption despite strict avoidance of crustacean and other "seafoods".

It is controversial to advise if fish as a "seafood" is beneficial or detrimental to children with AE in terms of fish atopy and potential heavy metal contamination.

Fish Atopy or Sensitization

According to our findings, only one-fourth of AE patients showed atopic fish sensitization and there is no difference in terms of eczema severity between the fish atopic and the non-fish atopic groups. In a previous study, we also documented no definite association between atopy to food allergens and eczema severity.[4] Hence, we conclude that there is no consistent correlation between fish atopy and eczema severity.

Heavy Metal Exposure

Due to increasing worldwide water pollution, fish might be a source of excessive heavy metals.[5,6,12,22,24-27] Body burden of mercury is associated with acute atopic eczema and total IgE in children from southern Germany.[28] Systemic dermatitis from mercury has also been reported.[29] Nevertheless, we did not find any abnormal levels of mercury in our patients and mercury levels were not found to correlate with any of the studied parameters. Levels of arsenic in food are fairly low. Nevertheless, levels of arsenic in fish and seafood may be high, because fish absorb arsenic from the water they live in.[24-26] Fish that contain significant amounts of inorganic arsenic may be a danger to human health. Bivariate analyses did not reveal statistically significant associations between AE or the body burden of arsenic and heavy metals.[7] Although blood levels of mercury and arsenic correlated with days of fish consumption, the levels of these metals generally did not exceed local normal reference values. Manganese has also been incriminated in causing neurotoxicity and allergic dermatoses in patients who consumed fish from contaminated areas.[25,30-32] We did not find abnormal manganese levels in our patients and the blood manganese levels did not correlate with eczema severity.

Zinc is the most widely studied metal in childhood dermatological conditions.[12,33] It is an important co-enzyme and antioxidant defense system in the skin. Typically, red meat (beef and pork) and seafood contain very high zinc.[34,35] Serum zinc levels were generally low in eczema[11] and in allergic children.[12,32,36] Zn levels, however, showed no correlations with eczema severity or quality of life.[12] We did not find any association between zinc levels and fish consumption in the present study. In a pilot study (unpublished data), zinc replacement did not seem to ameliorate AE severity.

Limitations

The present study was a cross-sectional analysis and

patterns of dietary changes were not evaluated. Ideally, at least two blood levels over a period of time should be measured to evaluate the consistence of our findings. Also, the exact amounts of fish intake could be determined. Distinction should be made between consumption of small fish versus big fish and non deep-water fish versus deep-water fish as the amount of zinc, mercury, arsenic, and manganese that they contain would be different. Nevertheless, retrospective documentation of dietary intake for a chronic relapsing disease was nearly impossible.

CONCLUSION

This study attempted to solve the many myths concerning fish consumption in AE. Suffice is to say that there is currently no evidence that patients with eczema have toxic levels of heavy metals associated with fish consumption, and that there was no difference in terms of fish consumption behavior, eczema severity, quality of life, and heavy metal levels between AE patients with or without fish sensitization. Nor is there any evidence to suggest that patients have milder eczema with more days of fish consumption. Based on these findings, it is sensible to advise parents to provide a balanced diet for their children with AE without the necessity to consume excessive amount of fish. Evaluation of levels of arsenic and mercury may be indicated if patients give a history of frequent seawater fish consumption. Fish should be avoided in the case of obvious fish allergy or anaphylaxis. Aggressive and expensive approaches such as chelation therapy should not be offered to these patients for "routine detoxification". There is no evidence to suggest that fish is bad for eczema (in terms of sensitization or heavy metals), or good for eczema (i.e. milder eczema with more days of fish consumption).[22]

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