Allergology International xxx (2017) 1–9

Contents lists available at ScienceDirect

Allergology International

journal homepage: http://www.elsevier.com/locate/alit

Original article

Exposure amount and timing of solar irradiation during pregnancy and the risk of sensitization in children

Hyun Yong Koh [a], Eunhae Cho [a], So-Yeon Lee [b], Woo Kyung Kim [c], Yong Mean Park [d], Jihyun Kim [e, f], Kangmo Ahn [e, f], Seung Won Lee [a], Mi Ae Kim [g], Myung-Il Hahm [h], Yoomi Chae [i], Kee-Jae Lee [j], Ho-Jang Kwon [k], Man Yong Han [l, *]

[a] CHA University School of Medicine, Seongnam, South Korea
[b] Department of Pediatrics, Childhood Asthma Atopy Center, Environmental Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea
[c] Department of Pediatrics, Inje University College of Medicine, Seoul, South Korea
[d] Department of Pediatrics, Konkuk University Hospital, Konkuk University School of Medicine, Seoul, South Korea
[e] Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
[f] Environmental Health Center for Atopic Diseases, Samsung Medical Center, Seoul, South Korea
[g] Department of Medicine, CHA University School of Medicine, Seongnam, South Korea
[h] Department of Health Administration and Management, College of Medical Science, Soonchunhyang University, Asan, South Korea
[i] Department of Medical Education, Dankook University College of Medicine, Cheonan, South Korea
[j] Department of Information and Statistics, Korea National Open University, Seoul, South Korea
[k] Department of Preventive Medicine, Dankook University College of Medicine, Cheonan, South Korea
[l] Department of Pediatrics, CHA University School of Medicine, Seongnam, South Korea

ARTICLE INFO

Article history:
Received 2 March 2017
Received in revised form
31 July 2017
Accepted 4 August 2017
Available online xxx

Keywords:
Aeroallergen sensitization
Allergic disease
Pregnancy
Solar irradiation
Vitamin D

Abbreviations:

25(OH)D3	25-hydroxyvitamin D
ISAAC	the International Study of Asthma and Allergies in Childhood
aORs	Adjusted odds ratios
DLNM	distributed lag non-linear models

ABSTRACT

Background: Solar irradiation affects sensitization to aeroallergens and the prevalence of allergic diseases. Little is known, however, about how the time and amount of solar irradiation during pregnancy affects such risks in children. We aimed to find out how solar irradiation during pregnancy affects sensitization to aero-allergens and the prevalence of allergic diseases in children.

Methods: This population-based cross-sectional study involved 7301 aged 6 years and aged 12 years children. Maternal exposure to solar irradiation during pregnancy was evaluated using data from weather stations closest to each child's birthplace. Monthly average solar irradiation during the second and third trimesters was calculated with rank by quartiles. Risks of allergic sensitization and allergic disease were estimated.

Results: Relative to the first (lowest) quartile, the adjusted odds ratio (aOR) for allergic sensitization in the fourth (highest) quartile was lowest within solar irradiation during pregnancy months 5–6 (aOR = 0.823, 95% CI 0.720–0.942, $p < 0.05$). During months 9–10, the aOR for allergic sensitization for the fourth was higher than the first quartile of solar irradiation (aOR = 1.167, 95% CI 1.022–1.333, $p < 0.05$). Similar results were observed when solar irradiation was analyzed as a continuous variable during months 5 (aOR = 0.975, 95% CI 0.962–0.989, $p < 0.001$) and month 9 (aOR = 1.018, 95% CI 1.004–1.031, $p = 0.003$). Increased solar irradiation during months 7–8 increased the risk of asthma (aOR = 1.309, 95% CI 1.024–1.674, $p = 0.032$).

Conclusions: Maternal exposure to solar irradiation during the second trimester of pregnancy associated with reduced aeroallergen sensitization, whereas solar irradiation during the third trimester was related to increased sensitization to aeroallergens.

Introduction

Atopic sensitization to aeroallergens and food allergens can result in the development of asthma,[1] allergic rhinitis[2] and food hypersensitivity[3] in children. Such atopic sensitization and allergic

* Corresponding author. Department of Pediatrics, CHA University School of Medicine, 351 Yatap-dong, Bundang-gu, Seongnam, Gyonggi-do 463-712, South Korea.
E-mail address: drmesh@gmail.com (M.Y. Han).
Peer review under responsibility of Japanese Society of Allergology.

http://dx.doi.org/10.1016/j.alit.2017.08.007

disease result from the combined interactions of genetic and environmental factors. Gestational environment *in utero* during fetal organogenesis[4,5] may influence the development of immune-modulating diseases, such as multiple sclerosis, type I diabetes and rheumatoid arthritis.[6] Similarly, allergic diseases[4,7] and sensitization are programmed *in utero* and these are affected by fetus size, maternal exposure to allergens and smoking, as well as by maternal nutrition and vitamin D status.[5,8] Postnatal solar irradiation can affect allergic sensitization,[9] asthma and anaphylaxis,[10] but there has been little to no research into temporal relationship between prenatal solar irradiation and the incidence of child's allergic sensitization or allergic disease afterbirth. Because immune response and epigenetic mechanism involved in allergic sensitization starts from early perinatal period as in developmental origins of health and disease (DOHaD) theory,[11] the solar irradiation controlled by maternal behavior which affects to environment *in utero* might have an influence to postnatal allergic sensitization susceptibility. In this instance, the fact that allergic disease susceptibility affected by gestational period should be helpful to plan the antepartum care.

The relationship between vitamin D levels during pregnancy and the risk of sensitization to foods and aero-allergens remains unclear. Lower 25(OH)D3 (25-hydroxyvitamin D) levels in cord blood have been associated with a higher risk of sensitization to foods and aero-allergens,[12–15] whereas other studies have failed to observe these correlations.[8,16–21] These discrepancies may be due to the biphasic effect of cord blood vitamin D levels on serum IgE concentrations[22] and to differences in genetic backgrounds of the participants.[14,23] Vitamin D concentrations at different time points during pregnancy may differ in their effects on allergic sensitization, as both the first fetal reactions to allergen exposure and T cell maturation occur during the second trimester.[4,24]

Exposure to sunlight exposure, not dietary vitamin D, is the major contributor to changes in 25(OH)D levels,[17,18,25,26] which in turn is associated with allergen sensitization. This study was therefore designed to investigate the relationship between the timing and amount of solar irradiation during pregnancy and the offsprings' sensitization to aeroallergens and development of allergic diseases.

Methods

Subjects

This cross-sectional study in Korean assessing the prevalence of allergic diseases among school aged children in 2010 involved 4003 subjects born in 2002–2003 (aged 6 years) and 4112 subjects born in 1997–1998 (aged 12 years) in 40 schools in 30 representative cities of Korea.[27] Participants were selected by a stratified, multiple-staged and countrywide probability sampling. The inclusion criteria were children born in 2002–2003 and born in 1997–1998 who were in school and completely replied to the questionnaire and allergic skin test. To remove selection bias, the number of students were enrolled in proportion to the population density of city where school was located on. Of the 7714 children who completed both the skin test and the questionnaire, 7301 were selected, 3613 children born in 2002–2003 and 3688 children born in 1997–1998. 413 children who had a disagreement or turned examination down were excluded. All of the children underwent skin tests for 18 types of aero-allergens and their parents completed questionnaires on basic demographic information and risk factors associated with allergic diseases.[28] The study design and protocol were approved by a Dankook University in Cheonan institutional review board (IRB approval number: DKUH IRB 2010-09-0260), and all participants provided a written consent.

Questionnaire

Parents completed standardized questionnaires that contained the International Study of Asthma and Allergies in Childhood (ISAAC) core health questions,[27] in addition to 27 items regarding general information, 29 items regarding living space and habits and 5 items assessing pre- and post-pregnancy socio-economic status, as well as current socio-economic status. For assessing allergic rhinoconjunctivitis, asthma and eczema with ISSAC questionnaire, we defined symptoms suggestive of allergic diseases as follows: those who had experienced itchy eczema episodes, or a problem with nasal symptoms or wheezing unrelated to a cold within 12 months of the survey.[27]

Solar irradiation and other climate information

Data on solar irradiation (MJ/m^2) and other climate information (temperature and humidity) in Korea, measured at 22 weather stations in April 2002–December 2003 and April 1997–December 1998, were obtained from the data archives of the Korea Meteorological Agency. The intensity of ultraviolet-B radiation was measured as minimal erythemal doses every 10 min using UV-biometers (Solar light, USA), with the highest intensity of each day regarded as the daily intensity. Monthly intensity was calculated as the average of the highest daily intensities. All participants were matched to one of the 22 weather stations closest to their place of birth. Daily levels of solar irradiation measured at the nearest weather station were approximated to solar irradiation exposure throughout the whole pregnancy period.

Skin prick test and total IgE measurement for allergic sensitization

All subjects were tested for atopic sensitization to 18 aero-allergens, i.e. *Dermatophagoides pteronyssinus* (Der p), *Dermatophagoides farinae* (Der f), *Tyrophagus putrescentiae* (Tyr p), cockroach, cat, dog, alder, birch, oak, Japanese cedar, orchard grass, bermuda grass, timothy, mugwort, ragweed, Japanese hop, alternaria, and *Aspergillus fumigatus* (Allergopharma, Reinbeck Germany). Details on the skin test protocol have been described previously.[28] In the skin prick test (SPT), a test was regarded as positive if a wheal was e 3 mm and controls showed adequate reactions. Non sensitization was defined participant who has no any reaction in SPT about all aeroallergen types. Mono- and poly-sensitization were single and multiple sensitization to aero-allergen panels, respectively. The amount of total IgE was measured using patient's serum by the IgE ImmunoCAP. High value of total IgE was defined if it was $\geq$100.[27]

Potential confounding factors

Potential confounding factors on univariate analysis included factors with a known risk for sensitization and those showing statistically significant differences. Factors associated with environment during pregnancy and infancy included maternal smoking during pregnancy, pets in the household before age 1 year, breast feeding history, number of siblings, remodeling or moving to a new house within 1 year, and age at first presentation to a childcare center. Factors associated with current status included monthly income, exposure to second-hand cigarette smoking, location of living space within a building, terms of the building, presence of a fabric sofa, and purchase of new furniture within 1 year. Other potential confounders of outcome included gender, *Z* scores of current BMI calculated for the Korean population,[29] and birth weight.

Please cite this article in press as: Koh HY, et al., Exposure amount and timing of solar irradiation during pregnancy and the risk of sensitization in children, Allergology International (2017), http://dx.doi.org/10.1016/j.alit.2017.08.007