Biomedical Research 2014; 25(4): 528-532 *ISSN 0970-938X*
http://www.biomedres.info

Astigmatism in twin infants is related to pregnant nutrition.

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Abstract

Astigmatism is a very common refractive error in infants. The etiology of astigmatism is poorly understood although it may involve pregnant environmental factors. The aim of this study was to examine the association between pregnant nutrition and the risk of infant astigmatism in twins. Total 28 pairs of twins (11 monozygotic and 17 dizygotic), whose mothers had been involved in this study since month 4-6 of pregnancy, received noncycloplegic refraction measurement by vision screening instrument at the age of 3 months. Detailed perinatal history and 24-hour dietary records were collected. Umbilical vein blood of the twins and vein blood of their mothers in month 4-6 of pregnancy were collected to measure micronutrients, including vitamin A, 25-(OH) vitamin D_3, calcium, iron, magnesium, and zinc. We found that he rate of astigmatism was significantly greater in twins from mothers with astigmatism than in those from mothers without astigmatism ($P<0.01$), but was not significantly associated with the mode of delivery, birth order, sex, birth asphyxia ($P>0.05$). Logistic regression analysis showed that morning sickness, BMD, Hb, maternal serum magnesium and vitamin A levels during mid-pregnancy, umbilical vein serum vitamin D3 and calcium levels and birth weight were correlated with astigmatism ($P<0.05$). In conclusion, the development of astigmatism in twins is related with pregnant nutrition and birth weight. Sufficient supply of nutrition during pregnancy may help prevent the development of astigmatism in twins.

Keywords: Astigmatism; Micronutrients; Twins; Vision screening

Accepted August 28 2014

Introduction

Several studies suggest that both genetic and environmental factors are involved in ocular growth, especially the development of refraction status, in the uterus [1,2]. Astigmatism detected in the infants is formed before birth [3]. There is a large amount of evidence suggesting that genetic factors are involved in astigmatism, although the degree and the mode of inheritance remain unclear [4,5]. In addition, environmental factors such as preterm birth are known to be related to visual impairment, oculomotor abnormalities, and refractive error at birth. Compared with full term infants, preterm infants have high rates of refractive error in myopia and anisometropia and a trend for the development of astigmatism [6,7].

Nutrition, as an important environmental factor, is known to be related to ocular growth after birth. Among children aged 2-11, serious nutritional imbalance within 6 months after birth would significantly increase the incidence of astigmatism [8]. Moreover, animal study indicated that refraction error was induced by insufficiency of vitamine D and calcium in young birds [9]. However, no studies have examined the involvement of nutrition condition during pregnancy in the etiology of astigmatism.

Twin studies provide unique opportunities to estimate the relative importance of genetic and environmental determinants of a disease such as astigmatism [4,5,9]. In this study we aimed to describe the occurrence of astigmatism in Chinese infant twins and to estimate the contribution of environmental factors to the variations in liability for astigmatism.

Subjects and Methods

Subjects

All mothers involved in this study gave informed consent and the study protocol was approved by Ethics Commit-

tee of Nanjing Medical University. Twin infants delivered at Jiangsu Province Maternity and Child Health Care Hospital between January 2008 and March 2009 were eligible for this study. 15 twin-pairs were excluded due to either their failure to complete the regular ophthalmic examination, or the evidence of a congenital eye diseases. Of 28 studied pairs of infants, 11 were monozygotic (MZ), consisting of 5 male pairs and 6 female pairs, and 17 were dizygotic (DZ), consisting of 8 male pairs and 6 female pairs, and 3 pairs of the opposite sex. Mothers of the twins received regular investigations on nutrition conditions in month 4-6 of pregnancy, and the results were recorded in detail. Pregnancy and delivery surveys were conducted, which included the method of conceiving (natural or artificial insemination), abnormal morning sickness (moderate or serious vomiting not limited to the morning), hypertension of pregnancy, the mode of delivery, birth order, the sex of infants, birth asphyxia, parents' astigmatism condition (measured with Weilun autorefractor). Twin birth weight was 1300-3600 g (medium 2602.08±475.81 g)，birth length was 40-50 cm (medium 47.95±2.39 cm), gestational age was 231-281 days (medium 259.92±8.29 days).

Nutritional assessment

Umbilical vein blood of the twins and vein blood of their mothers in month 4-6 of pregnancy were collected. Mothers' nutritional status was assessed through dietary survey, BMD (bone mineral density), hemoglobin (Hb) and nutrients determination in vein serum of mid-gestation. Umbilical vein blood of the twins was collected at birth to assess nutritional status of the twins and their mothers. At least one time of 24-hour dietary recording was conducted at the second and third trimester of pregnancy. BMD in mid-gestation was measured by Absorptiometry (model: Sunlight 7000, Israel). 25-(OH) vitamin D was detected by ELISA kit. Vitamin A was detected by high performance liquid chromatography (HPLC model: Shimadzu LC-10AT, Japan). Calcium, iron, magnesium and zinc were detected by atomic absorption spectrometry (AAS model: Shimadzu AA-6300, Japan).

Refractive detection

Refractive detection was performed in the twins of 3 months old by noncycloplegic autorefraction with an autorefractor (model: SureSight Weilun vision screening instrument, USA). Twins with the degrees of astigmatism C1.0D≤C<2.0D were grouped as group 1, twins with the degrees of astigmatism C≥2.0D as group 2.

Statistical analysis

Epi-data3.1 software was used to collect the data and build up the database, SPSS11.5 software was used for statistical analysis. Comparison between groups was analyzed by t test or analysis of variance (ANOVA). The relationship between astigmatism and environmental factors was analyzed by logistic regression analysis. $P<0.05$ was considered as statistically significant

Results

Rate of astigmatism in the twins and their parents

Rate of astigmatism in the twins at three months after birth was 52.58%, significantly higher than 14.28% of their parents ($P<0.05$). Rate of astigmatism had no significant difference between MZ and DZ ($P>0.05$).

Relationship of astigmatism with factors of pregnant mothers and twins

Rate of astigmatism was significantly greater in the twins from mothers who had astigmatism than in those from mothers without astigmatism ($F=6.33$, $P<0.01$). However, other variables were not significantly associated with the rate of astigmatism ($P>0.05$, Table 1).

Table 1. *Correlation of astigmatism with factors of pregnant mothers and twins*

Factors of mother	n	Astigmatism value	P	Factors of twins	n	Astigmatism value	P
conception model				zygosity			
natural	32	1.78±0.66	0.30	MZ	22	1.86±0.46	0.91
artificial insemination	24	1.93±0.76		DZ	34	1.89±0.78	
parents astigmatism				Sex			
positive	16	2.49±0.46	0.01	Male	29	1.99±0.68	0.16
negative	40	1.19±0.45		female	27	1.87±0.54	
hypertension of pregnancy				birth order			
positive	12	1.98±0.66	0.18	First	28	1.89±0.64	0.34
negative	24	1.83±0.86		second	28	1.85±0.73	
mode of delivery				birth asphyxia			
natural	8	1.78±0.85	0.07	positive	12	1.92±0.85	0.36
uterine incision	48	1.89±0.56		negative	44	1.84±0.59	

Table 2. *Logistic regression analysis of the risk factors for astigmatism*

Risk factors	β	P	OR	OR95%CI
morning sickness	0.29	0.03	1.40	1.10～5.13
gestational age	0.01	0.58	1.02	0.96～1.08
BMD	0.31	0.03	1.44	1.30～6.19
haemoglobin	0.53	0.03	1.69	1.03～2.78
mid-gestation vein serum				
calcium	-0.01	0.59	1.01	0.97～1.08
iron	0.06	0.50	1.06	0.89～1.26
zinc	1.10	0.24	3.02	0.46～19.46
magnesium	-0.33	0.03	1.39	1.03～1.89
vitamin A	0.03	0.00	1.03	1.01～1.06
vitamin D	-0.00	0.89	0.99	0.98～1.02
umbilical vein serum				
calcium	-0.05	0.02	1.04	1.03～1.08
iron	0.09	0.10	0.90	0.80～1.02
zinc	-0.61	0.14	1.85	0.86～3.97
magnesium	0.10	0.30	0.90	0.73～1.10
vitamin A	0.00	0.44	1.00	0.98～1.02
vitamin D	-0.02	0.02	1.02	1.00～1.04
Birth weight	-0.01	0.04	1.02	1.00～1.03
Birth length	0.21	0.10	0.80	0.62～1.05

Logistic regression analysis of risk factors in twin astigmatism

Multiple Logistic regression models were constructed to further investigate the effect of pregnant environmental and nutritional variables on the development of astigmatism in infants of 3 months old. With or without astigmatism as the dependent variable in the twins, the pregnancy-related factors were selected as independent variables, which included morning sickness, gestational age, birth weight and length, parental refractive status, nutrient conditions of mothers and twins such as vitamin A, 25- (OH) vitamin D3, calcium, iron, magnesium, and zinc. The results showed that morning sickness, BMD, maternal serum haemoglobin level during mid-pregnancy, and mid-gestation serum levels of magnesium and vitamin A were associated with increased risk of astigmatism. For factors associated with the infants, umbilical vein serum levels of calcium and vitamins D, and birth weight were associated with increased risk of astigmatism (Table 2). These data suggest that these pregnant environmental factors may contribute to higher astigmatism rate in the infants.

Discussion

Astigmatism is a refractive error in which the unequal curvature of one or more ocular refractive surfaces prevents light rays from focusing at one point on the retina. Varughese et al. found that detection rate of astigmatism (cylinder power of 1.0 D or worse) was 67.8 %, and concluded that astigmatism eye was formed in the uterus [3]. A study in Singapore showed that the incidence of amblyopia was 1.19% in 30-72 months old infants, with 71% of them caused by astigmatic refractive errors [10].

Genetic factors play important role in the development of astigmatism [4,5,11,12]. For example, Hammond et al. examined refractive error in 226 monozygotic (MZ) and 280 dizygotic (DZ) twin pairs aged 49 to 79 years, and found that genetic factor accounted for 47% to 49% of astigmatism [5].

The reason why twins were selected as the subjects for the study of astigmatism is not only that it is easy to investigate the effects of genetic factors [13], but also that twin pregnant woman need much more nutrients than single

pregnant woman during embryonic development, and pregnant mother and fetus during pregnancy are more susceptible to nutrient deficiencies or unbalance [14]. The rate of astigmatism in twins was reported to be significantly higher than in singleton [15]. These data suggest that astigmatism is not only affected by genetic factors, but also closely related to pregnant environmental factors.

We analyzed risk factors of pregnant mothers during pregnancy which may be related to eye embryonic development, and found that the formation of astigmatism was closely correlated with maternal and infantile nutrition. 1. Morning sickness: twins with mother's morning sickness had higher risk of astigmatism than those without mother's morning sickness, suggesting that the formation of astigmatism is associated with early nutritional deficiency of fetus. 2. During the second trimester or mid-pregnancy: BMD, hemoglobin, and serum levels of magnesium and vitamin A may be related to the occurrence of astigmatism. BMD reflects long-term nutritional status of calcium, while hemoglobin indicates nutritional status of iron. 3. During the last trimester: the occurrence of astigmatism may be related to serum levels of calcium and vitamin D in the twins during delivery, and birth weight. By surveying maternal dietary during this period, we found that most mothers' nutrient intake exceeded the singleton' reference, but 20% mothers had serum nutriment deficiency. In addition, the more birth weight, the more nutrition needs, and the more prone to inadequate nutrient supply. These data are consistent with the view that birth weight rather than gestation should be used as the criteria for the screening of refractive error, especially in developing countries where the incidence of intrauterine malnutrition is higher [16].

However, the mechanism how nutrient insufficiency contributes to astigmatism is unclear. Vitamin D receptors were found in the retina, cornea and optic nerve [17]. Vision development and refraction condition were affected by micronutrients such as vitamin A, calcium, iron and zinc [18]. If maternal nutrients such as magnesium, vitamin A and D during pregnancy are insufficient, fetal cornea development will be disrupted, decreasing the function of anti-traction. Further studies are needed to investigate the underlying mechanism.

To our knowledge, this is the first study to examine the association between pregnant nutrition and the risk of infant astigmatism in twins. Our data suggest that pregnant women of twins are more prone to pregnant malnutrition and the development of astigmatism in twins is related with pregnant nutrition and birth weight. Sufficient supply of nutrition during pregnancy may help prevent the development of astigmatism in twins.

Competing interests

The authors declare that they have no competing interest.

References

1. Grosvenor T. Etiology of astigmatism. Am J Optom Physiol Opt 1978; 55: 214-218.
2. Lyhne N, Sjolie AK, Kyvik K O, et al. The importance of genes and environment for ocular refraction and its determiners: a population based study among 20-45 year old twin. Br J Ophthalmol 2001; 85: 1470-1476.
3. Varughese S, Varghese RM, Gupta N, et al. Refractive error at birth and its relation to gestational age. Curr Eye Res 2005; 30: 423-428.
4. Grjibovski AM, Magnus P, Midelfart A, et al. Epidemiology and heritability of astigmatism in Norwegian twins: an analysis of self-reported data. Ophthalmic Epidemiol 2006; 13: 245-252.
5. Hammond CJ, Sniede H, Gilbert CE, et al. Genes and environment in refractive error: the twin eye study. Invest Ophthalmol Vis Sci 2001; 2: 1232-1236.
6. Birch EE, O'Connor AR. Preterm birth and visual development. Semin Neonatol 2001; 6: 487-497.
7. Cook A, White S, Batterbury M, Clark D. Ocular growth and refractive error development in premature infants without retinopathy of prematurity. Invest Ophthalmol Vis Sci 2003; 44: 953-960.
8. Dantas AP, Brandt CT, Leal DN. Ocular manifestations in patients who had malnutrition in the first six months of life. Arq Bras Oftalmol 2005; 68: 753-756.
9. Hodos W, Gregory R, Bock Organizer, Kate Widdows. Avian models of experimental myopia: environmental factors in the regulation of eye growth. Ciba Found Symp 1990; 155: 149-156.
10. Chia A, Dirani M, Chan YH, et al. Prevalence of amblyopia and strabismus in young Singaporean Chinese children. Invest Ophthalmol Vis Sci 2010; 51: 3411-3417.
11. Hashemi H, Hatef E, Fotouhi A, et al. Astigmatism and its determinants in the Tehran population: the Tehran eye study. Ophthalmic Epidemiol 2005; 12: 373-381.
12. Dirani M, Islam A, Shekar SN, et al. Dominant genetic effects on corneal astigmatism:the genes in myopia (GEM) twin study. Invest Ophthalmol Vis Sci 2008; 49: 1339-1343.
13. Martin N, Boomsma D, Machin G. A twin-pronged attack on complex traits. Nat Genet 1997; 17: 387-392.
14. Brody BL, Roch-Levecq AC, Klonoff-Cohen HS, et al. Refractive errors in low-income preschoolers. Ophthalmic Epidemiol 2007; 14: 223-229.
15. Hur YM, Zheng Y, Huang W, et al. Comparisons of refractive errors between twins and singletons in Chinese school-age samples. Twin Res Hum Genet, 2009; 12: 86-92.

16. Varghese RM, Sreenivas V, Puliyel JM, Varughese S. Refractive status at birth: its relation to newborn physical parameters at birth and gestational age. PLoS One. 2009; 4: e4469.
17. Bidmon HJ, Stumpf WE. 1, 25-Dihydroxyvitamin D3 binding sites in the eye and associated tissues of the green lizard Anolis carolinensis. Histochem J 2001; 119: 1625-1628.
18. Whatham A, Bartlett H, Eperjesi F et al. Vitamin and mineral deficiencies in the developed world and their effect on the eye and vision. Ophthalmic Physiol Opt 2008; 28: 1-12.

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