Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health 6 (2016) 361–366

Contents lists available at ScienceDirect

Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health

journal homepage: www.elsevier.com/locate/preghy

Sex differences in early growth during the first three years of life in offspring from mothers with pregnancy-induced hypertension

Takashi Mitsui, Hisashi Masuyama *, Takeshi Eguchi, Shoko Tamada, Eriko Eto, Kei Hayata, Yuji Hiramatsu

Department of Obstetrics and Gynecology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata, Okayama 700-8558, Japan

ARTICLE INFO

Article history:
Received 8 July 2016
Accepted 26 August 2016
Available online 13 September 2016

Keywords:
Pregnancy-induced hypertension
Fetal growth restriction
Catch-up growth
Toddler
Sex

ABSTRACT

Objectives: Newborns born to mothers with pregnancy-induced hypertension (PIH) are thought to be at high risk for lifestyle-related diseases, such as obesity and hypertension, in adulthood.
Study design: A longitudinal study of 78 pregnant women with PIH and their newborns, who visited Okayama University Hospital from 2009 to 2013.
Main outcome measures: We investigated the change in growth of offspring born to mothers with PIH and compared it with the standard growth curve in Japanese to examine whether there was rapid catch-up growth during the first 3 years of life.
Results: Subjects were 78 pregnant women with PIH and their offspring, who visited Okayama University Hospital from 2009 to 2013. Valid responses were obtained from 29 of 78 (37.1%) women. Body weight and length at birth were at the third percentile or less in females, and at the 10th percentile or less, in males. When body weight and length were compared at 6 months, 18 months, and 3 years old between male and female toddlers, male toddlers slowly caught up until 3 years old, but female toddlers rapidly caught up in the first 6 months. Furthermore, in newborns with fetal growth restriction caused by the intrauterine environment of PIH, differences in physical development between male and female toddlers were more remarkable.
Conclusions: There is a significant sex difference in catch-up growth during the first 3 years, which might be involved in lifestyle-related diseases in adulthood, suggesting continuous follow-up is necessary, especially for female offspring.

1. Introduction

The concept of fetal origins of adult disease is where a fetus exposed to poor nutrition *in utero* life and has fetal growth restriction (FGR) has an increased risk of lifestyle-related diseases, such as obesity and type 2 diabetes, hypertension, and cardiovascular disorders, in adulthood [1]. Not only the prenatal environment, but also various environmental factors after birth, such as breast milk and nutrition, are related to lifestyle-related diseases. This situation is widely recognized as the concept of development origins of health and disease [2]. With regard to this concept, Gluckman and Hanson proposed the idea that developmental plasticity, trade-off, and predictive adaptive responses of the environment in the developmental phase are associated with various diseases in adulthood [3,4]. When the intrauterine environment becomes worse because of maternal complications, such as pregnancy-induced hypertension (PIH) and malnutrition, the fetus becomes chronically hypoxic, with low nutrition, and asymmetrical FGR. There are various causes of FGR [5], including PIH. After birth, newborns who are born to mothers with PIH adapt their metabolism and endocrine function in the extrauterine environment. However, because nutrition after birth in the extrauterine environment during infancy is different from malnutrition of the fetal period in the intrauterine environment, infants have inappropriate predictive adaptive responses. This leads to development of lifestyle-related diseases, such as obesity, hypertension, and insulin resistance, in adulthood. Infants born to pregnant women with preeclampsia have higher blood pressure and a larger body mass index (BMI) in childhood and young adulthood [6], and another reports show that there is a sex difference in the risk of developing lifestyle-related diseases in the infants born to mother with preeclampsia [7,8]. Furthermore, Settler et al. reported that the greater the body weight gain in the first 4 months after the birth, the higher the risk of obesity in childhood [9]. Additionally, a rapid body weight gain

* Corresponding author.
E-mail address: masuyama@cc.okayama-u.ac.jp (H. Masuyama).

http://dx.doi.org/10.1016/j.preghy.2016.08.238
2210-7789/

in early infant life is associated with obesity in childhood and young adulthood [10].

Therefore, in this study, we investigated physical development of newborns who were born to mothers with PIH and compared it with the standard growth curve in Japanese. This study aimed to examine whether there was rapid catch-up growth during the first 3 years in male and female offspring.

2. Materials and methods

Subjects were 78 pregnant women with PIH and their newborns, who visited Okayama University Hospital from 2009 to 2013. PIH was diagnosed according to the definition of PIH by the Japan Society of Obstetrics and Gynecology [11]. FGR was defined as a fetal weight just before the birth that is below 1.5 standard deviations of the estimated Japanese standard fetal weight [12]. Small-for-gestational age (SGA) neonates were defined as having a body weight at birth <10th percentile for neonates of the same gestational age [13]. In this study, multiple pregnancies and pregnancies with chromosomal abnormalities and congenital disease in the fetus and newborns, and those who were not able to followed up during the first 3 years, were excluded. When newborns born to mothers with PIH reached 3 years of age, we sent a questionnaire to their parents and investigated the changes in physical development during the first 3 years. Percentile growth curves using data from an investigation of physical development in infants and toddlers in Japan were created [14]. Physical development curves of body weight, length, and BMI during the first 3 years were compared between male and female toddlers born to mothers complicated with PIH. Additionally, body weight and length of male and female toddlers with FGR born to mothers who were complicated with PIH were compared with the mean body weight and length from data of this physical development investigation at 6 months, 18 months, and 3 years old. Software downloaded from the Internet (www.niph.go.jp/soshiki/07shougai/hatsuiku/) was used for statistical analysis.

We used the Student's-*t* test, χ^2 test, and Friedman's test after the data were tested for normality of distribution. Student's-*t* test was used to entries of maternal age, body weight, BMI, body weight at delivery, body weight gain, the extent of FGR, weeks at delivery, neonatal body weight, length, BMI, Apgar score 1 min and 5 min. χ^2 test was used to entries of maternal gravidity, type of disease (onset), methods of delivery. Friedman's test was used to entries of type of disease. *P*–values <0.05 was defined as significant.

This study was approved by the Institutional Ethical Review Board of Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, and it conforms to the provisions of the Declaration of Helsinki. Informed consent was obtained from all patients for being included in the study.

3. Results

Valid responses were obtained from 29 of 78 (37.1%) women to whom we sent the questionnaire. Maternal and neonatal characteristics in the 29 women and offspring are shown in Table 1. Next, we compared the maternal and neonatal characteristics between male (n = 13) and female (n = 16) newborns. There were no significant sex difference in maternal age, pregnancy history, non-pregnant body weight, non-pregnant BMI, body weight at delivery, and the body weight gain during pregnancy. Additionally, there were no significant differences in the type of PIH, gestational weeks at delivery, the extent of FGR, and the methods of delivery between male and female newborns. There were also no significant differences in neonatal characteristics between male and female newborns (Table 2).

Table 1
Maternal and neonatal characteristics.

Maternal characteristics (*n* = 29)		Neonatal characteristics (*n* = 29)	
Age (years)*	33.9 ± 5.6	Sex	
Gravidity		Male	13 (44.8%)
Primigravida	21 (72.4%)	Female	16 (55.2%)
Multigravida	8 (27.6%)	Body weight (g)*	2311.5 ± 769.4
Body weight (kg)*	55.5 ± 11.3	Height (cm)*	45.6 ± 4.7
BMI (kg/m^2)*	22.5 ± 4.0	BMI (kg/cm^2)*	10.8 ± 1.9
Body weight at delivery (kg)*	62.9 ± 4.0	Apgar score 1 min*	7.5 ± 1.4
Body weight gain (kg)*	7.5 ± 4.7	Apgar score 5 min*	8.8 ± 0.5
Type		SGA	8 (27.6%)
Preeclampsia	16 (55.2%)		
Gestational hypertension	8 (27.6%)		
Superimposed preeclampsia	4 (13.8%)		
Eclampsia	1 (3.4%)		
Type (Onset)			
Early onset	10 (34.5%)		
Late onset	19 (65.5%)		
FGR (SD)*	−1.1 ± 1.5		
Weeks of delivery (week)*	36.8 ± 3.2		
Methods of delivery			
Vaginal delivery	9 (31.0%)		
Caesarean section	20 (69.0%)		

* Data are mean ± SD. FGR: fetal growth restriction, SGA: small for gestational age.

Table 2
Comparison of maternal and neonatal characteristics between male and female newborns who were born to mothers with PIH.

Variables	Male (n = 13)	Female (n = 16)	*P*-values
Maternal characteristics			
Age (years) *	35.2 ± 5.4	32.8 ± 5.4	0.23
Gravidity			
Primigravida	8 (61.5%)	13 (81.3%)	0.22
Multigravida	5 (38.5%)	3 (18.7%)	
Body weight (kg) *	57.8 ± 112.1	53.6 ± 10.6	0.34
BMI (kg/m^2)*	23.6 ± 4.3	21.6 ± 3.7	0.19
Body weight at delivery (kg) *	65.5 ± 11.4	60.9 ± 10.1	0.26
Body weight gain (kg) *	7.8 ± 4.4	7.4 ± 5.1	0.80
Type			
Preeclampsia	5 (38.5%)	11 (68.8%)	0.14
Gestational hypertension	5 (38.5%)	3 (18.8%)	
Superimposed hypertension	2 (15.4%)	2 (12.5%)	
Eclampsia	1 (7.7%)	0 (0.0%)	
Type (Onset)			
Early onset	6 (46.2%)	5 (31.3%)	0.33
Late onset	7 (53.8%)	11 (68.7%)	
FGR (SD) *	−0.8 ± 2.0	−1.3 ± 1.1	0.37
Weeks of delivery (weeks) *	37.1 ± 3.1	36.5 ± 3.5	0.59
Methods of delivery			
Vaginal delivery	5 (38.5%)	4 (25.0%)	0.35
Caesarean section	8 (61.5%)	12 (75.0%)	
Neonatal characteristics			
Body weight (g) *	2478.5 ± 889.0	2175.9 ± 655.0	0.34
Height (cm) *	46.4 ± 5.5	45.0 ± 4.1	0.43
BMI (g/cm^2) *	11.0 ± 1.9	10.6 ± 1.8	0.54
Apgar score 1 min*	7.5 ± 1.5	7.5 ± 1.3	0.94
Apgar score 5 min*	8.8 ± 0.6	8.7 ± 0.5	0.42
SGA	4 (30.8%)	4 (25.0%)	0.78

* Data are mean ± SD. FGR: fetal growth restriction, SGA: small for gestational age.

The physical development curves of body weight, length, and BMI from birth to 3 years old in male and female infants and toddlers were examined (Figs. 1 and 2). In male newborns, the mean birth weight was 2478.5 ± 889.0 g, birth length was 46.4 ± 5.5 cm, and BMI at birth was 11.0 ± 1.9 kg/m^2. These data were in the