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EFFECT OF FOLIC ACID SUPPLEMENTATION IN PREGNANCY PERIOD TO GROWTH AND DEVELOPMENT OF OFFSPRING: AN EXPERIMENTAL STUDY

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ABSTRACT

We experimented on animals to reveal the effect of folic acid supplementation in different pregnancy period to growth and development of offspring.

Background and Aim: The term "folic acid" specially means pteroylmonoglutamic acid and note as "PteGlu"after the front part of pteroic acid and glutamic acid. Nowadays, congenital neuroanomaly is growing in children so it is important to assess the effect of folic acid which can protect it.

Materials: Wistar white rats with 160-180g in body weight were used as experimental animals.

Methodology: The pregnancy white rats were divided into control group and study group and study group was divided into early, mid and late group according to the folic acid supplementation period. In control group, white rats were taken folate lake feed. In study group, white rats were taken 3.0mg/kg folic acid once per day in early period (first week), mid period (second week), late period (third week). To determine the effect on growth and development of offspring, we measure the length and weight of 156 young rats which were bred by 20 female white rats at 2 days after birth and did comparative analysis between control and study group. We took 5 young rats in each group to assess the effect on neurobehavioral development. Before initial motion test, we measure foreleg step response inertia time, response inertia time in balance beam test and correction rate of bilateral foreleg step in mustache irrigation bilateral foreleg step test and did comparative analysis between control and study group.

Result: At 2 days after birth, the length in mid and late study group was significantly bigger than control group ($P<0.05$, $P<0.01$). The length of young rats in mid group had tendency to be bigger than late group. And the weight in mid and late study group was significantly bigger than control group ($P<0.05$, $P<0.01$). The weight of young rats in mid group had tendency to be bigger than late group. In assessment the effect on neurobehavioral development, foreleg step response inertia time and response inertia time in balance beam test in mid and late study group was significantly shorter than control group($P<0.05$) and the value in mid group had tendency to be shorter than late group. And correction rate of bilateral foreleg step in mustache irrigation bilateral foreleg step test in study group had tendency to be shorter than control group but there was no significant difference.

Conclusion: The folic acid supplementation in mid and late period of pregnancy promotes growth and development of offspring and neurobehavioral development. And supplementation in mid period had tendency to be bigger.

Keyword; pregnancy period, folic acid supplementation, growth and development.

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INTRODUCTION

The term "folic acid" specially means pteroylmonoglutamic acid and note as "PteGlu" after the front part of pteroic acid and glutamic acid. In 1941, a research group took pure acidic material from 4t of spinach and called this material "folic acid" which means leaf. Folate plays necessary role in cellular metabolism as monocarbon transporter. These reactions are necessary for synthesis purine and pyrimidine nucleoside which is necessary for DNA synthesis.

One of the common functions of cellular folic acid is to deliver monocarbon to synthesis of purine and thymidine. The cells of neural tube which is dramatically separated during embryonic development needs large amount of nucleoside for replication of DNA. If the neuroepithelial cells deplete the intracellular pool of nucleotides, cell replication slows down and the development of niche is delayed. This delay in neural groove development may lead to the formation of neural tube defects. The concentration increase of homocysteine due to the depletion of folic acid seems to play important role in occurrence of neural tube defect. A research study shows that micronucleus which appears in depletion of folic acid is risk factor for development of Down's syndrome. Some researchers suggested that DNA methylation is impaired in depletion of folic acid and impairment of hemichromosome arrangement and chromosome separation due to former induce to occurrence of Down's syndrome. Also, folic acid deficiency is related to congenital anomaly such as congenital heart disease, fragile X syndrome, uranoschism and fetal anticonvulsive syndrome and complication of pregnancy such as ablatio placentae and habitual abortion of unknown origin.

It has already proved that pre-conceptional intake of folic acid supplements have a good effect on development of fetus and protect congenital neuroanomaly. Dystectia is congenital insufficient symphysis of encephalon and spinal cord due to asyntaxia of neural tube and it consists of anencephaly, encephalon hump, spinal cord disconnection syndrome and etc. It has proved that folic acid supplementation protective neural tube anomaly such as former.

But effect of folic acid supplementation in different pregnancy period on growth and development of fetus is still incorrect so we have done animal experiment to assess it. Nowadays, given the increasing incidence of congenital neurological malformations and neurodevelopmental disorders such as autism in children, it is important to understand the effect of folic acid on prevention.

1. METHODOLOGY

2.1. Materials

Wistar white rats with 160-180g in body weight were used as experimental animals.

2.2. Procedure

We divide 20 female white rats into 4 groups and each female so lock in cage with 3 males as to do pairing. Next day, we check the vaginal content and determine that it is in pregnancy 1 day if sperm and vaginal plus appear in smear.

The pregnancy white rats were divided into control group and study group and study group was divided into early, mid and late group according to the folic acid supplementation period. In control group, white rats were taken folate lack feed. In study group, white rats were taken 3.0mg/kg folic acid once per day in early period (first week), mid period (second week), late period (third week).

To determine the effect on growth and development of offspring, we measure the length and weight of 156 young rats which were bred by 20 female white rats at 2 days after birth and did comparative analysis between control and study group.

We took 5 young rats in each group to assess the effect on neurobehavioral development. Before initial motion test, we measure foreleg step response inertia time, response inertia time in balance beam test and correction rate of bilateral foreleg step in mustache irrigation bilateral foreleg step test and did comparative analysis between control and study group.

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2. RESULT

2.1. Effect of folic acid supplementation in different pregnancy period to growth and development of offspring

2.1.1. Change of length and weight of young rats according to the folic acid supplementation period

Table 1: Change of length and weight of young rats according to the folic acid supplementation period ($\bar{X}$±SE)

Division	Folic acid supplementation period	number	length (cm)	weight (g)
Control group	-	39	5.3±0.2	3.8±0.3
Study group	Early	37	5.7±0.3	4.1±0.2
	Mid	39	6.7±0.4**	5.5±0.4**
	Late	41	6.2±0.3*	4.7±0.3*

*: P<0.05, **: P<0.01

At 2 days after birth, the length was 6.7±0.4cm, 6.2±0.3cm in mid and late study group and it was significantly bigger than control group (P<0.01, P<0.05). The length of young rats in mid group had tendency to be bigger than late group.

Also, at 2 days after birth, the weight was 5.5±0.4g, 4.7±0.3g in mid and late study group and it was significantly bigger than control group (P<0.01, P<0.05). The weight of young rats in mid group had tendency to be bigger than late group.

2.2. Effect of folic acid supplementation in different pregnancy period to neurobehavioral development of offspring

2.2.1. Change of neurobehavioral development according to the folic acid supplementation period

Table 2: Change of neurobehavioral development according to the folic acid supplementation period ($\bar{X}$±SE)

Division	Folic acid supplementation period	Foreleg step response inertia time(s)	Response inertia time in balance beam test(s)	Bilateral foreleg step correction rate (%)
Control group	-	2.9±0.2	12.6±1.6	96.8±2.1
Study group	Early	2.8±0.3	12.0±1.6	97.3±3.0
	Mid	1.9±0.3*	7.5±1.0*	98.9±2.5
	Late	2.0±0.3*	7.7±1.1*	98.3±3.2

*: P<0.05(), n=5

In initial motion test, foreleg step response inertia time in mid and late study group was 1.9±0.3s 2.0±0.3s and it was significantly shorter than control group (P<0.05) and the value in mid group had tendency to be shorter than late group. Also, in balance beam test, response inertia time was 7.5±1.0s, 7.7±1.1s and itwas significantly shorter than control group (P<0.05) and the value in mid group had tendency to be shorter than late group. And in mustache irrigation bilateral foreleg step test, correction rate of bilateral foreleg step in study group had tendency to be shorter than control group but there was no significant difference.

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3. DISCUSSION

Pregnant women are at high risk of folate deficiency because pregnancy significantly increases folate requirement, especially during periods of rapid fetal growth. Folate deficiency during pregnancy can results in neural tube defects, NTDs. Folate deficiency in pregnancy may also increase the risk of preterm delivery, infant low birth weight and fetal growth retardation, as well as increasing homocysteine level in blood, which may lead to spontaneous abortion and pregnancy complication such as placental abruption and preeclampsia. [1]

Folic acid has a pivotal role in homocysteinemetabolism, and folate supplementation can lower levelsof homocysteine.Increased homocysteine is anindependent risk factor for vascular diseaseand hasbeen associated with placental abruption.[2] Folate status may play anessential role in ovulatory function, possibly through the metabolism of homocysteine.[3-5]

Previous studies have associated FA supplementation with reduced risk of ovulatory infertility[6]and decreased homocysteine in the follicular fluid, with a subsequent higher degree of follicular development and oocyte maturity in women undergoing IVF. [7-9]

In Denmark, women planning to conceive are advised to take a daily supplement of400μg folic acid (FA) until the 12th week of gestation to reduce the risk of neuraltube defects (NTDs).Starting FA supplementation before conception is an importantcomponent of effective prevention of NTDs.[10] But many women aren't taking FA in preconceptional or conceptional period. Despite campaigns promoting the FA recommendation in Denmark in 1999 and2001, women in the preconceptional period appear to have neither adequate dietaryintake of folate nor adequate supplementation from FA tablets or MV supplements.[11]

Research study shows that there was not statistical relationship between periconceptional FA supplementation andneonatal birth weight, body length, head circumference, chest circumference, and gestational age. The Supplementation of folic acid in early period of pregnancy and continuation after 12 weeks of pregnancy promote the growth of fetus. Periconceptional FA supplementation was associated with increased scores in CM and PS domains among 6-month-old infants ($P < 0.05$), and was a protective factor for possible delayed development of CM domain for 18-month-old infants. FA supplements use in early pregnancy was associatedwith increased scores in GC domain among 18-month-old infants (P=0.007). Continued supplementation with FA after the first trimester was associated with decreased risk ofdelayed development of FM and GC domains among 6-month-old infants. As mentioned before, folic acid supplementation in pregnancy period has significance in body development of fetus and neurobehavioral development after birth.

We revealed the effect of folic acid supplementation in different pregnancy period to growth and development of offspring in this study. According to our study results, at 2 days after birth, the length was significantly bigger than control group (P<0.05, P<0.01). The length of young rats in mid group had tendency to be bigger than late group. And the weight was significantly bigger than control group (P<0.05, P<0.01). The weight of young rats in mid group had tendency to be bigger than late group.

In assessment the effect on neurobehavioral development, foreleg step response inertia time and in balance beam test, response inertia time in mid and late study group was significantly shorter than control group(P<0.05) and the value in mid group had tendency to be shorter than late group. And in mustache irrigation bilateral foreleg step test, correction rate of bilateral foreleg step in study group had tendency to be shorter than control group but there was no significant difference.

As a result, the folic acid supplementation in mid- and late period of pregnancy promoted gestational development and neurobehavioral development of offspring. And supplementation in mid period had tendency to be bigger.

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4. CONCLUSION

The folic acid supplementation in mid period of pregnancy is very important in growth and development of offspring and neurobehavioral development. And supplementation in late period wasn't great significant as compared with supplementation in mid period.

REFERENCES

1. Ibrahim I. A. A. and Yusuf A. J.Quantitative determination of iron and folic acid in Lactuca sativa; (Lettuce) plant, Advances in Applied Science Research, 2015, 6(7):112-115.

2. Marlies E.W. et al.: Antepartum haemorrhage of unknown origin and maternal cigarettesmoking beyond the first trimester, Australian and New Zealand Journal of Obstetrics and Gynaecology 2012; 52: 161-166.

3. Ebisch IM, Thomas CM, Peters WH, Braat DD, Steegers-Theunissen RP.The importance of folate, zinc and antioxidants in the pathogenesis and prevention of subfertility. Hum ReprodUpdate 2007;13:163-74.

4. Joshi R, Adhikari S, Patro BS, Chattopadhyay S, Mukherjee T. Free radical scavenging behavior of folic acid: evidence for possible antioxidant activity. Free Radic Biol Med 2001;30:1390-9.

5. Ruder EH, Hartman TJ, Goldman MB. Impact of oxidative stress on female fertility. CurrOpin Obstet Gynecol 2009;21:219-22.

6. Chavarro JE, Rich-Edwards JW, Rosner BA, Willett WC. Use of multivitamins, intake of B vitamins, and risk of ovulatory infertility. Fertil Steril 2008;89:668-76.

7. Szymanski W, Kazdepka-Zieminska A. Effect of homocysteine concentration in follicular fluid on a degree of oocyte maturity. Ginekol Pol 2003; 74:1392-6.

8. Ebisch IM, Peters WH, Thomas CM, Wetzels A M, Peer PG, Steegers-Theunissen RP. Homocysteine, glutathione and related thiols affect fertility parameters in the (sub)fertile couple. Hum Reprod 2006;21:1725-33.

9. Boxmeer JC, Brouns RM, Lindemans J, Steegers EA, Martini E, Macklon NS, et al. Preconception folic acid treatment affects the microenvironment of the maturing oocyte in humans. Fertil Steril 2008; 89:1766-70.

10. Predictors of preconceptional folic acid ormultivitamin supplement use: a cross-sectionalstudy of Danish pregnancy planners, Clinical Epidemiology, 2012:4 259-265.

11. Heidi T Cueto et al.: Folic acid supplement use and menstrual cycle characteristics: a cross-sectional study of Danish pregnancy planners, Clinical Epidemiology, 2012:23 267–290

Doi: 10.2016-37245516/; DOI Link :: https://doi-ds.org/doilink/06.2025-76455185/ASIO-JEPCR/V8/I1/1040