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Morphology of Mice Fetus After High Dose Intake of Vitamin A By Mother Mice Japan Strain

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Abstract: Vitamin A mostly used as an antioxidant product as its effective, easy to get, and cheap. The said effect of vitamin A is congenital defect of mice fetus, which related with teratogenesis as a side effect of hypervitaminosis A. hypertaminosis A mechanism is blocking genetic expression when gene mutation and change the nucleotide line on DNA that caused defected on embriogenic beginning. The aim of this research is to find out the morphology effect of mice fetus after high dose vitamin A intake on mother mice Japan strain. The research method that we used is experimental with postest only group design. The populations are healthy female mice japan strain. Sampling technique that we used is simple random sampling, which divided into 4 group, control group nd 3 different treatment group. Based on research result, there was an effect of high dose vit A consumption, into number of living birth rate, congenital defect birth, intra uterus mortality rate , and morphology defect (P<0,05). Its better to give social education about the benefit of Vit A consumption, and the danger of it to woman in fertile age, and also for couple on fertile age, also doing controlling and monitoring on vit A distribution.

Keywords: Morphology, mice fetus, vitamin A

INTRODUCTION

Vit A has been used a lot on anti oxidant product like in cosmetics, shampoo, and many other product, which the using dose are lack of control. Aside of that, the Vit A is one of the most important nutrition which needed by our body. Every food nutrition, minerals, and vitamins that important during pregnancy, will crossed membrane placenta and will be accumulated on fetus body, to help the growth and body formation of the fetus (Katzung, 1998).

The fetus morphology can be turn into abnormal as an effect of abnormal growth, that caused by several items that identified as teratogen item. The teratogn word came from greek language, which Teras means monster and genesis means the origin of. So, teratogenesis can be defined as the origin of a monster or congenital defect process. Most famous teratogen item is thalidomide. The pregnant women who consume thalidomide, especially on the third week and eight week, will have Fakomelia, which signed with congenital defect of shorter body part or even not formed at all. (Almahdy, 1993).

In several research it shows that chemical item that has teratogenetic character, is vitamin A. its been weel known that Vitamin A can caused serious health problem, but little know how teratogenisis of hipervitaminosis A happen and still need further research. (Lu FC, 1994). Meanwhile, like most known, many pregnant woman has xeroftalmia as an effect of vitamin A deficiency, and has to consume high dose vit A that cause hypertaminosis. meanwhile in Indonesia its really easy to find vit A, without even need doctor prescription, until the used of vit A become out of control and very possible to cause hypertaminosis A (Limbong T, 2005).

Based on that description, the author feel attracted to researching about fetus morphology, after high dose vit A intake by oral, on mother mice japan strain.

METHOD

The type of research that we used here is experimental with postest only group design. (Zainuddin, 2000). The research was take place on Pharmacy Lab, Math NadScience Faculty, and Biology Lab, Medicine Faculty of Andalas University. The research was did it on August 18 – September 08, 2010. Sample

population of this research are healthy female mice japan strain. The test that apply to mice japan strain, that fit with criteria of sample inclusion minimum 4x5 mice = 20 mice. Considering the possibility of dead mice, so in each group we 10% (2 mice) extra. With that calculation in total we need 30 female mice for this research.

RESULT AND DISCUSSION

Result

Based on normality trial we found variable of mice fetus body weight, number of mice uterus pocket, number of life mice fetus and number of defect mice fetus data, in normal distribution, means we can do parametic test of One way anova.

Table 1. The Average of mice fetus body weight mus mukulus female japan strain, in a group of control and treatment group.

Group	Body Weight of Fetus (gram) (Mean ± SD)	Min	Mak	p
Control	1,03 ± 0,15	0,9	1,2	0,143
PI (Vitamin A		0,8	1,4	0,143
Dose 3.250 IU/KgBB)	0,97 ± 0,24			
PII (Vitamin A		0,6	0,9	0,143
Dose 6.500IU/KgBB)	0,79 ± 0,11			
PIII (Vitamin A		0,9	1,1	0,143
Dose 13.000 IU/KgBB)	0,01 ± 0,12			

In table 1, anova test found point of P >0,05 which mean theres no significant difference of both group of mice.

Table 2. The Average number of female mice mus muskulus japan strain uterus bag between control group and treatment group.

Group	Number of mice Uterus bag (Mean ± SD)	Min	Mak	p
Control	10,20 ± 1,34	9,0	12,0	0,750
PI (Vitamin A		9,0	11,0	0,750
Dose 3.250 IU/KgBB)	9,60 ± 0,89			
PII (Vitamin A		8,0	12,0	0,750
Dose 6.500 IU/KgBB)	9,60 ± 1,67			
PIII (Vitamin A		6,0	12,0	0,750
Dose 13.000 IU/KgBB)	9,00 ± 2,55			

From table 3, the anova test found point of P >0,05 which means theres no significant difference of number of mice uterus bag in both group.

Table 3. The average of living birth rate of female mice mus muskulus japan strain, between control group and treatment group.

Group		Alive born mice fetus (Mean ± SD)	Min	Mak	p
Control		10,20 ± 1,34	9,0	12,0	0,000
PI (Vitamin A			8,0	10,0	0,000
Dose IU/KgBB)	3.250	9,00 ± 0,71			
PII (Vitamin A			5,0	8,0	0,000
Dose IU/KgBB	6.500	6,80 ± 1,34			
PIII (Vitamin A			1,0	6,0	0,000
Dose IU/KgBB	13.000	4,00 ± 1,87			

From table 3, anova test, it found point of p <0,05 which means there is significant differentiation, of average decreasing birth rate of living mice in a control group and treatment group. By that, we can continue with post hoc test bonferroni to see clearer if there is significant difference of average number of living mice birth rate.

Table 4. Average Loving Fetus Percentage.

Treatment Group	K	PI	PII	PIII
K	-	1,000	0,007	0,000
PI	1,000	-	0,126	0,000
PII	0,007	0,126	-	0,030
PIII	0,000	0,000	0,030	-

Keterangan :

K = Control without any treatment
PI = Treatment by giving Vitamin A Dose 3.250 IU/KgBB
PII = Treatment by giving Vitamin A Dose 6.500 IU/KgBB
PIII = treatment by giving Vitamin A Dose 13.000 IU/KgBB

Based on result of posthoc test bonfferoni, on table 3.3.1, its can be seen that the average living fetus in control group and T I shown significant difference P>0,05, while control group and P II also shows significant difference p <0,05, and between control group and P III also shows theres significant difference of p<0,05.

Table 5. The average mice mus muskulus japan strain fetus with congenital defect birth in control group an treatment group.

Group	Fetus Mice Born abnormal (Mean ± SD)	Min	Max	p
Control	0,00 ± 0,00	0,0	0,0	0,018
PI (intake of Vitamin A Dose 3.250 IU/KgBB	0,20 ± 0,45	0,0	1,0	0,018
PII (Intake of Vitamin A Dose 6.500 IU/KgBB	1,00 ±1,00	0,0	2,0	0,018
PIII (Intake of Vitamin A Dose 13.000 IU/KgBB	2,20 ±1,79	1,0	5,0	0,018

From table above, the anova test we found was point of P<0,05, which means there is significant difference, by increasing average number of mice fetus that born with congenital defect in control group and treatment group. Its means it is suggested to continue the research with post Hoc Test Bonfferoni, to see more clearly the significant difference of total number of mice that born with congenital defect.

Table 6. the Average differentiation of number of mice fetus that born with congenital defect in control group and treatment group.

Treatment Group	K	PI	PII	PIII
K	-	1,000	0,907	0,026
PI	1,000	-	1,000	0,049
PII	0,907	1,000	-	0,536
PIII	0,026	0,049	0,536	-

Information :

K = Control without any treatment
PI = Treatment by giving Vitamin A Dose 3.250 IU/KgBB
PII = Treatment by giving Vitamin A Dose 6.500 IU/KgBB

PIII = Treatment by giving Vitamin A Dose 13.000 IU/KgBB

Based on post hoc test bonfferoni, on table 5.5.1, it can be seen that the averae mice fetus born with congenital defect on control group and treatment group didn't shows any significant difference p>0,05, also in control group and P II didn't show any significant difference p >0,05, while control group and P IIIshows there was significant difference on p <0,05.

Table 7. Data of mice fetus born dead which not normally distributed and continue with non parametric test.

Group		Born Mice Fetus	p
		Death Intra Uterus (Mean Rank)	
Control		6,00	
PI (Vitamin A Dose IU/KgBB	3.250	7,30	0,014
PII (Vitamin A Dose IU/KgBB	6.500	13,40	
PIII (Vitamin A Dose IU/KgBB	13.000	15,30	

Based on Kruskal Wallis test, it shows that the average of death fetus born in intra uterus, in control group and P I, P II, P III, shows significant difference in P <0,05 and on 3 treatment group P III has the most high rate of mice fetus born death in intra uterus.

3.1 The observation to the fetus which got fixation with Bouin's liquid

Fetus that got fixation in Bouins liquid will get harder and turn into yellow. The observation found that there were change on eyelid, ear, the shape of tails, number of finger on front and back feet, anal genital gap and also a cleft palate, and it were found on treatment group.

From the observation we did, there were real difference of both control and treatment group. On control group, each fetus has two eyelid, two ears, normal shape of tail, and four normal feet with four finger on front feet, and five finger on back feet, have anal genital gap, and no cleft palate, while in treatment group we found many awkward body defect.

DISCUSSION

Jepang body weight of fetus mice mus muskulus japan strain

The result research on table 5.2 shows the average weight of fetus in every treatment groups are (PI = 0,97 + 0,24, PII = 0,79 + 0,11 and PIII = 1,01 + 0,12), this result are lower compares to control group 1,026 + 0,12.

Based on anova test we got a point of p = 0,143 (p>0,05) means theres no significant difference of average body weight of mice fetusbetween control group and all treatment group (PI, PII, PIII), because mice fetus body weight can be affected by how many fetus inside the mother womb. This is the same with result with research of Winknjosastro H (2002), who says that getting many the number of fetus in one mother, the body weight will getting smaller and also in contrary.

Number of mice mus muskulus japan strain fetus that born live.

Based on result of anova test we get point of p = 0,000 (p<0,05), means theres significant difference on a number of mice fetus born live in a control group and treatmen group (PI. PII, PIII). The following analysis by using post hoc test bonfferoni found that the average mice fetus born live in control group and treatment group showing no significant different p = 1,000 (p>0,05), its means the intake of Vit a dose 3.250 IU/KgBB didn't affected the number of live born mice fetus, while in control group and P III shows significan difference p = 0,007 (p<0,05), and control group with p III also significant difference p = 0,000 (p<0,05). Its means the intake of high dose vitamin A can affected the number of born live mice fetus.

This is the same with Yong T (2000) research which applied in two groups with treatment of giving high dose vitamin A to a pregnant white rat (Rattus Novergicus) through intra amnion, where resulted with finding 73.1% intrauterine dead fetus, and 18.9% of fetus didn't develop. This was the effect of alltrans retinoat which have teratogenic character, in big amount will cause somatic cell mutation at the beginning of

embryonic cell which affected organogenesis and resulted with failure development of early embrio. (Granner, 2009).

Based on research result that collected and theory about theres an effect of high dose vitamin A intake to the number of born live of mice fetus, that's why it continue with following research to find optimal dose of vitamin A intake that will not have teratogenic effect.

Number of Mice mus muskulus japan strain Fetus that born with defect

By using Anova test we get point of P=0,018 (p<0,05) which means there is significant difference on increasing number of fetus born with congenital defect on control group and treatment group. Further analysis by using post hoc test bonfferoni found that average fetus born defected in control group and P I didnt shows significant difference PI= 1,000 (p>0,05), also with control group and P II didn't shows significant difference P = 0,907 (p>0,05), while in control group and P III shows significant difference p= 0,026 (p<0,05). Its means that by having high dose vitamin A intake can affected to defected birth and kind of defect that appears.

Its fit with statement that made by Maryam S (2003), Limbong T, 2005 which says, Vitamin A, when you consumed in high dose can cause the symptom of many kind toxicity and individualistic and depends on how long we consumed until we stop that cause the failure of embryonic cell migration which cause slowing down the development and cause birth defect.

From the research it can be seen that the increasing of birth defect happen on the highest dose vit A intake (13.000 IU/KgBB), compares to ywo other group treatment and also control group. And this is why we need to do socialization on how to consume the vitamin A, the benefit, the harm especially to women on fertile age and couple on fertile age

Number of Dead mice mus muskulus japan strain fetus

Base on Kruskall – wallis test, it found that average fetus born dead in intrauterus, between control group and PI, P II, P III, shows significant difference p = 0,014 (p>0,05), and between three treatment on P III, they have significant point in intrauterus dead of mice fetus.

It also the same with research of Lestari (2004), who also found that vitamin A intake by intraperitoneal on pregnant white rat (rattus novergicus), can cause the increasing number of dead embrio inside the uterus, and the malformation external and internal, the defect on bone development and aksial frame and body part.

From another research it can be seen that there is an increasing number of intra uterus dead mice fetus because of the intake of Vitamin A (13.000 IU/KgBB), compares to 2 treatment group and control group, so, the distribution of Vitamin A need to be control and monitoring, cannot be included in free market medicine.

The description of kind of defect that appears on mice mus muskulus japan strain fetus after high dose vitamin A intake.

Fetus that been put on Bouin liquid had turn hard and yellow, it can be used to observe the outer layer and clip. The observing parameters are eyelid, ears, feet and finger. The result of the observation shows that group with high dose vitamin A intake 13.000IU/KgBB, have the highest rate of body defect compares to others two group, especially in a cavum abdomen formation, frame, and finger, that fit with teratogenic mechanism theory of hipertaminosis A, which disturbed the organogenesis of early embrio, especially on gastrulasi and neurolasi period.

This result also the same with research in India which using pregnant white rat, it found that high dose vitamin A intake by intra amnioncan cause 71%of fetus born alive and have congenital malformation, such as platoschizis (cleft palate), and other for of malformation of body part. (Mohanty S, Singh G: 2000.

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