

The Effect of Torbangun Leaves Tea on Msg-Induced Fetal Development Disorder in Mice

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Abstract. The safety of MSG on the fetus has not been confirmed yet. The objective of this research is to determine the effect of tea of torbangun leaves on fetal development disorder of mice. The present study is experimental with a Completely Randomized Design (CRD). Data obtained were then analyzed by ANOVA, with $p < 0,05$ as the level of significant. The comparison of mean values \pm SEM increase number of live fetuses group C1-T1 ($4,60 \pm 0,93$; $11,40 \pm 0,87$), $p=0,018$. The comparison of mean values \pm SEM decrease number of embryo re-sorption percentage group C0-C1 ($00,00 \pm 00,00$; $36,74 \pm 15,13$), group C1-C2 ($36,74 \pm 15,13$; $00,00 \pm 0,00$), group C1-T1 ($36,74 \pm 15,13$; $00,00 \pm 0,00$), and group C1-T2 ($36,74 \pm 15,13$; $15,00 \pm 22,36$), $p=0,020$. This study concluded that T1 group is giving the best effect on increasing life fetuses and decreasing embryo re-sorption percentage.

Keyword: Fetal Development Disorder, Monosodium Glutamate (MSG), Mice, Pregnancy

Abstrak. Keamanan MSG pada janin belum dikonfirmasi. Tujuan penelitian ini adalah untuk mengetahui pengaruh teh daun torbangun terhadap gangguan perkembangan janin mencit. Penelitian ini eksperimental dengan Rancangan Acak Lengkap (CRD). Data yang diperoleh kemudian dianalisis dengan ANOVA, dengan $p < 0,05$ sebagai tingkat signifikan. Perbandingan nilai rata-rata \pm SEM meningkatkan jumlah janin hidup kelompok C1-T1 ($4,60 \pm 0,93$; $11,40 \pm 0,87$), $p = 0,018$. Perbandingan nilai rata-rata \pm SEM menurunkan jumlah kelompok persentase serpihan embrio C0-C1 ($00,00 \pm 00,00$; $36,74 \pm 15,13$), kelompok C1-C2 ($36,74 \pm 15,13$; $00,00 \pm 0,00$), kelompok C1-T1 ($36,74 \pm 15,13$; $00,00 \pm 0,00$), dan kelompok C1-T2 ($36,74 \pm 15,13$; $15,00 \pm 22,36$), $p = 0,020$. Penelitian ini menyimpulkan bahwa kelompok T1 memberikan efek terbaik pada peningkatan janin hidup dan menurunkan persentase serpihan embrio.

Kata Kunci: Gangguan Perkembangan Janin, Monosodium Glutamate (MSG), Tikus, Kehamilan

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1. Introduction

Monosodium glutamate (MSG), almost easy to find in the world. Everybody maybe has tasted, but this product still controversial for the benefit of healthy [1]. When Dr Ho Man Kwok

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mengirim surat kepada The New England Journal of Medicine, 1968, who said, that he got a syndrome after ate food in China's Restaurant. That's we called Chinese Restaurant Syndrome (CRS), and then the issue about the safety of MSG was asking. CRS's syndrome was felt no sense on the neck, to arm, and back for about 2 hours, the syndrome will go [2].

In Medan, Indonesia, some people consume MSG with the higher dose, approximately half spoon every one bowl of noodle. Consumption of MSG with high doses will increase free radical (will increase lipid peroxidation process, which is signed by increased of malondialdehyde (MDA) [3]. The body will increase three enzymes to overcome those radical, that is super oxide dismutase (SOD), catalase dan peroxidase glutheparone. Those enzymes will increase the production of glutathione (anti-radical). Herbals have antioxidant, which can catch the free radical. One of them is to ban gun leaves. Torbangun leaves contain iron (zinc), carotenoids, polyphenol and antioxidant [4].

2. Methodology

Leaves of torbangun were collected from Karo, Sumatra, Indonesia. The leaves separated, cleaned, air-dried, coarsely powdered, and added by aquades, and boiled with 90^o Celsius, for 15 minutes. The extract of toboggan leaves is called in-fusion or tea.

Healthy 30 females of Double Ditsch Webster (DDW) mice were mated with healthy ten males of DDW mice. The next day, if we found vagina plug, in the female, we called the copulation were done, and the day was we called the zero-days of pregnancy 5.

We divided 30 pregnant mice into six groups. Group C0 (negative control, which received 0,3 ml aquades), group C1 (positive control, which received 4mg MSG per gram body weight each day), group C2 (positive control, which received 0.14 g tor-bangun leaves tea per 20g body weight each day), group T1 (treated with 4mg MSG/g body weight and 0.0728g torbangun leaves tea /20g body weight each day), and group T2 (treated with 4mg MSG /g body weight and 0.14g torbangun leaves tea /20g body weight each day). And group T3 (treated with 4mg MSG /g body weight and 0.28g torbangun leaves /20g body weight each day). All of the mice were killed with cervical dislocation and then dissected for the ovarium and fetuses removal.

Then, we observe the live fetuses, the body weight of fetuses, dead fetuses, embrio resort, implantation and corpus luteum. The results were expressed as the mean and analyzed using one-way ANOVA. Data were computed by statistical analysis using SPSS software. Differences between the data were con-sidered significant at $p < 0.05$.

3. Result

Data of fetal development were expressed in table 1.

Table 1. Fetal Development

G r o u p	Live fetuses	Body weight of fetuses (g)	Embryo resorp	Dead fetuses	implantation	Corpus luteum
C0	10.2	1.26	0	0	10.2	22
C1	4.6	1.35	3	0	7.6	20.6
C2	9	1.18	0	0.6	9.6	21.6
T1	11.4	0.94	0	0.4	11.8	26.2
T2	6.6	1.66	0.6	0	7.2	19.2
T3	9.4	1.28	0	0	9.4	21.8

The result is statistically significant on means of both live fetuses ($p = 0,018$) and embryo resorption ($p = 0,003$).

4. Discussion

Many factors influence fetuses life, such as implantation period disorder, and pra implantation or pasca implantation. Preimplantation disorder period does not allow the fetuses reached and moved into the endometrium, then the fetuses will fall and finally lost, that we called aborted.

In normal condition, fetal implantation failed at approximately 10%-15%. Out of 70-75% survived implantation, an approximately survive up to second week up is 58% and 16% are normal. Therefore only 42% of ovum will meet the spermatozoa would have survived. However, out of this number, some will be aborted afterwards or delivered abnormally [5].

In this research, we found that among the control group (C0) preimplantation lost is 56.43% which is normal and others groups are more or less similar.

Giving MSG 4mg/gBW (C1) can cause the decreased number of live fetuses with mean is 4 [6], then control group (C0) 10.2, which is significantly, with $p = 0.018$. The meaning is giving high doses of MSG during pregnancy caused the dangerous effect on the development of fetuses. These results concordant with Sabri [5] and Sufitni [7].

This study shows that the daily consumption of 4mg/g body weight of MSG significantly increased the number of embryo resorption in C1 (mean = 3) than in C0 (mean = 0) ($p = 0,003$).

It proves that consumption of high dose MSG during pregnancy can lead to the dangerous effect of the development of fetuses such as increasing the number of embryo resorption, consistent with other previous studies [5].

Increased embryo resorption in T1 group, maybe caused by the high dose of consumption MSG, and then increased MSG metabolic, and then will increase free radical, and oxidative stress have done. Giving tea of torbangun leaves, with the best dose 0.28g/20gBW/day during pregnancy, which has given MSG, caused positive effect, increased number of live fetuses, and decreased number of embryo resorption. That's condition likely control group.

The best dose for tea of torbangun leaves is a T3 group (0.28g/20gBW/day) because we still found dead fetuses in T1 group and embryo resorption in T2 group.

The decreasing of survival mammalian's embryo caused by dysfunction of mitochondria, and decreasing of available of ATP. During embryo development, metabolic cells will produce ROS in extracellular. The effect of ROS on embryo development is normally blocking development of an embryo. More and more product of embryo development, more ROS would produce. After fertilisation, the beginning of embryo development is based on gen expression from its maternal. Then, the expressions will avoid ROS, with the helping of GSH (growth stimulating hormone) from its maternalc [8].

Mice embryo genes are activated with 2 stage cells. Without expression genes from embryo maternal to avoid ROS, will cause the embryo need higher ATP for their development. Oxidative stress also cause vary damaged in cells, included lipid peroxidation layers, amino acid oxidation, apoptosis and necrosis, which decreasing successfully embryo product in vitro [9].

Death of fetus is very few so that will not be significant for statistical result. Meaning that this is a normal case. Some implantation and corpus luteum on C1 group, almost same as others groups. This research concordant with Sabri [5] and Sufitni [7].

After that, this research shows that high consumption rate of MSG will cause damage in preimplantation and pasca implantation. MSG consumption in early pregnancy will damage embryo until gastrulation phase (forming three germinal layers on the embryo, when started the first beginning of primitive streak). Primitive streak in mice did on pregnancy 6,5 day. Damaged embryo on gastrulation phase, is difficult to fix. If we cannot reducing our consumption of MSG, then we should consume some antioxidants.

5. Discussion

Giving high doses of MSG on mice during pregnancy will give embryotoxic effect, characterized by decreasing the number of live fetuses and increasing the number of embryo resorption

significantly. But, giving them tea of Torbangun leaves can reduce embryotoxic of MSG effect, particularly they are giving together will increase the number of live fetuses and decrease the number of embryo resorption.

REFERENCES

- [1] E. A. Berkes and K. M. Woessner, "Monosodium glutamate," *Food Allergy: Adverse Reactions to Food and Food Additives*, p. 342, 2003.
- [2] R. K. Bush, S. L. Taylor, and S. L. Hefle, "Adverse reactions to food and drug additives," *Allergy: principles and practice*, vol. 2, pp. 1183–1198, 1998.
- [3] K. Beyreuther *et al.*, "Consensus meeting: monosodium glutamate—an update," *European journal of clinical nutrition*, vol. 61, no. 3, p. 304, 2007.
- [4] C. M. Santosa and T. Hertiani, "Phytochemical compounds and the effect of 'bangunbangun' leaves (*Coleus amboinicus*, L.) water extract on phagocytosis activity of neutrophil cell rat (*Rattus norvegicus*)," *INDONESIAN JOURNAL OF PHARMACY*, pp. 141–148, 2005.
- [5] E. Sabri, "Efek Perlakuan Ekstrak Andaliman (*Zanthoxylum Acanthopodium*) Pada Tahap Praimplantasi Terhadap Fertilitas Dan Perkembangan Embrio Mencit (*Mus Musculus*)," *Efek Perlakuan Ekstrak Andaliman (*Zanthoxylum Acanthopodium*) Pada Tahap Praimplantasi Terhadap Fertilitas Dan Perkembangan Embrio Mencit (*Mus Musculus*)*, 2007.
- [6] T. W. Sadler, *Langman's medical embryology*. Lippincott Williams & Wilkins, 2011.
- [7] Sufitni -, Delyuzar -, and E. Sabri, "Efek Pemberian Madu terhadap Lesi Hepar Maternal Mencit Terpapar Monosodium Glutamate (MSG) selama Masa Kehamilan," *1*, vol. 22, no. 2, May 2013.
- [8] P. F. N. Silva, "Physiology of peroxidation processes in mammalian sperm (Thesis).[Utrecht (Netherland)]: Utrecht University," 2006.
- [9] Y. Kitagawa, K. Suzuki, A. Yoneda, and T. Watanabe, "Effects of oxygen concentration and antioxidants on the in vitro developmental ability, production of reactive oxygen species (ROS), and DNA fragmentation in porcine embryos," *Theriogenology*, vol. 62, no. 7, pp. 1186–1197, 2004.