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## Number of foetus in pregnant *Mus musculus* which was injected by anti Qa2 and given mild regular exercise: endothelial dysfunction animal model to induce preeclampsia

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# Number of foetus in pregnant *Mus musculus* which was injected by anti Qa2 and given mild regular exercise: endothelial dysfunction animal model to induce preeclampsia

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**Abstract.** Preeclampsia community guideline (PRECOG) defined preeclampsia as a condition which was identified by the diastol blood pressure  $\geq 90$  mmHg and proteinuria in  $\geq 20$  weeks of pregnant. Basic mechanism of preeclampsia was endothelial dysfunction. One of preeclampsia's impacts was intra uterine fetal death. It could be signed by less number of foetus. One of ways to prevent preeclampsia's process was mild regular exercise. This research's goal was analyzing the effect of mild regular exercise to number of foetus in pregnant *Mus musculus* which was injected by anti QA2 as endothelial dysfunction animal model to induce preeclampsia. The design was experimental. It used 6 *Mus musculus*/group. The groups were control (normal pregnant/K1), pregnant *Mus musculus* which was injected by anti QA2 (endithelial dysfunction model/K2), pregnant *Mus musculus* which was injected by anti QA2 and given mild regular exercise since early pregnant (K3), and pregnant *Mus musculus* which was injected by anti QA2 and given mild regular exercise since 1 week before pregnant (K4). Statistical analyze used Kruskal Wallis Test ( $\alpha=0,05$ ). It showed there was no significant different of foetus' number among all groups. The conclusion was there was no effect of mild regular exercise to number of foetus in pregnant *Mus musculus* which was injected by anti QA2 as endothelial dysfunction animal model to induce preeclampsia.

## 1. Introduction

*Preeclampsia community guideline* (PRECOG) defined preeclampsia as a condition which was identified by diastol blood pressure  $\geq 90$  mmHg and proteinuria in  $\geq 20$  weeks of pregnant [1]. Basic mechanism of preeclampsia was endothelial dysfunction, that could give global impact [2]. Preeclampsia could give impacts to mother and foetus. One of its impact in foetus was intra uterine fetal death and neonatal death [3]. One of signs that could show impact of preeclampsia was number of foetus.

One of ways to prevent preeclampsia's process was mild regular exercise. Mild regular exercise could increase cardiorespiration function that was suitable for hypertension like preeclampsia [4]. Mild regular exercise would increase interleukin 6 (IL6) which would induce interleukin 10 (IL10) production as anti inflammation agent [5]. Mild regular exercise also increased endogen antioxidant such as superoxide dismutase (SOD), katalase, and glutathione peroxide [6]. Inflammation and oxidative stress were preeclampsia's mechanisms, so mild regular exercise was assumed to prevent endothelial dysfunction as preeclampsia's process.



One of ways to make endothelial dysfunction in animal model was injecting anti QA2 to block placental QA2 expression. Placental QA2 expression was similar with placental *human leucocyte antigen-G* (HLAG) expression in human. Blocking of HLAG was predictor of endothelial dysfunction [7].

This research's goal was analyzing the effect of mild regular exercise to number of foetus in pregnant *Mus musculus* which was injected by anti QA2 as endothelial dysfunction animal model to induce preeclampsia.

## 2. Methods

This research was true experimental using post test only with control group design. This research used female *Mus musculus* that was mated by male *Mus musculus* 1:1. Female *Mus musculus* with positive vaginal plug were used in the research. The vaginal plug was the sign those female and male *Mus musculus* were mated and the pregnant was called 0 day.

*Mus musculus* that were used must be 3 months, healthy, bodyweight 15-25 grams, well moving, no wound found in the body, and clear eye. This research used 6 pregnant *Mus musculus*/groups. The duration of research was 5 weeks, consisted of acclimatization, mating female and male *Mus musculus*, intervention, and termination.

All of female *Mus musculus* were injected by pregnant mare serum gonadotropine (PMSG) and human chorionic gonadotropine (HCG) to equate oestrus cycle. Female *Mus musculus* was injected by 5 IU PMSG intra peritoneal, after 48 hours they were injected again by HCG 5 IU intra peritoneal. After that, female *Mus musculus* were mated by male *Mus musculus* 1:1.

Tomorrow morning after mating, female and male *Mus musculus* were seperated. Female *Mus musculus* were examined if they had positive vaginal plug or not. Pregnant *Mus musculus* were who had positive vaginal plug, and randomize into 4 groups (6 pregnant *Mus musculus*/group).

The location was in Laboratory of Embriology, Faculty of Veterinery, Airlangga University. This research consisted of 4 groups: K1 (control, normal pregnant), K2 (pregnant *Mus musculus* which was injected by anti QA2 as endothelial dysfunction model), K3 (pregnant *Mus musculus* which was injected by anti QA2 and given mild regular exercise since early pregnant), and K4 (pregnant *Mus musculus* which was injected by anti QA2 and given mild regular exercise since 1 week before pregnant).

Mild regular exercise used treadmill with no angle. Treadmill used speed on 7 cm/second for 1 minute, 11 cm/second for 2 minutes, and 14 cm/second for 15 minutes. This exercise was done since early pregnant for K3, and 1 week before pregnant for K4. The exercise was done once in 2 days.

The termination was done in the 19<sup>th</sup> day of pregnant. The abdomen was dissected to open the uterus, and the number of foetus was calculated.

## 3. Results and Discussion

Data of this research was taken by calculating the number of foetus in the uterus of *Mus musculus* after termination. Mean of the number showed in table 1. Data was in normal distribution but not homogen, so it was analyzed by Kruskal Wallis Test.

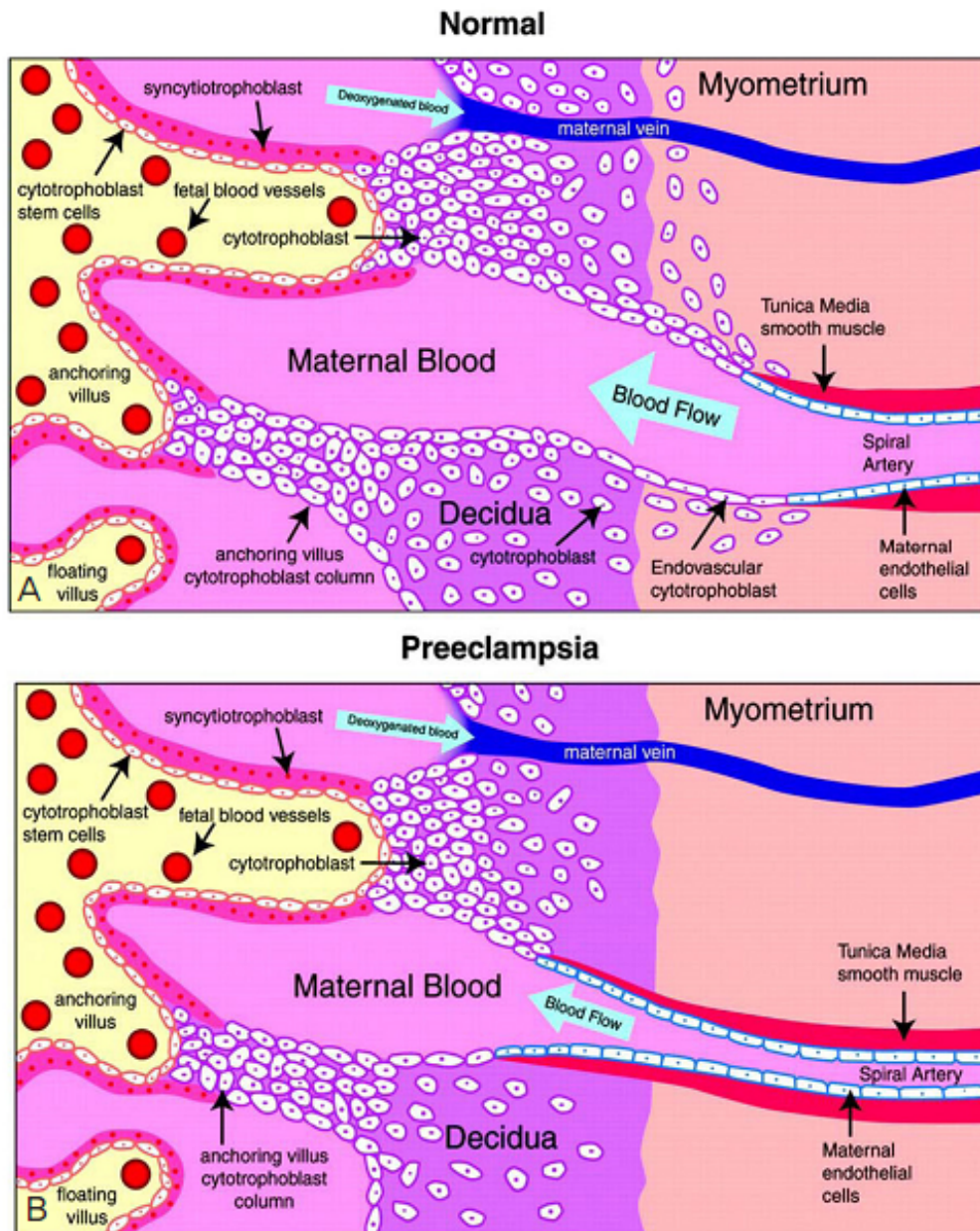
**Table 1.** Mean of foetus number in all of group.

GROUP	MEAN	SD	p VALUE	$\alpha$ VALUE
K1	10	1,095	p=0,111	0,05
K2	8,5	1,76	(Kruskal Wallis Test)	
K3	7,8	8,18		
K4	10,7	2,33		

p value > 0,05 means there was no significant differences (K1: control/normal pregnant; K2: pregnant *Mus musculus* which was injected by anti QA2 as endothelial dysfunction model; K3: pregnant *Mus musculus* which was injected by anti QA2 and given mild regular exercise since early pregnant; and K4: pregnant *Mus musculus* which was injected by anti QA2 and given mild regular exercise since 1 week before pregnant).

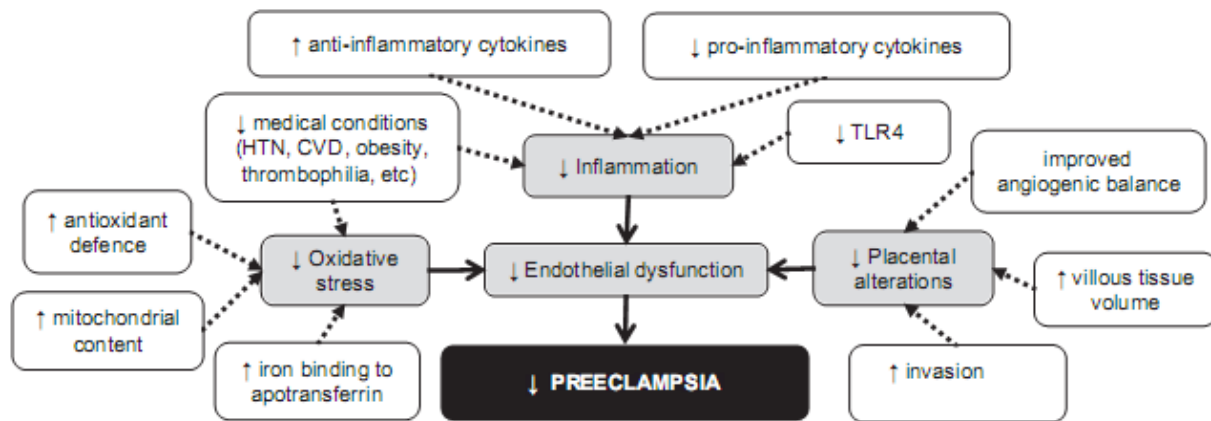
Table 1 showed that number of foetus in normal pregnant (K1) was more than in endothelial dysfunction model (K2). That fact could be caused by placental abnormality. Preeclampsia's placenta

had infarct and sclerosis of blood vessels. So, it caused the failure of endovascular invasion and inadequate of spiral artery's remodelling (Figure 1). This condition made oxygen and nutrition to foetus decreased [8]. Decreasing of oxygen and nutrition could make intra uterine fetal death or resorbtion of foetus in *Mus musculus*, so the number of foetus became less.



**Figure 1.** Comparison of placentation in preeclampsia and normal pregnant [8].

Table 1 also showed that number of foetus in K3 was less than K2. K3 was given mild regular exercise since early pregnant, and K2 was endothelial dysfunction animal model. It showed that mild regular exercise since early pregnant was not suitable enough for reducing the impact of preeclampsia to foetus. It could be caused by exercise in this case could not produce enough IL10 and endogen antioxidant as the protection of body to preeclampsia process. But if the exercise was done since 1 week before pregnant, it could increase the number of foetus. Exercise 1 week before pregnant could as early initiation of body process. If it was continued until pregnant, it was a chronic effect that made positive effect to the body. So, the regular exercise 1 week before pregnant could produce enough IL10 and endogen antioxidant to prevent the impact of preeclampsia's process especially to foetus. Process of anti inflammation and antioxidant from exercise like Figure 2.



**Figure 2.** Mechanism of exercise to prevent preeclampsia [9].

Enough IL10 and endogen antioxidant could activate endothelial cell to make its function became better [10]. So, the endothelial dysfunction did not happen, and endovascular invasion became adequate to distribute oxygen and nutrition to foetus. It prevented intra uterine fetal death.

Table 1 showed that Kruskal Wallis test had no significant differences, so there was no different number of foetus in all groups. It showed that the production of IL10 and endogen antioxidant was not enough significantly to stabilize the pregnant *Mus musculus* with endothelial dysfunction model. It was similar to Tomic *et al.* (2013) that showed there was no significant difference in intra uterine growth restriction and ather perinatal outcomes. In this research, the causes were decreasing of glucose level, frequency, duration and intensity of the exercise [11].

Another reason of no significant difference in this research was the type of exercise that was given to the groups. The exercise in this research was treadmill with no angle. Research of Kurniawati (2015) showed positive effect of exercise in pregnant women significantly, using aquarobic. Aquarobic was mild exercise, it could increase oxygen consumption and make the muscle strong. The result of her research was pregnant women in the third trimester had steady blood pressure and heart rate after given aquarobic for 1 month, twice in a week, and the duration of aquarobic in each exercise was 1 hour [12].

But we could see the different in descriptive data. So, the mild regular exercise actually had given positive effect but it was need to analyze more about the type of exercise to optimize the effect.

#### 4. Conclusion

The conclusion was there was no significant effect of mild regular exercise to number of foetus in pregnant *Mus musculus* which was injected by anti QA2 as endothelial dysfunction animal model to induce preeclampsia.

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