Mephenamic Acid Treatment Toward Follicles Development and Progesterone

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Abstract. Mefenamat acid is anti-inflammation non steroid which can hamper prostaglandin synthesis in the body tissue by hampering siklooxigen enzyme. The purpose of this research is to find out the influence of mefenamat acid toward the follicles development and progesterone level. This research his experimental laboratory method. The subject of the research divided into five groups randomly selected and have been homogenized. One group as control group and others as experimental group with various dos age of Mephenamic Acidtreatment. The data is analyzed to discover average difference the quantity off ollicles and blood progesterone level using one way Anova test. The results of this research is confirmed the significantly difference of Grafian follicles, yello wish corpus luteumand proges terone level as the influence of Mephenamic Acidin 0.5 mg/kg, 1mg/kg, 1.5 mg/kg, and 2 mg/kg; while there was no significantly difference intertiary follict les development. The decrease of corpus luteumis caused by mefenamat acid activity to hamper the prostaglandin synthesis in the body tissue by hampering siklooxigen enzyme. Prostaglandincan make follicles swelling and cause follicles fracture and make ovulation. The granulosis cell will makecorpus luteumwhich secreted progesterone hormone. Mephenamic Acid was proven to avoid ovulation that blocked the formation of yello wish corpus luteum result ingin the decreased of blood progesterone level.

Keywords: Blood Progesterone Level, Experimental, Follicles Development, Mephenamic Acid,

1. Introduction

Nonsteroidalanti inflammatory drugs (NSAIDs) is a medicine which often used the fertilize woman in the world. [1]Nonsteroidalanti inflammatory drugs (NSAIDs) is chemical compound which has anti inflammation, analgesic, and antipyretic activity. It is very useful medicine used in all the world.[2]. Nonsteroidalanti inflammatory drugs (NSAIDs) also can reduce artritis pain because of sikloksigenase hampering. [3]. Mefenamat acid is also the group of Nonsteroidalanti inflammatory drugs (NSAIDs) which has effect anti inflamation, analgetic, and antipieuretic.[4][5]. The work of mefenamat acid as Nonsteroidalanti inflammatory drugs (NSAIDs) is hampering the prostaglandin synthesis by hampering the work of cyclooxygenase enzyme (COX-1 & COX-2).[6][7][8][9]The enzyme system COX catalized the important prostaglandin biologically. An isoenzyme, namely,COX-2, active in ovarium during the follicle development. The hampering of COX-2 by inhibitor of NSAID and COX-2 estimate can cause the follicle syndrome of folikel luteinized unrupturedreversibel (LUFS). The syndrome is signed with the ovulation failure. [1]

Nonsteroidalanti inflammatory drugs (NSAIDs) has proven to hamper the ovulation and reduce the progesteron level for young woman and can disturb the fertilize seriously.[10]. The result of research

after 10 days of NSAIDs using, there is the decrease of progesterone significantly. NSAIDsalso influence the follicle dominantly.[11]. The NSAIDscan influence the ovulation, it need more attention although the potential complication has explained in medical literature, more than two decade. [1]
The result of Brouwer J (2017) find out that the woman with rheumatoid arthritis, using NSAIDs tend to get ovulation postponing which can explained, compared with the people with rheumatoid arthritis without NSAIDs. The data shows there is a relationship between conception and NSAIDs using. The using of mefenamat acid to avoid premature ovulation of dissimulation still being debatable, viewed from the cost for medicine to avoid the expensive premature increasing. Based on the background above, to get more oosit, it is hoped the embryo gotten is more and it is ovulation e to transfer the embryo more than one to make the possibility of pregnancy, so the purpose of this research is to find out the influence of mefenamat acid giving toward the follicle development and progesteron level from the mice whose gotten the PMSG and HCG. It is hoped the research will give positive suggestion to choose the medicine for avoiding the ovulation for the reproduction technique treatment.

2. Methods

It is laboratory experimental by using posttest only control group design.This research used adult woman mice (Musmusculus) with the weight about 20 gram. The research used 30 miece which divided into 5 groups. Control group(P1) is given aqua dest,t reatment group(P2,P3,P4,and P5)is given mefenamat acidperoralwith the dosage 0,5mg/kgBB, 1mg/kgBB,1,5mg/kgBB,2mg/kg BB of weight which stimulated withPMSG5 IUdanHCG5 IU before, and the result is compared with control.
Difictationo varium with the solution during 24 hours. The making of histology preparation by HematoxylinEosin (HE).The supply is examined under the microscope with the zoom100x,seen from 5 views. The measurement of progesterone by using Elisa method.Five groups is compared by using one direction Anova test. The next test is using LSD(leastsignificant difference),while the number of olikelde Graaf and corpusluteum used Kruskal-Wallis test because the data is heterogenetic.

3. Results

a. The differentiate of Mice Ovarium Follicles Follicle Development (Musmusculus) as the result of mefenamat acid giving

The research shows that mefenamat acid giving with the doses 0,5 mg/Kg BB, 1 mg/Kg BB,1,5 mg/Kg BB, 2 mg/Kg BB cause the meaningful differentiate toward the number of follicle. From the research is gotten the higher folikel de Graaf of groupP2, P3, P4, dan P5, and the number of corpus is lower. Forfolikeltersier, the number is the same because folikeltersier still can develop becomefolikel de Graaf before ovulation. For control group, the number of corpus luteumis higher, the number of folikel de Graafis the same between group P2 and P3, while, the number offolikeltersier is higher than group P2. The number of folikel de Graafas increase as the increasing of mefenamat increasing while the number of corpus will decrease. The result of Anova one folikeltersiergot the meaningless differentiate. ($p > 0,05$) and the result of kruskal-Wallis test show the number of folikel de Graafandcorpusluteumgot meaningful different terdapatperbedaan ($p < 0,05$).
The number of *corpus luteum is caused by the activity of mefenamat acid which has work mechanism by hampering the prostaglandin synthesis in the body tissue with hampering the siklooxigen enzyme* (COX-1 dan COX-2).[6].Prostaglandinhas a role for follikel swelling, it caused ovulation, the rest of granulose will form *corpus luteum*because the yellowish color will secret the progesterone hormone. Unfertilized oosit will cause *corpus luteum*become white corpus.
Normal menstrual cycles require the maturation of the complex feedback system of the hypothalamic-pituitary-gonadal (H-P-G) axis. The mature system involves orderly and sequential release from the pituitary of luteinizing hormone (LH) and follicle- stimulating hormone (FSH), in response to gonadotropin-releasing hormone from the hypothalamus. This results in the growth and maturation of follicles in the ovary, oocyte maturation, and estrogen and progesterone secretion. In the initial follicular phase of a normal menstrual cycle, increasing levels of FSH stimulate the maturation of an ovarian follicle as well as the secretion of estrogen. Estrogen, in turn, stimulates endometrial proliferation. In an ovulatory midcycle, the rising level of estrogen switches from a negative feedback mechanism on both LH and FSH to a positive mechanism. The resulting surge of LH precipitates the release of an oocyte from a mature follicle. The second half of the menstrual cycle, the luteal phase, is character- ized

primarily by secretion of progesterone as well as estrogen by the corpus luteum formed by the residual follicle.[12]

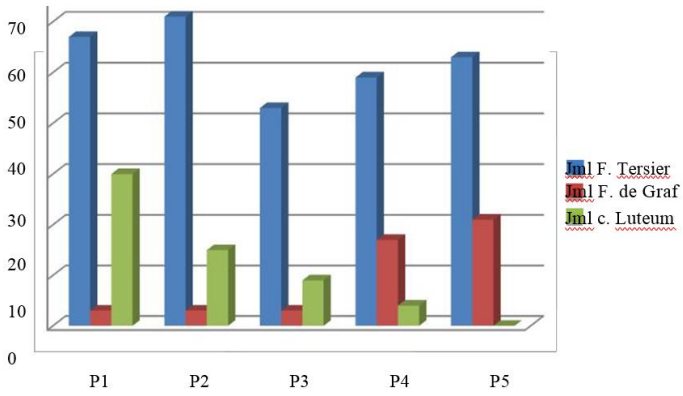

Figure 1.The graphic of folikelnumber of miceovarium of all treatment group.

b. The differentiate of progesterone level of mice blood (*Musmusculus*) because of mefenamat acid giving.

The result of mice blood examination to measure progesterone level is gotten the decrease of progesterone level as the increasing of mefenamat acid doses given. It caused the number of *corpus luteum*is lower for P2, P3, P4, and P5, while for control group is gotten the high progesterone level. It caused the number of *corpus luteum*of control group is higher than group P2, P3, P4, and P5 so the level of progesterone level is higher than another treatment group.

The result of anova test one direction, the level of progesterone get the meaningful differentiate ($p < 0,05$). The result of BNT shows that the progesterone levelget meaningful differentiate for group P1 – P2, group P1 – P3, group P1 – P4, group P2 – P5, group P3 – P5, and group P4 – P5. For group P2 has the average progesterone level is higher than group P3, P4, and P5, while for control group (P1) the average of progesterone level is higher than another group.

Mefenamat acid is NSAIDs group which work by reducing prostaglandin level[2][13][14].Progesteron level will decrease doses group 0,5 mg/Kg BB, 1 mg/Kg BB,1,5 mg/Kg BB, 2 mg/Kg BB caused the use of mefenamat acid to avoid the ovulation by hampering prostaglandin synthesis in the body tissue (COX-1 & COX-2).[6][15]. The prostaglandin itself has the role to freeze the follicle swelling which caused the break of follicle with the ovulation.The follicle will collapse after ovulation, get into luteal phase, and menstrual cycle will begin. The rest of granulosis cell will form the *corpus luteum*because the colour is yellowish and secrete the progesterone hormone. The increasing mefenamat acid doses given the corpus luteum also will increase and will influence the level of low progeteron level.

Progesteronis the steroid hormone which involved the estrus and pregnancy cycle.Progesteron produce the corpus luteum in ovarium after ovulated in adrenal gland which located near the kidney, also in placenta during the pregnancy. The increasing of progesterone level means the ovulation has happened and the level of progesterone in the midluteal phase. [16].

The research of [17]there is an ovulation disturbance for the patient whose getdiklofenak, naproksen&etorikoksib significantly. Diklofenakis the highest ovulation resistor compared with two others medicine (naproxen &etoricoxib). There is the decrease of progesterone level compared with control group significantly. The conclusion, this research will has dangerous effect for the woman fertilize.

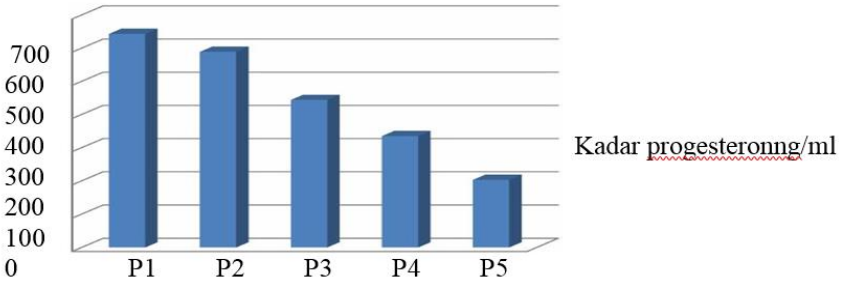

Figure 2. The graph of progesteron of miceblood.(ng/ml)for manytreatment group.

4. Conclusion

There is a meaningful difference between the fol like development, fol like de Graaf, corpus luteum, and protester on level because of mefenamic acid giving doses 0,5mg/Kg BB,1mg/Kg BB,1,5mg/Kg BB, 2mg/Kg BB but there is no meaningful difference for fo likely tarsier.

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