Mefenamic acid treatment to ward follicles development and progesterone level

S Aminah¹, D Lutfiasari², D K Prasetyanti³, M E Fitriasnani 4

¹,²,³,⁴ Health Sciences Faculty Kadiri University, Selomangleng street 1, Kediri, Indonesia

Email: sitiaminah@unik-kediri.ac.id

Abstract. Mefenamic acid is anti-inflammation non-steroid, which can hamper prostaglandin synthesis in the body tissue by hampering the siklooxigen enzyme. The purpose of this research is to find out the influence of Mefenamic acid toward the follicles development and progesterone level. This research is an experimental laboratory method. The subject of the research divided into five groups randomly selected and have been homogenized — one group as a control group and others as an experimental group with various dosages of Mefenamic acid treatment. The data is analyzed using a one-way Anova test. The results of this research are confirmed the significant difference of Grafian follicles, yellowish corpus luteum and progesterone level as the influence of Mefenamic acid. While there was no significant difference in tertiary follicles development. The decrease of corpus luteum is caused by Mephenamic acid activity to hamper the prostaglandin synthesis in the body tissue by hampering the siklooxigen enzyme. The prostaglandin can make follicles swelling and cause follicles fracture and make ovulation. The granulosis cell will make corpus luteum, which secreted progesterone hormone. Mefenamic acid was proven to avoid ovulation that blocked the formation of yellowish corpus luteum resulting in decreased blood progesterone level.

Keywords: Mefenamic acid, follicles development, blood progesterone level

1. Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) is a medicine which often used the fertilize woman in the world. [1] Nonsteroidal anti-inflammatory drugs (NSAIDs) is a chemical compound which has anti-inflammation, analgesic, and antipyretic activity. It is a very useful medicine used in all the world.[2]. Nonsteroidal anti-inflammatory drugs (NSAIDs) also can reduce arthritis pain because of sikl oksigenase hampering. [3]. Mefenamic acid is also the group of Nonsteroidal anti-inflammatory drugs (NSAIDs), which has an effect on anti-inflammation, analgesic, and antipyretic.[4][5]. The work of Mefenamic acid as Nonsteroidal anti-inflammatory drugs (NSAIDs) is hampering the prostaglandin synthesis by hampering the work of the cyclooxygenase enzyme (COX-1 & COX-2).[6][7][8][9] The Enzyme system COX catalyzed the important prostaglandin biologically. An isoenzyme, namely, COX-2, active in ovarium during the follicle development. The hampering of COX-2 by an inhibitor of NSAID and COX-2 estimate can cause the follicle syndrome of follicle luteinized unruptured reversible (LUFs). The syndrome is signed with the ovulation failure. [1]

Nonsteroidal anti-inflammatory drugs (NSAIDs) has proven to hamper the ovulation and reduce the progesterone level for a young woman and can disturb the fertilize seriously.[10]. The result of research after ten days of NSAIDs using, there is a decrease of progesterone significantly. NSAIDs also influence the follicle dominantly.[11]. NSAIDs can influence ovulation. It needs more attention, although the potential complication has explained in medical literature, more than two-decade. [1]

The result of Brouwer J (2017) finds out that the woman with rheumatoid arthritis, using NSAIDs tend to get ovulation postponing, which can be 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 Mefenamic acid to avoid premature ovulation of dissimulation still be debatable, viewed from the cost for the medicine to avoid the expensive premature increasing. Based on the background above, to get more post, 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 Mefenamic acid giving toward the follicle development and progesterone level from the mice whose gotten the PMSG and HCG. It is hoped the research will give positive suggestions to choose the medicine for avoiding ovulation for the reproduction technique treatment.
2. Methods

It is a laboratory experimental by using the posttest only control group design. This research used adult woman mice (Mus musculus) with a weight of about 20 grams. The research used 30 mice divided into five groups. Control group (P1) is given aqua dest, treatment group (P2, P3, P4, and P5) is given Mephenamic acid per oral with the dosage 0.5 mg/kg bb, 1 mg/kg bb, 1.5 mg/kg bb, 2 mg/kg BB of weight which stimulated with PMSG 5 IU dan HCG 5 IU before, and the result is compared with control.

Dictation ovarium with the solution for 24 hours. The making of histology preparation by Hematoxylin Eosin (HE). The supply is examined under the microscope with the zoom 100x, seen from 5 views — the measurement of progesterone by using the Elisa method. Five groups are compared by using one direction Anova test. The next test is using LSD (least significant difference), while the number of likely de Graaf and corpus luteum used the Kruskal-Wallis test because the data is heterogenous.

3. Results And Discussion

1. The differentiate of Mice Ovarium Follicles Follicle Development (Mus musculus) as the result of Mefenamic acid giving

The research shows that Mephenamic acid giving with the doses 0.5 mg/Kg BB, 1 mg/Kg BB, 1.5 mg/Kg BB, 2 mg/Kg BB causes the meaningful differentiate toward the number of the follicle. From the research is gotten, the higher likely de Graaf of group P2, P3, P4, dan P5, and the number of the corpus is lower. For follicle terrier, the number is the same because the follicle terrier still can develop become follicle de Graaf before ovulation. For the control group, the number of corpus luteum is higher. The number of follicle de Graaf is the same between-group P2 and P3, while the number of follicle terriers is higher than group P2. The number of follicle de Graaf as increases as the increasing of Mephenamic increasing while the number of corpus will decrease. The result of Anova one follicle terrier got the meaningless differentiate. (p> 0.05) and the result of the Kruskal-Wallis test shows the number of follicle de Graaf and corpus luteum got meaningful different (p < 0.05).

The number of corpus luteum is caused by the activity of Mefenamic acid, which has a working mechanism by hampering the prostaglandin synthesis in the body tissue with hampering the siklooxigen enzyme (COX-1 dan COX-2).[6]. Prostaglandin has a role for follicle swelling, and it caused ovulation. The rest of the granulose will form a corpus luteum because the yellowish color will secret the progesterone hormone. Unfertilized posit will cause a corpus luteum to become a 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 hypothalumus. 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 anovulatory 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 characterized primarily by secretion of progesterone as well as estrogen by the corpus luteum formed by the residual follicle.[12]
2. The differentiate of progesterone level of mice blood (Mus musculus) because of Mefenamic acid giving.

The result of mice blood examination to measure progesterone level is gotten the decrease of progesterone level as the increasing of Mefenamic acid doses given. It caused the number of corpus luteumis lower for P2, P3, P4, and P5, while the control group is gotten the high progesterone level. It caused the number of corpus luteum of the control group is higher than group P2, P3, P4, and P5, so the level of progesterone level is higher than in 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 level gets 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 the control group (P1), the average progesterone level is higher than in another group.

Mefenamic acid is NSAI Ds group which work by reducing prostaglandin level[2][13][14]. Progesterone 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 Mefenamic acid to avoid the ovulation by hampering prostaglandin synthesis in the body tissue (COX-1 & COX-2).[6][15]. The prostaglandin itself has a role in freezing the follicle swelling, which caused the break of the follicle with the ovulation. The follicle will collapse after ovulation, get into the luteal phase, and the menstrual cycle will begin. The rest of the granulosa cell will form the corpus luteum because the color is yellowish and secrete the progesterone hormone. The increasing Mephenamic acid doses given the corpus luteum also will increase and will influence the level of low progesterone level.

Progesterone is the steroid hormone which involved the estrus and pregnancy cycle. Progesterone produces the corpus luteum in ovarium after ovulated in the adrenal gland located near the kidney, also in the placenta during the pregnancy. The increasing of progesterone level means the ovulation has happened and the level of progesterone in the mid-luteal phase. [16].

The research of [17] there is an ovulation disturbance for the patient who gets diclofenac, naproxen & etoricoxib significantly. Diclofenac is the highest ovulation resist or compared with two other medicine (naproxen & etoricoxib). There is a decrease in progesterone levels compared with the control group significantly. The conclusion, this research will have a dangerous effect on the woman fertilize.
4. Conclusion
There is a meaningful difference between the follicle development, follicle de Graaf, corpus luteum, and progesterone level because of Mefenamic acid giving doses 0.5 mg/KgBB, 1 mg/KgBB, 1.5 mg/KgBB, 2 mg/KgBB but there is no meaningful difference for follicle terrier.

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