EFFECT OF GIVING CELECOXIB ON URIC ACID LEVEL ON MICE

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ABSTRACT

Celecoxib is a breakthrough for pain relievers under the trade name Celebrex®, which is a Non-Steroid Anti-Inflammatory drug with its activity as an analgesic, antipyretic and anti-inflammatory. The purpose of this study was to find out the effect of celecoxib on blood uric acid levels of female white mice was induced with fresh cow liver extract. Experimental animals were divided into five groups, namely the control group (-), the control group (+) and the three dose groups, respectively 0.26, 0.52 and 1.04 mg/20 g. Observations were made on 7, 14 and 21 days with the Enzymatic Photometric method. The results showed that administration of celecoxib suspension at a dose of 0.26, 0.52 and 1.04 mg/20 g did not affect blood uric acid levels when compared with controls (P> 0.05).

Keywords: Celecoxib, Non-steroidal anti-inflammatory, Uric Acid,

INTRODUCTION

Celecoxib is a breakthrough for pain relievers under the trade name Celebrex®, which is a Non-Steroid Anti-Inflammatory drug (NSAID) with its activity as an analgesic, antipyretic and anti-inflammatory. This Celecoxib includes Non-Steroid Anti-Inflammatory which selectively inhibit the enzyme cyclooxygenase 2 (COX-2) and was permitted to circulate in 1999 (Meek *et al*., 2010). In the form of white powder, difficult to dissolve in water, dissolved in methanol, ethyl acetate and acetone (Raval *et al*., 2010). Refoxocib is also classified as a selective NSAID against the COX-2 enzyme in which its chemical structure is similar to celecoxib. Refoxocib was introduced in 1999 and obtained permission to circulate in Indonesia starting from 2001. However, this drug has been withdrawn from circulation since 2004 due to an increase in cardiovascular risk in the form of heart attacks and strokes due to thrombotic events. Celecoxib and Refoxocib can be used as uric acid medicine because Refoxocib is a circulation permit (Zarghi & Arfaei, 2011).

After being withdrawn, this study was conducted to see the effect of Celecoxib on uric acid levels in white mice. Uric acid is the final product of purine degradation in the body. Uric acid including weak acid with pKa 5.4 in the form of white crystals, odorless and tasteless, and very difficult to dissolve in water (Hediger, 2004). Uric acid is produced in the liver, bone marrow and muscles. In these organs, there are anti-oxidase enzymes that can convert purines into uric acid, mainly with the presence of xanthine oxidase (Murray, 2012; Suyono, 2001).

Uric acid disorders are caused by high levels of uric acid in the blood, causing a buildup of crystals in joint areas that can cause pain (Murray, 2012; Milind *et al*., 2013). To reduce this pain is usually given NSAID (Ong *et al*., 2007). However, there have been no clinical reports about the effect of Celecoxib on uric acid levels. The purpose of this study was to find out the effect of celecoxib on blood uric acid levels of female white mice with the Enzymatic Photometric method. The results of this study are expected to be additional input for pharmacists, researcher, and physician in providing drug treatment appropriately and rationally so that the risk of errors in the use of NSAID drugs can be minimized and drug interactions can be avoided.

MATERIAL AND METHODS

Tools and Materials

The equipment used includes Analytical scales, animal scales, animal cage, oral needles, measuring cup, micropipette, drop pipette, test tube, test tube rack, Erlenmeyer, beker glass, centrifuge, centrifuge tube, spatula, mortar and stamfer, Philips 50/60 Hz blender, tweezers, label, knife, spectrophotometer, Genesis Thermospectronic 20. The materials used in this study were Celecoxib (Celebrex®), Na-CMC, distilled water, fresh cow liver, reagent Uric Acid FS TBHBA (DiaSys®) consisted of:

Reagent 1
- Phosphate buffer pH = 7,0 100 mmol/L
- TBHBA (2,4,6-tribromo-3-hidroksibenzoic acid)1 mmol/L

Reagent 2

- Phosphate buffer pH = 7,0100 mmol/L
- 4aminoantypyrine 0,3 mmol/L
- K4[Fe(CN6)]10 µmol/L
- Peroxidase (POD) ≥ 2 kU/L
- Uricase ≥ 30 U/L

Standard: UricAcid 6mg/dl (375µmol/L)

Reaction Principle:

$$\text{Urid Acid} + H_2O + O_2 \xrightarrow{\text{Uricase}} \text{Allantoin} + CO_2 + H_2O$$

$$\text{TBHBA} + \text{4-aminoantypyrin} + 2\,H_2O_2 \xrightarrow{\text{POD}} \text{Quinonimine} + 3H_2O$$

Methods

Celecoxib was obtained from the identified Matrix Laboratories factory. The experimental animals used in this study were 75 white mice aged ± 3 months. Mice were grouped into 5 groups. Each group of mice was placed in a separate cage. Before the study was carried out, mice were adapted for 7 days and given standard food. Animals fulfill healthy requirements if during the observation they do not show significant weight changes (<10%) and visually do not show unhealthy symptoms. Production of preparations has been conducted as follows:

Liver Homogenate

- 100 grams of fresh cow liver washed, cut into small pieces, put in a blender tube, plus 25 ml distilled water, then blended until smooth, strain and put into a container.

Making Na CMC 0,5%

- Weighing Na-CMC as much as 0.125 g, then developed in distilled water as much as ± 2.5 ml then scoured homogeneously and sufficiently with distilled water until 25 ml.

Making Test solutions

- The test solution was made by suspending Celecoxib in 0.5% Na CMC, where the test substance was weighed according to the dose then added 0.5% Na CMC which had been developed, then crushed to a homogeneous period and diluted with distilled water until the volume needed.

The dose of Celecoxib in humans is used 100, 200 and 400 mg. After being converted into mice, it was obtained 0.26 mg/20 g, 0.52 mg/20 g, and 1.04 mg/20 g.

Data Analysis

Data processed statistically using two-way Variance Analysis (ANOVA). If it is significantly different then proceed with Duncan's New Multiple Range Test (DNMRT) at the smallest significant difference level of 1% and 5%

RESULTS AND DISCUSSION

Table 1. The effect of Celecoxib administration on uric acid levels of average on average female white mice on days 7, 14, and 21

Treatment	Average serum of uric acid levels on the day			Total	Average ± SE
	7	14	21		
I	2,32 ± 0,28	3,18 ± 1,43	4,37 ± 0,57	9,87	3,29 ±
II	3,24 ± 0,72	4,03 ± 1,50	2,86 ± 0,95	10,13	3,37 ±
III	1,67 ± 0,55	2,62 ± 0,98	2,76 ± 1,61	7,05	2,35 ±
IV	2,97 ± 0,99	2,38 ± 1,11	2,19 ± 0,35	7,54	2,51 ±
V	3,82 ± 1,98	1,97 ± 0,61	2,34 ± 0,06	8,13	2,71 ±
Total	14,02	14,18	14,52	42,72	14,24
Total ± SE	2,80 ±	2,84 ±	2,90 ±	8,54	2,85

Description :
I = negative control group
II = positive control group
III = Celecoxib dose 0.26 mg / 20g BB
IV = Celecoxib dose 0.52 mg / 20g BB
V = Celecoxib dose 1.04 mg / 20g BB

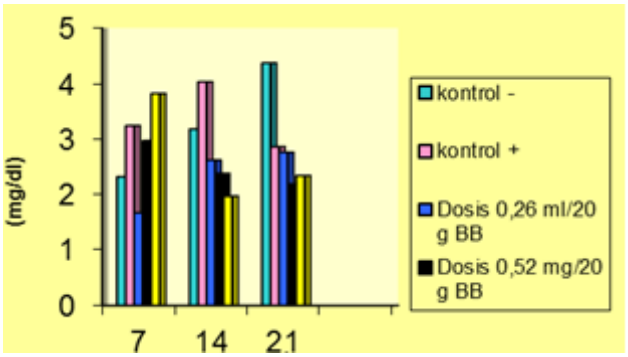

Figure 1. A bar chart of the relationship between serum uric acid levels and female white mice time

In this study celecoxib was suspended in 0.5% Na-CMC which served as an inert carrier and celecoxib powder was evenly dispersed. Celecoxib suspension was given orally in experimental animals with various levels of doses of 0.26 mg/20 g, 0.52 mg/20 g, and 1.04 mg/20 g. The use of Celecoxib dose was 0.26 mg/20 g, 0.52 mg/20 g, and 1.04 mg/20 g is based on multiples of 2 (Zarraga & Schwarz, 2007).

In this study, experimental animals were given induction of the uric acid formation is the extract of cow liver as much as 0.5 mL/20 g orally for 7 consecutive days before treatment and continued during treatment, thus uric acid levels are high so that the effect of oral administration of celecoxib can be known. Selection of cow liver extract to increase uric acid levels in experimental animals because this cow liver contains 150-1000 mg of a purine for every 100 g of cow liver. Celecoxib is given orally because this route of administration is more commonly used, easy to

administer, safe and it does not hurt experimental animals (Lascelles *et al*., 2007).

Measurement of uric acid levels in the blood of mice is carried out by enzymatic methods which involve enzymatic uric acid oxidation reactions. The selection of the above measurement method is based on the simple process, namely the level of uric acid is directly known, is more sensitive and is a common method used in clinical laboratories (Pasalic *et al*., 2012).

ANOVA test results (in table I), there was a significant effect on the decrease in blood uric acid levels in mice, where animals with the lowest doses of Celecoxib (0.26 mg/20 g) showed a decrease in the highest blood uric acid levels of 2.35 mg/dl. Whereas with increasing doses of 0.52 mg/20 g and 1.04 mg/20 g there was an increase in blood uric acid levels of mice, 2.51 mg/dl and 2.71 mg/dl.

The results of this study, if calculated using statistics, we can compare the control group (+) with the celecoxib group with a dose of 0.26 mg/20 g, the celecoxib dose group 0.52 mg/20 g, and the celecoxib group 1.04 mg/20 g. Likewise, the control group (-) with celecoxib group dose 0.26 mg/20 g, celecoxib group 0.52 mg/20 g, with significant differences between control (+) and control (-) with the dose of celecoxib have different abilities in reducing uric acid levels, on the other hand, giving celecoxib with other doses, there was no significant difference, there was no difference in reducing blood uric acid levels (Burns & Wortmann, 2012). However, after analyzing with Duncan 's, it did not show any effect of giving celecoxib to blood uric acid levels of mice.

CONCLUSION

From the results of the study, it can be concluded that the administration of celecoxib at various doses (0.26 mg/20 g, 0.52 mg/20 g, and 1.04 mg/20 g) does not affect uric acid levels in the blood for 21 days.

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