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Allopurinol Administration: When is More Effective?

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***Abstract*—Objectives: The objective of the study was to determine the appropriate administration time of allopurinol between morning and night administration. Method: This research was conducted in a controlled and open label. Eleven patients (six in night and five in morning) were fulfilled the criteria. Results and Discussion: no significant difference in the uric acid reduction between night and morning administration (p 0.435). However, night administration of allopurinol showed lower uric acid level reduction (-2.45 vs -0.98). In adverse reactions events, the night administration of allopurinol contributed to nausea and flatulence. Conclusion: Allopurinol provides better uric acid reduction at night but should be caution of the side effects.**

Keywords: allopurinol, uric acid, hyperuricemia

I. INTRODUCTION

The reports of The Global Burden of Disease, stating that the incidence of hyperuricemia is relatively common in the Asian region[1]. Indonesia hyperuricemia prevalence reached 24.7% with the three highest regions, East Nusa Tenggara (33.1%), West Java (32.1%) and Bali (30%)[2]. Hyperuricemia can lead to several risks such as pain, mortality, and morbidity of cardiovascular disease, urolithiasis, and kidneys damage [3-5]. Allopurinol is the first line of choice in the treatment of hyperuricemia by various guidelines such as the American College of Physicians (2016), European League Against Rheumatism (2016), Australian and New Zealand (2015), 3e Initiative, Multinational Evidence, Expertise, Exchange Initiative (2013), American College of Rheumatology (2012), and British Society of Rheumatology (2007)[6]. However the most effective allopurinol administration time in reducing uric acid concentrations is still unknown. Therefore, we conducted a study to determine the best administration time to reduce uric acid levels.

II. MATERIAL AND METHOD

A. Procedure

Design Study

The study was an open label, controlled and non-randomized, which conducted from February to April 2019. The inclusion criteria was hyperuricemia diagnosed, informed consent approved, not pregnant, not suffering from chronic renal failure, and not in chemotherapeutic. Patients who met the criteria were divided into two groups, first group received allopurinol 100 mg once daily in the morning and the second group received allopurinol once daily at night for 10 days. The study was approved by Kesbangpol with number 007/1190 / KESBANGPOL / 2018.

Determination of Uric Acid

On day 1 the patient was examined for fasting uric acid levels (Baseline level) on both groups. At the end of the study, on the 10th-day patients was examined again for fasting uric acid levels. The difference between the last day of examination and the first day (baseline) were used to determine the comparison of the decrease in uric acid concentration on both groups. The uric acid examination was using Easy Touch GCU 3 in 1.

B. Data Analysis

The data were analyzed using the t-test method using SPSS version 16.00.

III. RESULTS

Table 1. Patients Characteristic

Patients Characteristic		
Gender	∑	%
Male	6	54,5
Female	5	45,5
Total	11	100
Age		
26-35	1	9,1
46-55	3	27,3
56-65	4	36,4
> 65	3	27,3
Total	11	100

Male was dominated compared to the female (54.5% vs 45.5%). In addition, patitents with age of 56-65 were dominated on this study

Table 2. Uric Acid Concentration

No	Group	Patients Number	Average ± SD	p
1	Night	6	-2.450 ± 3.7591	0.435
2	Morning	5	-0.980 ± 1.4873	

The night administration was give a better decrease in uric acid concentration compared with the morning group, although the difference was not statistically significant (p 0.435).

Table 3. Adverse Effect Incidence

No	Group	Patients Number	Adverse Effect Incidence	Manifestation
1	Night	6	2	Nausea and Bloating
2	Morning	5	-	No AE was Observed

The night administration group of allopurinol showed a better reduction effect compared to the group given allopurinol in the morning. However, the night administration group gave manifestations of side effects such as nausea and flatulence in 2 patients compared to the morning group which none experienced side effects. There was no research subjects withdrawal on this study.

IV. DISCUSSION

Based on the results of the study in patients characteristic showed male was more dominated on hyperuricemia disease, this condition may due to the genetic differences that result in different functions[7]. Estrogen in female can increase uric acid excretion in the kidneys[8]. However, after menopause, the risk of hyperuricemia in female is increased[9]. Allopurinol is effective to reduce the uric acid concentration in hyperuricemia disease, and night administration is better than morning in uric acid reduction (-2.450 ± 3.7591 vs -0.980 ± 1.4873). Allopurinol decreases the concentration of uric acid through the inhibition of the xanthine oxidase enzyme which converts xanthine to uric acid [10]. The better results at night time administration of allopurinol may be due to the uric acid production that occurs at night and the highest concentration of gout occurs at night[11]. Furthermore, the attack of hyperuricemia can increase during the night and early morning, it may be due to at 2:00 a.m - 6:00 a.m. the body temperature ranges between 36.4 ° C and this lower body temperature in the early hours of the morning potentially causing a higher risk of crystallization of uric acid, which triggers gout attacks [11]. However, the night administration group was give manifestations of side effects such as nausea and flatulence.

V. CONCLUSION

Allopurinol provided better uric acid reduction at night administration but should be caution of the side effects.

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