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EFFECTS OF SIDAGURI (SIDA RHOMBIFOLIA L) ON URIC ACID AND C-REACTIVE PROTEIN (CRP) IN PATIENTS WITH GOUTY ARTHRITIS

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ABSTRACT

Introduction: Gouty arthritis is a metabolic disease associated with a high diet of purines and alcohol consumption. Monosodium urate crystal accumulation (MSU) in joints and soft tissues is the main trigger of inflammation in gouty arthritis. This disease can adversely affect the quality of life of the patient. Increased levels of uric acid in the blood (hyperuricemia) is the main cause of gouty arthritis. One of the medicinal plants is sidaguri (Sida rhombifolia L), has been known to have the potential of antigout and anti-inflammatory activities by inhibiting nitric oxide.

Method: This randomized controlled trial was conducted in Adam Malik Hospital and Prof. Dr. Boloni Hospital Medan from April- October 2018. Patients randomized to receive Sidaguri extract (Sida Rhombifolia L) and meloxicam or placebo and meloxicam in a double-blind technique. Sample size of each of group was 20 patients. Data were statistically analyzed.

Result: 40 Gouty arthritis patients divided into 2 groups: Sidaguri group (20 patients) and Placebo group (20 patients). Based on the T-dependent test, there was significant differences of uric acid and CRP serum before and after treatment between Sidaguri group and Placebo group in Gouty arthritis patients (p=0.0001).

Conclusion: There was significant differences between uric acid levels and CRP before and after treatment of Sidaguri.

KEYWORDS : Sidaguri, Gouty Arthritis, Uric Acid, CRP

1. INTRODUCTION

Gouty arthritis is a metabolic disease associated with a high diet in purines and alcoholic consumption. Monosodium urate crystal accumulation (MSU) in joints and soft tissues are the main triggers for inflammation in gout arthritis. Gout arthritis is the third most common type of arthritis after osteoarthritis and other rheumatic diseases (disorders of joint supporting components, inflammation, overuse).[1]

This disease disrupts the quality of life of the patient. Increased levels of uric acid in the blood (hyperuricemia) is the main cause of gout arthritis.2 Problems arise when deposition of monosodium urate (MSU) crystals are formed within the joints and surrounding tissues. These needle-shaped crystals cause an inflammatory reaction which, if continued, will cause severe pain that often accompanies gout arthritis.[3]

NHANES III 1988 to 1994 data in the United States showed that gout arthritis affects more than 3 million men who age 40 or older, and 1.7 million 40 year-old or older women.4 In 2007 to 2008, the number of patients with gouty arthritis increased to 8.3 million, in which the number of people with gout arthritis in men amounted to 6.1 million patients and women 2.2 million. This shows that the prevalence of gouty arthritis in the United States has increased in the past two decades.[5]

In Indonesia there has not been much epidemiological publication about gout arthritis. According to the Health Service of Central Java Province, the number of cases of gout arthritis from year to year has increased in comparison with other non-infectious diseases cases. In 2007 the number of cases of gout arthritis in Tegal by 5.7% increased to 8.7% in 2008, from medical record data at Kardinah General Hospital during 2008 recorded 1068 patients both inpatients and outpatients who examined uric acid levels 40% of whom suffer from hyperuricemia.[6]

Changes in traditional lifestyle to modern lifestyle are the main triggers of gout arthritis. Most cases of gout arthritis have a primary cause background, thus requiring long-term control of uric acid levels. A good communication with patient is needed to achieve therapeutic goals. It can be obtained by education and a low purine diet is good. Other prevention in the form of decreased alcohol consumption and weight loss.[7]

Indonesia is the world's biodiversity mega-flashlight, and ranks second richest in the world after Brazil. In Indonesia is estimated to live around 40,000 plant species, there are 9,600 species of plants as nutritious medicinal plants and approximately 300 new species used as a traditional medicine by the traditional medicine industry. Therefore, it is necessary to develop traditional medicines in a sustainable and integrated manner so that Indonesia's natural wealth can be maximally utilized to improve public health services.8 One of the medicinal plants is sidaguri plant (Sida rhombifolia L)that has been known with potential as antigout and has anti-inflammatory activity by inhibition of nitric oxide. In relation to the background, the data, and the results of the above study, the researcher wanted to know how the influence of Sidaguri (Sida rhombifolia L) on the inflammatory process in gout arthritis patients by checking inflammatory marker ie C-Reactive Protein (CRP) and serum uric acid as biomarker of gout arthritis, before and after getting sidaguri extract treatment.

2. METHOD

2.1. Patient Selection

The research was conducted in a randomized controlled clinical with parallel design method with treatment group (Sidaguri Group) and control group (Placebo group) independently and randomized. Samples to be used in this study were all patients with the diagnosis of Gout Arthritis at Haji Adam Malik Hospital Medan and in Prof. Dr. Boloni hospital Medan starting from April 2018 until October 2018. The sample size for each study group was 20 patients. Blood sampling was performed at the cubital fossa area of the study subjects for Uric Acid and CRP examinations one day before getting treatment and 30 days later. A randomized double blind method was obtained in treatment groups receiving Sidaguri extract (Sida Rhombifolia L) with meloxicam and a control group that received placebo-containing drugs with Meloxicam in simple random sampling with some sealed envelopes that were not transparent and given odd and even numbers on the rolled of paper in it. Inclusion criteria was subjects with age above 17 years both men suffering from Arthritis Gout disease. Subjects receive informed consent for physical and laboratory examination and use Sidaguri (Sida rhombifolia L) drugs and NSAID-containing drugs from start to finish desired by the Medical Research Ethics Committee of USU Medical Faculty. Exclusion criteria was patients with impaired liver, kidney function, and diseases that cause an inflammatory reaction.

2.2. STATISTICAL METHODS

Data analysis was performed through univariate and bivariate analyses using the SPSS 22nd version (SPSS Inc., Chicago) with a 95% confidence interval. Bivariate analysis was performed using T-dependent test with significance p<0,05.

3. RESULT

Among 20 patients who received Sidaguri extract (Sida rhombifolia L), 13 (65%) were male and 7 (35.00%) were female. Based on the education level, 3 (15.00%) patients had elementary education, 1 (5%) had junior high school, 14 (70%) had senior high school and 2 (10%) were bachelor. Based on respondents' work, 2 (10%) patients worked as civil, 6 (30%) were farmer, and 12 (60%) were self-employed. In placebo group, 12 (60%) were male and 7 (35.00%) were female. Based on the education level, 4 (20%) patients had elementary education, 4 (20%) had junior high school, 11 (55%) had senior high school and 1 (5%) were bachelor. Based on respondents' work, 2 (10%) patients worked as civil, 5 (25%) were farmer, and 13 (65%) were self-employed.

Table 1. Baseline Characteristic in Sidaguri and Placebo Group

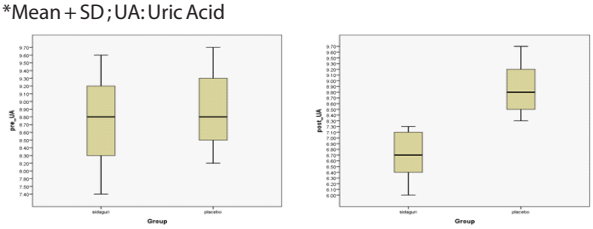
Characteristic	Sidaguri Group n=20	Placebo Group n =20
Gender, n (%)		
Male	13 (65)	12 (60)
Female	7 (35)	8 (40)
Age, n (%)		
40 – 50	7 (35)	1 (5)
51 – 60	9 (45)	10 (50)
61 – 70	4 (20)	9 (45)
Education level, n (%)		
Elementary	3 (15)	4 (20)
Junior high school	1 (5)	4 (20)
Seniorhigh school	14 (70)	11 (55)
Bachelor	2 (10)	1 (5)
Work, n (%)		
Civil Servant	2 (10)	2 (10)
Farmer	6 (30)	5 (25)
Self-employed	12 (60)	13 (65)

The mean ± SD value of uric acid pre-treatment and post treatment were 8.65 + 0.64 and 6.68 + 0.39 respectively in Sidaguri group, and 8.85 + 0.43 and 8.86 + 0.42 respectively in placebo group. In this study, a T-dependent test showed that there was significant differences of uric acid serum before and after treatment in Sidaguri group (p=0.0001) but there was no differences of uric acid serum before and after treatment in Placebo group (p=0,776) (Table 2).

Table 2. Comparison of serum levels of Uric Acid (Pre Treatment and Post Treatment) in Sidaguri Group and Placebo Group

Variables	UA Pre Treatment	UA Post Treatment	p value
Sidaguri Group*	8.65 + 0.64	6.68 + 0.39	0.0001
Placebo Group*	8.85 + 0.43	8.86 + 0.42	0.776

*Mean + SD ; UA: Uric Acid



(A) (B)

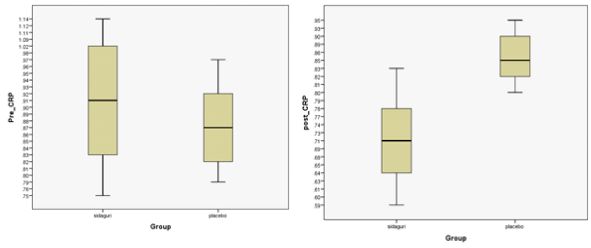
Figure 1. Box Plot of Uric Acid levels in Sidaguri Group and Placebo Group (a) Pre treatment (b) Post treatment

The mean ± SD value of CRP serum level pre-treatment and post treatment were 0.92 + 0.12 and 0.71 + 0.08 respectively in Sidaguri group, and 0.87 + 0.06 and 0.87 + 0.05 respectively in placebo group. In this study, a T-dependent test showed that there was significant differences of CRP serum before and after treatment in Sidaguri group (p=0.0001) but there was no differences of CRP serum before and after treatment in Placebo group (p=0,368) (Table 3).

Table 3. Comparison of serum levels of CRP (Pre Test and Post Test) in Sidaguri Group

Variables	CRP Pre treatment	CRP Post Treatment	Sig.
Sidaguri Group*	0.92 + 0.12	0.71 + 0.08	0.0001
Placebo Group*	0.87 + 0.06	0.87 + 0.05	0.368

CRP : C-Reactive Protein, *Mean + SD



(A) (B)

Figure 2. Box Plot of CRP levels in Sidaguri Group and Placebo Group (a) Pre treatment (b) Post treatment

3. Discussion

Sidaguri extract showed a better response on day-30 based on the change of uric acid level compared to placebo, which descreased significantly from 8.65 to 6.68 while placebo group did not show a significant decrease.

This result is in line with experimental research conducted by Rizky, et al (2018) who examined the effect of the combination of sidaguri leaf extract and red ginger rhizome in patients with hyperuricemia. The results concluded that the combination of ethanol extract of Sidaguri (Sida rhombifolia L) leaves had better antihyperuricemia activity than the control group.9 Research conducted by Iswantiny, et al (2014) proved the potential of antigout in sidaguri. This study showed that extract of sidaguri flavonoids has an inhibitory power against xantine oxidase enzymes up to 71% and spectrophotometric measurements show that the flavonoid extract has a competitive inhibition mechanism.10 Research conducted by Harahap, et al (2017) also concluded that the extract of sidaguri (Sida rhombifolia L.) has an effect in decreasing uric acid through inhibition of xanthine oxidase enzymes (p <0.05).[11]

A statistical significant decrease of CRP serum level was shown in sidaguri group, which falling from 0.923 to 0.708, but not in control group, which only decrease from 0.869 to 0.866.

These results are in line with research conducted by Marpaung, et al (2018) who reported a decrease of CRP level average in patients with osteoarthritis patients after consuming Sidaguri (Sida rhombifolia L.) leaf extract, and further explained that sidaguri has an anti-inflammatory effect (p <0.005). Research conducted by Tanumihardja, et al (2016) found that sidaguri ethanol extract had an anti-inflammatory effect as proven by a significant decrease in CRP levels when compared with the control group (p <0.005).[12]

Several studies have reported various phytochemical content in various parts of the sidaguri plant, especially in the leaves. In general, the leaves contain alkaloids, calcium oxalates, tannins, saponins, phenols, amino acids, and essential oils. Sidaguri stems contain calcium oxalate and tannins. While the root part contains alkaloids, steroids and efedrine. Isolation and identification of a

mixture of steroids, porphyrins, flavones, and alkaloid Indoquinolones were carried out in ethanol extracts of leaf and stem sidaguri plants. Rough extract of sidaguri flavonoids is shown to inhibit XO up to 55% and to decrease uric acid. The flavonoids contained in the extract of Sidaguri leaves have the effect of xanthine oxidase inhibition, therefore reduce the production of excess uric acid. Levels of uric acid expressed through urine by diuresis process, in this case sidaguri plants have diuretic effects.[13,14]

Some studies also mention that sidaguri has anti-inflammatory benefits. Phytochemical compounds contained in Sidaguri are alkaloids and ecdysteroids which play an important role in inhibiting prostaglandin biosynthesis by blocking cyclooxygenase. The active compound of β-sitosterol in sidaguri plants also has an anti-inflammatory activity by inhibition of nitric oxide. Other compounds suspected of having anti-inflammatory activity in the leaves of Sidaguri are flavonoids and saponins.[15,16]

4. CONCLUSION

There were significant changes in uric acid and CRP levels in patients with gouty arthritis after consuming sidaguri (Sida rhombifolia L.) extract.

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