# Comparison of C-Reactive Protein Levels and Erythrocyte Sedimentation Rates to Osteoarthritis Patients with Sidaguri Extract Treatment within 1 Month and 2 Month

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Abstract: Osteoarthritis (OA) is defined as a heterogeneous condition that leads to joint sign and symptoms caused by defective integrity of articular cartilage and inflammation. CRP is a sensitive acute phase reactant with levels rapidly rising in many inflammation conditions. ESR is an indirect measure of the level of inflammation in the body. The management of OA limited in the pain and inflammation control with any NSAID. Meloxicam is one of NSAID that inhibits the synthesis of prostaglandins by inhibiting at least 2 cyclo-oxygenases (COX) isoenzymes. Sidaguri plant (*Sida rhombifolia L.*) is one of the most important species of the medicinal part in Indonesia as anti-inflammation, by inhibition of nitric oxide and protein denaturation inhibitions. Our study recruited 50 patients with OA divided into two groups, patients who get Meloxicam and Sidaguri (n = 25) and patients with Meloxicam and placebo (n = 25). There were significant differences before, one month, and two months after therapy with p-value <0.001, and the Sidaguri combination with meloxicam is better in reducing CRP and ESR levels.

## 1 INTRODUCTION

According to the American College of Rheumatology (ACR), osteoarthritis (OA) is defined as a heterogeneous condition that leads to joint sign and symptoms which are caused by defective integrity of articular cartilage. (Sarzi-Puttini et al., 2005)

OA is one of the most common chronic disorder among the elderly. WHO Scientific Group on Rheumatic Diseases data found that approximately 40% of people over the age of 70 years developed this disease. More than 65 years of age are at risk of having OA. The prevalence of OA was 80% and have some degree of limitation of movement. (Organization, 2003) The disease is characterized by degenerative process and mechanical disturbance with the gradual erosion of joint cartilage. Prevalence of OA was found to increase with age and enzymatic sequence that triggers a response which ended in the destruction of joints. (Dahaghin et al., 2005)

Assessment of pain usually used in OA is the visual analog scale (VAS). The pain VAS is self-completed by the respondent. The score is classified as 1 to 4 (on a 0-10 scale). The mild pain is treated with non-opioid analgesics with or without adjuvant therapy, 5 to 6 scale as moderate pain treated with non-opioid analgesics, weak opioid analgesics with or without adjuvant therapy, and 7 to 10 as severe pain treated with strong opioids analgesics with or without adjuvant therapy. (Jensen et al., 2003)

The ACR use non-steroidal anti inflammatory drugs (NSAIDs) as the main drug of OA. The Agency for Healthcare Research and Quality (AHRQ) reported the use of non-opioid analgesics for OA as primary and secondary treatment. The European League Against Rheumatism (EULAR) recommendations for the management of OA recommend paracetamol as the first line treatment, with topical agents such as topical NSAID and capsaicin. The American Heart Association Scientific Statement on the use of NSAIDs and the American College of Cardiology Foundation consensus recommend reducing the risk of gastrointestinal (GI) adverse events in patients using antiplatelet and NSAID therapy. (Hochberg et al., 2012)



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Meloxicam is one of NSAID member of oxicam class that inhibits the synthesis of prostaglandins in cells settle in a specially designated tube of anticoagulated blood, an effect that is altered by proteins associated with an inflammatory response (Assasi et al., 2015)

CRP is merely an indicator or biomarker of a disease process that is caused by cell death due to inflammation. C-reactive protein (CRP) is a protein produced by the liver as a response of inflammation and infection. It is an extremely sensitive acute phase reactant with levels rapidly rising 1000 times or more in many disease condition. ESR is an indirect measure of the level of inflammation in the body. ESR measures the rate at which red blood body tissue by inhibiting at least 2 cyclo-oxygenases (COX) isoenzymes. (Davies and Skjodt, 1999) From an international perspective, WHO has agreed to promote the use of traditional medicine, complementary medicine for health that focuses on people centered on health services and encourages the use of security and the efficacy of the traditional medicines related to licensing and products, training and practitioners. (Aditama, 2014)

Sidaguri plant (*Sida rhombifolia L.*) is one of the most important species of the medicinal part in Indonesia as anti-inflammation. The anti-inflammatory activity effects by inhibition of nitric oxide and protein denaturation inhibitions. Potent anti-inflammatory effect of root of Sidaguri on rat periapical lesion model caused by β-sitosterol, a sterol isolated of different species of Sidaguri, which is reported to have anti-inflammatory properties, similar to hydrocortisone and oxyphenbutazone. (Khalil et al., 2006)

# 2 METHODS

## 2.1 Patient Selection

This randomized, independently and a double-blind controlled clinical trial was performed from April 2017 until November 2017 in Haji Adam Malik Hospital and Prof. Dr. Boloni Hospital in Medan. This Study enrolled patients diagnosed with osteoarthritis. CRP, ESR, RFT, LFT levels were measured from blood samples collected from the cubital fossa area at one day before treatment, 30 days and 60 days later. The patients were randomly divided into two groups: one group with sidaguri extract and meloxicam and the other group with meloxicam and placebo, in simple random sampling with some sealed envelope that was not transparent and given odd and even numbers on the rolled of paper in it.

## 2.2 Inclusion and Exclusion Criteria

In inclusion criteria, all the subjects aged over 40 years of both men and women with OA, with VAS ≥ 4, no impaired liver and kidney function and other causes of inflammatory reaction.

## 2.3 Statistical Methods

To display epidemiological data of the subject of the research, we used tabulation to show the descriptive picture. Data were processed and analyzed using SPSS Version-24 program with $p < 0.05$ significance.

# 3 RESULT

This study involved 50 patients who fulfilled the inclusion criteria, the patients were equally divided into two groups: patients who received Meloxicam with Sidaguri ( n=25) and the other group who received Meloxicam with placebo (n=25). The patients were monitored before treatment, one month and two months after treatment. Nine patients (69,2%) who received Meloxicam therapy and placebo were male. Meanwhile, 21 patients (56,8%) who received meloxicam and sidaguri were female. The baseline characteristics showed no significant differences between the two groups (p-value =0,017)

Table 1. Basic characteristics

| Characteristics | | Therapy | | P-Value |
|---|---|---|---|---|
| | | Meloxicam& Placebo (MP) | Meloxicam&Sidaguri (MS) | |
| Gender | Male | 9 (69.2%) | 4 (30.8%) | 0.107 |
| | Female | 16 (43.2%) | 21 (56.8%) | |
| Age | | 58.92 ±10.43 | 59.64 ± 11.39 | 0.817 |

Table 2: Significance Test Differences in laboratory results based on Meloxicam and Placebo Therapy

| Variable | Mean | n | Standard Deviation | P-Value |
|---|---|---|---|---|
| ESR-PRE | 22.88 | 25 | 2.205 | <0.001 |
| ESR-1 month | 22.40 | 25 | 2.217 | |
| ESR- 2 months | 21.44 | 25 | 1.873 | |
| CRP-PRE | 0.876 | 25 | 0.2437 | <0.001 |
| CRP-1 month | 0.836 | 25 | 0.2515 | |
| CRP- 2 months | 0.764 | 25 | 0.2079 | |
| SGOT-PRE | 19.45 | 25 | 4.342 | <0.001 |
| SGOT-1 month | 22.76 | 25 | 4.560 | |
| SGOT-2 months | 23.67 | 25 | 4.628 | |
| SGPT-PRE | 21.05 | 25 | 7.239 | <0.001 |
| SGPT-1 month | 23.87 | 25 | 7.538 | |
| SGPT- 2 months | 22.96 | 25 | 7.760 | |
| UREUM-PRE | 30.786 | 25 | 17.875 | <0.001 |
| UREUM-1 month | 36.709 | 25 | 18.786 | |
| UREUM-2 months | 38.912 | 25 | 19.074 | |
| CREATININ-PRE | 0.876 | 25 | 0.265 | <0.001 |
| CREATININ-1 month | 1.120 | 25 | 0.298 | |
| CREATININ-2 months | 1.368 | 25 | 0.321 | |

Table 3: Significance Test Differences in laboratory results based on Meloxicam and Sidaguri Therapy

| Variable | Mean | n | Standard Deviation | P-Value |
|---|---|---|---|---|
| ESR-PRE | 23.89 | 25 | 1.689 | <0.001 |
| ESR-1 month | 12.98 | 25 | 3.309 | |
| ESR- 2 months | 11.32 | 25 | 3.867 | |
| CRP-PRE | 1.309 | 25 | 0.245 | <0.001 |
| CRP-1 month | 0.762 | 25 | 0.158 | |
| CRP- 2 months | 0.639 | 25 | 0.142 | |
| SGOT-PRE | 19.59 | 25 | 7.987 | <0.001 |
| SGOT-1 month | 25.68 | 25 | 8.142 | |
| SGOT-2 months | 27.52 | 25 | 9.043 | |
| SGPT-PRE | 22.81 | 25 | 14.986 | <0.001 |
| SGPT-1 month | 27.47 | 25 | 13.782 | |
| SGPT- 2 months | 29.56 | 25 | 12.908 | |
| UREUM-PRE | 23.90 | 25 | 11.703 | <0.001 |
| UREUM-1 month | 27.51 | 25 | 10.678 | |
| UREUM-2 months | 30.91 | 25 | 10.002 | |
| CREATININ-PRE | 0.79 | 25 | 0.156 | <0.001 |
| CREATININ-1 month | 0.83 | 25 | 0.179 | |
| CREATININ-2 months | 0.98 | 25 | 0.190 | |

Our study revealed a statistically significant improvement based on laboratory results include CRP, liver function, renal function, and ESR before, after 1 month and 2-month Meloxicam and placebo treatment with p-value <0.001. (Table 2 )

A statistically significant improvement laboratory results include CRP, liver function, renal function, and ESR before, after 1 month and 2 months after Meloxicam and Sidaguri treatment also revealed p-value < 0.001. (Table 3)

The mean ESR after 2 months Meloxicam and Placebo therapy was 66.72, while the mean ESR after 2 months Meloxicam and Sidaguri therapy were 16.06. There is a statistically significant

difference between ESR-2 months treatment with MP and ESR-2 months treatment with MS with p-value <0.001.

The mean CRP after 2 months with MP therapy was 0.825, while the mean CRP after 2 months with MS therapy was 0.903. There is a statistically significant difference between CRP-2 months treatment with MP and CRP-2 months treatment with MS with p-value 0.003.

Table 4: Significance Test of difference between post-therapy ESR and post-therapy CRP in both groups and VAS score

| Variable | Therapy | N | Mean | Standard Deviation | P-Value |
|---|---|---|---|---|---|
| **ESR** | Meloxicam& Placebo | 25 | 66.72 | 2.098 | <0.0001 |
| | Meloxicam&Sidaguri | 25 | 16.06 | 2.855 | |
| **CRP** | Meloxicam& Placebo | 25 | 0.825 | 0.234 | 0.003 |
| | Meloxicam&Sidaguri | 25 | 0.903 | 0.182 | |

# 4 DISCUSSION

This study included 50 samples, divided into two groups. It was found that OA was predominantly in women (43.2% and 56.8%). Subject's age in both groups were not significantly different (58.92 ± 10.43 and 59.64 ± 11.39) with p-value 0.817. The prevalence of OA is rising along with the age due to its irreversibility. Therefore, age has a major role as an important risk factor in osteoarthritis and it is much more common in women than men. (Glyn-Jones et al., 2015)

Increased level of CRP and ESR was found in both groups before therapy with either meloxicam and Sidaguri or meloxicam with placebo. On the other hand, CRP and ESR levels after 30 days and 60 days are lower, and statistically significant with p-value <.0.001. According to Mishra et al. there is a significantly increased CRP level in patients with OA (Mishra et al., 2012).

A significant improvement was found in the meloxicam group compared to placebo while comparing meloxicam with placebo and meloxicam with Sidaguri resulted in a statistically different outcome in CRP and ESR. Systemic inflammation is reflected by CRP, even it is not specific for OA. Its level can reach up to 100 times of normal range. CRP levels will diminish rapidly when tissue damage and inflammation recede and return to baseline in 24-48 hours. CRP levels are steady in plasma and are not influenced by diurnal variation. (Kandy, 2016)

Meanwhile, ESR could rise in the following condition: acute inflammatory processes, acute and chronic infections, tissue damage (necrosis), rheumatoid, collagen disease, malignancy and physiological stress conditions (e.g. pregnancy), thus it is not a specific indicator. ( Kee, 2008)

From the study results, it can be concluded that mean ESR in patients receiving meloxicam and placebo treatment group was 66,72 while in meloxicam and sidaguri-treated patient, the mean ESR was 16.06 with p-value <0.0001. This implied that meloxicam and sidaguri treatment was preferable in decreasing ESR over meloxicam and placebo treatment. Moreover, mean CRP levels found in meloxicam and placebo group was 0.825 while in meloxicam and the sidaguri group was 0.903 with p-value 0.003, succeeded by clinical improvement observed from decreasing VAS (*p* =0,003*)*.

Several studies found the anti-inflammatory effect in Sidaguri. It contains an alkaloid, ecdysteroid, flavonoids, and saponins, which is believed can inhibit the production of prostaglandin (as cyclooxygenase blockers). Moreover, it is also found that β-sitosterol in the Sidaguri also has anti-inflammatory properties. (Mah et al., 2017)

The author acknowledges the limitation of this study. The study had a smaller sample size. We recommend further study with larger samples to confirm this finding.

# 5 CONCLUSIONS

There were significant differences before, one month, and two months after therapy with p-value <0.001 in both group and the Sidaguri combination with meloxicam is better in reducing CRP and ESR levels.

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