Taurine Intakes Increase Superoxide Dismutase Activity in Knee Osteoarthritis

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Abstract. The aim of this research was to determine the correlation between taurine intake with superoxide dismutase (SOD) activity in knee osteoarthritis (OA) patients. In OA, there is a state of oxidative stress that will increase the progression of osteoarthritis and the risk of disability. Superoxide dismutase is an enzymatic antioxidant which can suppress the increase of free radicals since early time. Taurine is known to have several roles in the human body, such as antioxidants, anti-inflammatory and chondroprotective. This study used cross sectional design involving 56 knee OA subjects' grade II-IV, aged 40-60 years old that were recruited through consecutive sampling. Taurine intake was obtained by semiquantitative FFQ method. The SOD activity in whole blood was measured using RANSOD SD 125 with spectrophotometric method. The statistical analysis that had been done used SPSS with a correlation test. The intake of taurine was 59.77 mg per day and the SOD activity was 274.97 Unit per mL. This research found a significantly positive correlation (r = 0.284, p = 0.034) between taurine intakes and SOD activity in patients with knee OA. For the conclusion the taurine intake may have a role with the SOD activity in patients with knee OA.

Keywords: superoxide dismutase, taurine, knee osteoarthritis

1. Introduction

Osteoarthritis (OA) is a degenerative disease of the joints and synovium which characterized by an imbalance between cartilage synthesis and degradation resulting in joint remodelling. Worldwide, the World Health Organization (WHO) estimates that the prevalence of OA in 2020 will increase by 18% in women and 9.6% in men over the age of 60 years [1]. In Indonesia, based on data from Indonesia Basic Health Research (Riset Kesehatan Dasar) 2013, the prevalence of arthritis disease based on diagnosis from the health provider was 11.9%, while based on clinical symptoms was 24.7%. [2] Knee OA is the most common type of OA with the prevalence of 12.7% in female and 15.5% in male.[3]

Osteoarthritis is a multifactorial disease. There are several factors which may precipitate the occurrence of OA, including age, sex and nutritional status associated with nutrients.[4] In OA there is an increased expenditure of proinflammatory mediators which lead to increased reactive oxygen species (ROS) formation. This increase contributes to the occurrence of oxidative stress which is marked by an imbalance between oxidant and antioxidant. [5] Antioxidants are substances which play a role in suppressing the ROS formation. One of the enzymatic antioxidants, superoxide dismutase
SOD), works against free radicals by breaking off the radical chain reaction from the beginning by catalysing superoxide to hydrogen peroxide. [6] Research conducted by Amzoui et al. [7] found that there was a decrease in SOD activity in the blood of patients with knee OA. A decreased in SOD activity will cause an increase of superoxide and peroxynitrite production, activation of degradation enzyme such as matrix metalloproteinase (MMP), degradation of DNA, inhibition of collagen and proteoglycan synthesis, and apoptosis of chondrocyte, that eventually aggravate the disease progression. [8]

Taurine is a conditionally essential amino acid which is formed as the result from methionine and cysteine metabolism. Although taurine does not participate in protein synthesis, but it has a variety of roles in the body, including as an anti-inflammatory, chondroprotective, and as an antioxidant. In relation to antioxidants, taurine in some studies is known to have a role in the activity of SOD. [9] This is supported by study from Oliviera [10] which found that taurine can prevent a decrease in SOD activity.

Research on nutrient in relation to taurine and SOD activity in OA are still limited to animal experiments and other diseases. Based on this, the researcher felt it was necessary to conduct a study to determine the correlation between these two factors as an effort to suppress the formation of free radicals and to prevent deterioration and disability in OA patients.

2. Experimantal Methods

This study used a cross-sectional design and was conducted in the Orthopaedic outpatient clinic of Bhayangkara Hospital, Sukanto Hospital and Cipto Mangunkusumo National Centre Hospital from April to May 2018. The calculation of minimum sample quantities needed was calculated using the sample formula for correlation study [11] with the total number of subjects required was 56 subjects. Subjects were obtained using the consecutive sampling method. The inclusion criteria of the subjects consisted of male and female patients, aged 40-60 years with body mass index (BMI) ≥ 18.5 kg/m², diagnosed with II-IV grade knee OA by an orthopaedic or rheumatology specialist and signed the informed consent. Exclusion criteria include patients with trauma or knee joint surgery, patients with rheumatoid arthritis disease, chronic obstructive pulmonary disease, diabetes mellitus, congestive heart failure, chronic kidney disease and other chronic inflammatory diseases based on medical records. The subjects’ characteristics were age, gender, menopause status, smoking habit, BMI and nutritional status. Data collection were taken through interview and measurement. Anthropometric measurements were performed by measuring height and weight. Measurement of nutritional status was done by using body mass index (BMI) parameters based on Asia Pacific classification. Smoking status was obtained using Brinkman Index.

2.1. Assessment of dietary taurine intake

Data for dietary taurine intake were obtained through interview using semi-quantitative Food Frequency Questionnaire (FFQ) for the last 1-month.

2.2. Superoxide dismutase activity analysis

The activity of SOD in blood was taken from cubiti vein and measured using a kit from RANSOD SD 125 with spectrophotometry method. The blood samples then were sent and measured in Biochemistry Laboratory of Faculty of Medicine Universitas Indonesia.

2.3. Statistical analysis

Data was processed using Statistical Package for Social Sciences (SPSS) version 20. Normality data test was done by using Kolmogorov-Smirnov test. If the data was normally distributed (p>0.05), the data was presented in the mean and standard values, otherwise if the distribution was not normally distributed (p<0.05) the data was presented in the median (minimum-maximum) value. The correlation between dietary intake of taurine and SOD activity was analysed using Spearman correlation test.
3. Result and Discussion
3.1. Subject characteristics
In this study, as shown in Table 1, the mean age of the subjects was 50.75±6.17 years old. There were 50 female subjects (89.3%), higher than that of the male subjects with only 6 subjects (10.37%). Furthermore, as many as 33 (66%) of the female subjects were already in their menopause while the other 17 (34%) female subjects were not. The high number of OA in menopause women are in line with the research conducted by Heidari [12] that stated the prevalence of knee OA in women were greater than that of in men in age below 55 years old, and the risk increases 1.84 times after women reached menopause. This is due to the decreased level of estrogen at the time of menopause.

The median for BMI in this study was 29.16 (22.5-44.3) kg/m², with 27 (48.2%) and 23 (41.1%) of the subjects were in second grade and first grade obesity. The results are similar with Purcel[13] who found that 62% of knee OA patients were obese, with most of them in second grade obesity. Furthermore, obesity increases the pressure on the knee joint and the expenditure of proinflammatory mediators thereby inflicting damage. Meta-analysis suggests that a five-kilograms reduction in body weight may reduce 50% of knee OA risk while an increase of five BMI units may increase 35% of knee OA risk. [14; 15] Based on the smoking habit, this study found that 53 (94.6%) of the subjects had no smoking habit. This result is consistent with Dube et al. [16] who stated that there was no relationship between smoking habit and narrowing of joint spaces on the subject with knee OA.

| Variable                        | Total          |
|---------------------------------|----------------|
| Age, (years)                    | 50.75 ± 6.17*  |
| Gender, n (%)                   | Male 6 (10.37) |
|                                 | Female 50 (89.3) |
| Menopause status, n (%)         | Menopause 33 (66) |
|                                 | Not menopause 17 (34) |
| Body Mass Index, (kg/m²)        | 29.16 (22.5-44.3)** |
| Nutritional status, n (%)       | Normal 4 (7.1) |
|                                 | Overweight 2 (3.6) |
|                                 | Obese 1 23 (41.1) |
|                                 | Obese 2 27 (48.2) |
| Smoking habit, n (%)            | Non-smoker 53 (94.6) |
|                                 | Light smoker 2 (3.6) |
|                                 | Moderate smoker 0 (0) |
|                                 | Heavy smoker 1 (1.8) |

*Mean ± Standard deviation
**Median (Minimum-Maximum)

3.2. Subjects’ dietary taurine intake
Based on FFQ semiquantitative, the median of dietary taurine intake was 59.77 (15.96-278.57) mg per day. This result is similar to Zhao et al’ [17] data which stated that dietary taurine intake per day on male subjects in different regions of China was between 34-80 mg per day. This result was lower when compared with study from Kim et al. [18] in two groups of women in urban and rural areas (fisheries) which found 114.9±78.7 and 215.9±187.9 mg dietary taurine intake per day.

Humans are estimated to be able to synthesize taurine as many as 1-3% of the total sulfuric amino acid intake [19] or equivalent to 50-125 mg per day [20]. Taurine biosynthesis occurred in the human liver with cysteine sulfonic acid decarboxylase (CSAD) enzyme as a catalysator in the process. However, human liver has limited activity of CSAD enzyme, thus requiring taurine intake from the
outside to maintain taurine homeostasis [19; 21]. Furthermore, a high amount of taurine can be found in food that contains animal protein, and only a small amount of taurine found in plant protein [21].

3.3. Superoxide dismutase activity
From Table 2, the median for SOD activity in this study was 274.97 (152.48-360.97) Unit/ml and as much as 36 (64.3%) of the subjects showed increased of SOD activity and 18 (36.1%) with normal SOD activity. The result is consistent to Maneesh et al. [22] who found an increase in blood SOD activity in the knee OA group when compared to the controls. Similar result was also stated by Surapaneni et al. [23] who found that in knee OA subjects, there is an increase activity in blood SOD when compared to the controls. Increased SOD activity in this study illustrated the adaptive process of the body as an effort to prevent the occurrence of oxidative stress state. [22; 23; 24]

| Variable          | Total               |
|-------------------|---------------------|
| SOD activity (Unit/mL) | 274.97 (152.48-360.97)** |
| Decrease, n (%)    | 2 (3.6)             |
| Normal, n (%)      | 18 (32.1)           |
| Increase, n (%)    | 36 (64.3)           |

Unit / ml: unit per millilitre
** Median (minimum-maximum)

3.4. Correlation between dietary taurine intake and superoxide dismutase activity
This study found significantly positive correlation with weak strength (r = 0.284, p = 0.034) between dietary taurine intake with SOD activity. The result of this study is consistent with Das [25] who used rats as study subjects. The study showed that the taurine increased SOD activity compared to that of control. Furthermore, similar results were also stated by Vanitha et al. [26] who used oxidative-induced group of rats as subjects, found that taurine supplementation could increase the activity of SOD.

Taurine increases SOD activity through several mechanisms. Taurine derivatives, taurine chloramine (TauCl) can inhibit the NFkB inflammatory pathway and suppress the formation of nitric oxide (NO) and NADPH oxidase complex (NOX) thereby suppressing ROS formation. TauCl can also increase the activation of Nrf2 which is a transcription factor for the synthesis of various antioxidants including SOD. The taurine itself conjugated with the mitochondrial tRNA forming 5-taurinmetiluridin that will increase the respiratory chain activity thus reducing the diversion of electrons which contribute to superoxide formation. In addition, taurine may also increase the expression of SOD mRNA thus increasing the secretion of SOD. [27; 28; 29]

4. Conclusion
The results of this study showed a correlation between dietary intake of taurine with SOD activity in knee OA patients. Based on this result, it can be concluded that dietary taurine intake contributed to the activity of SOD in knee OA patients. Educating patients is needed especially in the selection of food sources of taurine which is widely found in animal protein such as fish, meat, chicken; as an effort not only to increase the dietary taurine intake but also to meet the dietary recommended protein intake of patients with knee OA.

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