The sodium does not affect joint pain and functional activity of knee osteoarthritis patients

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Abstract

Background: The sodium may aggravate synovial inflammation and cartilage thinning. This incidence can cause joint pain and reduce functional activity. Not many people know the effect of sodium on the incidence of osteoarthritis.

Objective: This study aims to determine the relationship between sodium in the body and knee joint pain which results in functional activity.

Methods: The quantitative descriptive study used accidental sampling. The study was conducted at three outpatient polyclinic orthopedics of hospitals and was approved by the Health Ethics Committee. All data were collected during the interview. The Semi-Quantitative Food Frequency Questionnaire and the Nutrisurvey Indonesia 2007 application were used as a tool to collect daily sodium intake (mg). Knee joint pain score was measured using the Visual Analog Scale (VAS), while functional body activity was measured using the Western Ontario McMaster Osteoarthritis Index (WOMAC). The Pearson and Spearman test ($P<0.05$) were used as a correlation test.

Results: 80 subjects were recruited according to the inclusion criteria. Characteristics of the subjects were pre-elderly (32, 40%), women (74, 92.5%), body mass index ≥30 kg/m^2 (54, 67.5%) and occupation (43, 53.75%). Average sodium intake = 2090.78±1084.33 mg, VAS score = 6.28±1.95 and WOMAC score = 32.65±14.88. The correlation sodium, VAS, and WOMAC were not significant ($P=0.196$, $P=0.372$).

Conclusions: Increased sodium intake is not associated with knee joint pain and functional body activity.

Introduction

Osteoarthritis (OA) is a chronic degenerative disease of the joints with uncertain multi-etiology. The biggest clinical outcome of OA is joint pain.[1] Pain especially in the morning or after less than 30 minutes of inactivity is a symptom of OA. OA occurs predominately in women and obese. Changes in joint structures such as sclerotic, osteophytes, sarcopenia, subchondral sclerosis, thin-

ning of the synovial membrane are common in OA.[2] All of the changes above will cause joint pain.[3] The appearance of pain in the sensi will reduce the daily functional activities of the body.

Based on data from the Centers for Disease Control and Prevention (CDC) shows that the prevalence of OA that has been diagnosed by doctors is expected to increase in the next few years. It is estimated that by 2040 78.4 million (25.9%) of the total adult population or >18 years will suffer from arthritis. The incidence of joint disease is 8.1% of the total population of Indonesia. The percentage of events for women (8.5%) is greater than for men (6.1%). The number of proportions is obtained at the age of 15 or >75 years with the number always increasing to 18.95% in 2018.[4]

OA is classified into primary (idiopathic) and secondary such as trauma, joint structure surgery, joint malalignment, systemic inflammation,[5] increased biomechanical loading,[6] abnormal joints at birth, and joint genetics. Primary OA is a combination of risk factors with increasing age and obesity.[7] The incidence of OA is inseparable from environmental factors,namely the pattern of sodium salt intake.

Every human body requires sodium of 2% of the total minerals. Normal sodium levels in serum are 310-340 mg/dL. Sodium is one of the micronutrients needed in the body. Research conducted by the national research council says that the recommended sodium intake per day is 1100-3300 mg.[8] The average sodium intake for adults in the world exceed 2000 mg/day,[9] while the average sodium intake for adult in Indonesia is 2702 mg per day or 2.7 grams.[10] Based on the Regulation of the Indonesian Minister of Health, it is stated that for men aged 50-64 years the nutritional adequacy rate of sodium is 1300 mg, for women 1400 mg; while men aged 65-80 years is 1100 mg, women 1200 mg.[11] The level of sodium consumption in the United States reaches 4000-5000 mg/day. The high consumption of sodium in the US is due to the high consumption of fast food.[8] Packaged factory-processed food will have a sodium content 10 times greater than food prepared at home.[12,13]

Interleukin-17 (IL-17) is a proinflammatory cytokine secreted by TH-17 through sodium induction.[13,14] A high sodium environment in the body activates the p38/MAPK pathway. Nuclear 5/NFAT5 T cells and serum glucocorticoid kinase 1 (SGK1) are activated.[14] SGKI also promotes IL-23R expression, due to activation of TH-17 differentiation both *in vitro* and *in vivo*.[15] The process of increasing cartilage catabolism,[16] decreasing chondrocyte secretion, and inhibition the formation of collagen II aggregation and degradation, will occur as a result of IL-17 secretion.[17] Production of TNF-alpha, IL-6, IL-1, IL-6 and other proinflammatory cytokines will synergize with IL-17A in OA to increase inflammation.[18,19] Tissue inflammation can also form through increased sodium content in the body.[16] It is concluded that the IL-17 functional polymorphism would significantly lead to OA in the knee.[20] In fact, other studies also state that knee joint pain can be caused by an increase in IL-17.[21,22]

Sodium is present in the body in balance and is needed in metabolic processes. However, an increase in sodium intake above the standard requirement, causes a surge that will activate the body's immune system. It never pays attention to this in managing the daily sodium diet. Many factors can cause knee joint pain, one of which is high sodium content in the body. Further study is needed to determine the relationship between knee joint pain and its effect on the functional activity of OA patients through Visual Analog Scale (VAS) and Western Ontario McMaster Osteoarthritis Index (WOMAC) measurements.

Materials and Methods

The research was approved by the health ethics commission from 3 research hospitals, namely Brawijaya Army Hospital in Surabaya, Airlangga University Hospital in Surabaya, and Aisyiyah Islamic Hospital in Malang Indonesia. Data collection was carried out at the outpatient orthopedic June – December 2021. The needs of the research subjects were calculated using a formula based on the OA population in each research hospital.

All subjects in the study were selected by orthopedic specialists following the guidelines of the American College of Rheumatology (2019).[23] The subjects were sampled according to the time of visit to the orthopedic polyclinic at each hospital. The method of collecting subjects by accidental sampling follows a cross sectional model. The inclusion criteria were women, age 45-70 years, Kelgreen Lawrence (KL) knee OA level 2 or 3, not taking a weight loss diet program, not taking paracetamol and Nonsteroid Antiinflammation Drugs 1 days before, not corticosteroid injection last 2 weeks or hyaluronic acid injection last 3 months and sign the informed consent. We did not use KL-4 because the risk factors for OA are complex, and the level of pain and functional activity tends to be in the severe category. The results are feared to be biased. The KL level was determined by an orthopedic specialist based on the results of knee radiographs. Autoimmune diseases, gout and patients who have undergone knee joint surgery were exclusion criteria.

Research materials

Subject characteristics data (age, gender, occupation) were collected during the participant's interview. BMI was measured using weight/height (kg/m^2). The sodium intake data were collected by using the Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ).[23] The sodium intake questionnaire consists of 75 questions (3 staple foods, 22 animal side dishes, 2 vegetable side dishes, 4 vegetables, 6 drinks, 6 cooking spices, 32 lists of foods with sodium content >100 mg/100 gram of material). The SQ-FFQ used has been validated using Lawshe's content validity ratio (CVR) which was one of the methods widely used to measure content validity. The results of the SQ-FFQ validation were CVR = 1. To obtain the weight of sodium intake (mg/day) the Nutrisurvey Indonesia 2007 application was used based on food intake data in the SQ-FFQ for each subject. Based on the Regulation of the Minister of Health of the Republic of Indonesia of 2019, the standard daily sodium requirement for men is 36-49 = 1500 mg, 50-64 years = 1300 mg, 65-80 years = 1100 mg while for women it is 1500 mg, 1400 mg, 1200 mg for same age.

VAS and WOMAC in this study were used to measure knee joint pain and functional body activity. The knee joint pain score is divided into 5 levels, namely (normal = 0, mild = 1-3, moderate = 4-6, severe = 7-9, very severe = 10) while WOMAC was a functional body instrument consisting of 3 subscales namely pain, stiffness, and limited physical function. On the pain subscale there are 5 questions of pain intensity, the intensity of pain felt by the joints, when walking, climbing stairs, resting, and at night. While the stiffness subscale consists of 2 questions regarding the intensity of joint stiffness in the morning and evening. In the physical function limitation subscale, there were 15 questions, which consist of knee ability when going up and down stairs, standing up from sitting, standing strength, bending to the floor, walking on a flat surface, getting in/out of a car, shopping, putting on and taking off socks, lying down and getting out of bed, showering, strength/ability when sitting, and the last is the question of knee ability to go to the toilet. WOMAC answer score was normal = 0, mild = 1, moderate = 2, severe = 3, very severe = 4; while for total score category mild

= 0-24, moderate = 25-48, severe = 49-72, very severe = 73-96. The data on sodium intake and pain (VAS, WOMAC) were collected during the participant interviews in hospitals.

Research statistics

The type of data obtained was in the interval scale (sodium, WOMAC) and ordinal (VAS). All data collected were analyzed by statistical analysis of Person correlation to test the relationship between sodium and WOMAC ($P<0.05$) and Spearman correlation to test the relationship between sodium and VAS ($P<0.05$). The software used for statistical analysis is IBM SPSS version 23.

Results

The number of subjects obtained from 3 research hospitals is 80 people. Army Hospital in Brawijaya Surabaya had 32 subjects, Airlangga University Hospital had 19 subjects and Aisyiyah Islamic Hospital Malang had 29 subjects. The number of subjects for each hospital is obtained from a formula according to the prevalence of OA events among the population of patients in that hospital. OA patients who come to the orthopedic outpatient polyclinic were given therapy according to their complaints. The use of anti-inflammatory analgesic drugs was given by the hospital can be in the form of tablets, capsules, creams or injections. The type of drugs prescribed by an orthopedic doctor depends on the severity of OA and the degree of pain. All prescribed drugs were in accordance with OA treatment guidelines. The class of drugs prescribed to the subject is listed in Table 1. Based on the data on the characteristics of the subjects, it was found that they were women (74, 92.5%), pre-elderly (32, 40%), BMI ≥30 (kg/m^2) (54, 67.5%) and worked outside the home (≥8 hours/day) (43, 53.75%). The subjects' average sodium intake per day was 2090.78±1084.33. These results were above the needs of individual standards based on age and sex. Knee joint pain score = 6.28±1.95 and the value for functional activity parameters = 32.65±14.88 were included in the moderate category (Table 2). Statistical tests were carried out between Sodium, VAS and WOMAC (Table 3). It was positive significance results for BMI and WOMAC ($P=0.031$) but not for the VAS parameter ($P=0.368$). While the relationship between sodium, VAS, and WOMAC was no significance between the three (Table 4).

Table 1. Types of drugs given to subjects in 3 research hospitals.

Peroral	Injeksi	Krim
Meloxicam 15 mg	Osflex (Na Hyaluronate)	Flamar emulgel
Parasetamol 500 mg	Aragan (Na Hyaluronate)	Lafalos 20 gr
Kodein 20 mg	Triamcinolon acteonida	Hot in DCL 30 gr
Valisanbe 2 mg		
Myonal 50 mg (Eperisone)		
Glukosamin 250 mg		
Osotovel (Kalcitriol)		
Neurodex, Neurosanbe		
Methylprednisolon 16 mg		
dexketoprofen 25 mg		
Na.Diklofenak 50 mg		
Gabapentin 100 mg		
Mecobalamin		
Vit D		
Kalsium laktat		
Vit B Komplek		

Discussion

In this study, women with the aged 56-65 yo were the most prevalent characteristic of OA patients. The elderly (>55 yo) can cause a decrease in the body's metabolic processes and even a decrease in bone strength and muscle mass (sarcopenia). Sarcopenia, stiffness, limitation of joints, and thinning of the cartilage layer can increase friction in the joints which causes strong pain. Elderly women tend to have experienced menopause. Decreased estrogen hormone can increase the risk of developing OA,[24] through cytokine dysfunction as a result of unstable estrogen receptor expression.[25] In addition, reduced estrogen secretion also causes the accumulation of adipose fat which results in obesity. Estrogen also affects a person's moody effects psychologically

Table 2. Characteristics of subjects and research variables.

Characteristics	Frequency (%) x 108	Mean ± SD
Gender		
Men	6 (7.5)	
Women	74 (92.5)	
Age, yo*		59.46±8.25
46-55, Early age	27 (33.75)	
56-65 Pre-elderly	32 (40)	
≥66 Elderly	21 (26.25)	
BMI, kg/m^2		27.57±4.46
(18,5- 24,99) normal	11 (13.75)	
(25- 29,99) overweight	15 (18.75)	
(≥ 30) obese	54 (67.5)	
Occupation		
Not	37 (46.25)	
Yes	43 (53.75)	
Sodium, mg**		2090.78±1084.33
Below	18 (22.5)	
Above	62 (77.5)	
VAS		6.28± 1.95
Mild	8 (10)	
Medium	45 (56.25)	
Moderate	27 (33.75)	
Severe	0	
WOMAC		32.65± 14.88
Mild	23 (28.75)	
Medium	43 (53.75)	
Moderate	14 (17.5)	
Severe	0	

*Standard of the Minister of Health of the Republic of Indonesia, 2009; **Standard of the Minister of Health of the Republic of Indonesia, 2019. SD, standard deviation; BMI, body mass index.

Table 3. Association of Characteristics of Subjects, VAS and WOMAC.

Characteristic	Sodium	VAS	WOMAC
Gender	0.155	0.707	0.514
Age, yo	0.569	0.781	0.338
BMI, kg/m^2	0.586	0.368	0.031*
Occupation	0.078	0.387	0.446

Table 4. Association of sodium intake with VAS and WOMAC.

Variables	VAS	WOMAC
Sodium	0.196	0.372

so that women who have reached menopause tend to have minimal activity. Even a study conducted by Roman-Blas *et al.* (2009) said that estrogen deficiency was shown in an experimental post-menopausal rat model, resulting in subchondral bone resorption and articular cartilage degeneration.[26] All due to decreased estrogen in cartilage and others can cause joint pain and reduce functional activities primarily in the elderly.[27]

At this time education about healthy lifestyles is needed for a better quality of life. The savory taste of food further enhances the subject's appetite. This results in an excess of nutrients above the standard requirement. Lack of exercise and mistakes in choosing food can cause weight gain to reach obesity. Obesity can increase the prevalence of OA through joint overload which can cause friction, inflammation and pain.[28] More than half of the subjects fall into the category of obesity. The load on the joints due to obesity can further thin the cartilage and trigger synovial inflammation. The formation of osteophytes and subchondral thickening are one of the body's ways to increase joint strength in managing the load. Obesity causes a decrease in the sensitivity of pain receptors in the skin when a stimulus occurs. Stimulation of nociceptors to the descending pathway and causing pain perception are influenced by different individual characteristics.[29] The WOMAC is a questionnaire that asks about the frequency of the subject's daily activities so that it can describe the functionality of the knee joint while the VAS only describes the intensity of knee joint pain at this time. WOMAC gives significant results with obesity. The appearance of joint pain is not stagnant but dynamic depending on the risk factors that influence it. The sensitivity to the elderly has been reduced. This is due to the reduced density of unmyelinated fibers in the peripheral nervous system, resulting in a slowing of nerve conduction.[30] Likewise the use of drugs in the elderly, their effectiveness may be also decrease. This can be shown by the use of anti-inflammatory and analgesic drugs (Table 1) has not been able to relieve knee joint pain. A WOMAC questionnaire is better able to describe the incidence of knee joint pain than just looking at an emotional picture such as the VAS. In addition, excessive activity and the majority use of the knee joint can also cause OA and knee joint pain. As many as 53.75% of the subjects were in the occupation category, which means more than 8 hours a day doing routine work outside the home.

Based on the results of statistical analysis related to the relationship between sodium intake and knee joint pain and the degree of functional activity of the body, it has not yielded significant results. Sodium is the main component of table salt, it is also used as a seasoning and food preservative. Salt is one of the needs which is a complement to food needs and is a source of electrolytes for the human body. The sodium content reaches 10x in processed and packaged foods. The sodium content in the body should be in a state of balance. Hyponatremia is associated with organ dysfunction such as kidney or ADH (Antidiuretic Hormone) whereas hypernatremia with the common symptoms of thirst, caused by excessive sweating, diarrhea and excessive vomiting, can lead to brain dysfunction, confusion, seizures and coma. The role of sodium in the incidence of OA is related to Interleukin-17 (IL-17).[14,15] High sodium can activate the p38/MAPK pathway which affects the activation of activated T cell nucleus 5/NFAT5 and serum glucocorticoid kinase 1 (SGK1).[16] NFAT5 also influences sodium inducing inflammatory pathways. SGK1 promotes IL-23R expression and increases Th-17.[17] Th-17 is in charge of secreting IL-17, which is a proinflammatory cytokine that causes cartilage destruction, decreased secretion chondrocytes, collagen II degradation, and upregulation MMPs.[31] IL-17 is an early mediator of collagen breakdown in cartilage.[20,21] One of the risks of knee OA is caused by an increase in the IL-17 functional polymorphism.[21]

High intake of sodium cause destruction and inflammation in OA.[19,20]

Based on the Regulation of the Minister of Health of the Republic of Indonesia, the total sodium intake of 2090.78±1084.33 mg/day is classified as above the standard requirement and cause of OA but high sodium intake is not positively correlated with knee joint pain. According to Kellgreen Lawrence, knee joint pain and severity of OA do not correlate with high serum or synovial sodium concentrations.[32] At the degree of severity of OA level 4, the subject may not experience joint pain while those at levels 1-2 may already experience severe joint pain.[33] Pain receptors in the skin are influenced by biopsychosocial factors, there is intramolecular interaction when there is a change in biopsychosocial factors. Biopsychosocial factors allow disease to be seen as the result of interacting mechanisms at the cellular, tissue, organismal, interpersonal and environmental levels.[34]

Most of the subjects were pre-elderly where pain sensitivity to the pre-elderly had decreased. This is due to reduced density of unmyelinated fibers in the peripheral nervous system resulting in a slowdown in nerve conduction.[33] The limitation of this study is that sodium intake cannot be measured every day. Measurements were carried out assuming the pattern of sodium intake in the previous 7 days and 30 days.

Conclusions

Increased sodium intake is not associated with knee joint pain and functional body activity. High sodium intake can cause OA although does not correlate it. Knee joint pain and functional body activity are influenced by many other factors, both internal and external. Future research is needed to determine the main factors and risk confounders of knee joint pain and functional body activity in OA patients

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