Original Article

The Effect of Curcumin Ointment on the Quality of Life of Older Adults with Knee Osteoarthritis: A Randomized Placebo Clinical Trial

Neda Jamali, Mohsen Adib-Hajbaghery, Alireza Soleimani

Trauma Nursing research Center, Faculty of Nursing and Midwifery, Kashan University of Medical Sciences, 1Department of Internal Medicine, Kashan University of Medical Sciences, Kashan, Iran

ORCID:
Neda Jamali: 0000-0002-4686-2170
Mohsen Adib-Hajbaghery: 0000-0002-9518-4329
Alireza Soleimani: 0000-0002-0526-7623

Background: Knee osteoarthritis (KO) is one of the most common health problems affecting the quality of life (QOL) in older adults. Objective: Because improving the QOL is one of the important therapeutic goals, this study aimed to investigate the effect of curcumin ointment on the QOL in older adults with KO. Methods: This double-blind randomized clinical trial was performed from February 20, to June 22, 2019, on 72 older adults with KO referring to the office of a physician in Kashan, Iran. The individuals with eligibility criteria were recruited sequentially and were randomly assigned to two groups of 36 to apply either curcumin 5% ointment or Vaseline ointment twice daily for 6 weeks around the knee. The Osteoarthritis Knee and Hip Quality of Life questionnaire was used to measure the patients’ QOL at the beginning of the study, and at the end of the 4th and 6th weeks. The Fisher’s exact test, independent samples t-test, Friedman test, and repeated-measures analysis were used for data analysis. Results: The mean baseline QOL scores in the intervention and the placebo groups were 55.98 ± 8.12 and 58.75 ± 7.86 (P = 0.160) which then changed to 59.21 ± 7.98 and 60.01 ± 8.23 at the end of the 4th week and to 65.83 ± 8.81 and 60.26 ± 7.25 at the end of the 6th week, respectively. Repeated-measures analysis showed that over time, the use of curcumin ointment could significantly increase the mean QOL score in the intervention group (P = 0.001). Conclusion: Topical administration of 5% curcumin ointment can significantly improve the QOL in older adults with KO. Therefore, this ointment might be considered a complementary therapy to improve the QOL of patients with KO.

KEYWORDS: Curcumin, Knee, Older adults, Osteoarthritis, Quality of life

INTRODUCTION

Knee osteoarthritis (KO) is one of the most common health problems in older adults.[1] Due to its progressive nature, KO causes joint stiffness, pain, muscle weakness, mobility impairment,[2] disability, falls, depression, and impaired quality of life (QOL).[3,4] The prevalence of osteoarthritis is 60%–90% in people 65 years and older.[5] The prevalence of KO in Iranian older adults has also been reported as 63.1%.[6] Iranian older adults are more prone to knee joints injuries due to habits and lifestyle factors such as sitting on the ground, the shape of toilets, inadequate exercise activities, and standing cooking and housekeeping practices.[6] Joint surgery, medications, and protective modalities are commonly used to treat KO.[7] However, surgeries are expensive and medications have side effects – especially in older adults who suffer multiple organ dysfunctions.[8] Besides, the effects of walking aids, physiotherapy, hydrotherapy, weight loss, and lifestyle

For correspondence: Dr. Mohsen Adib-Hajbaghery, Trauma Nursing research Center, Faculty of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, Iran.
E-mail: adib1344@yahoo.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 license, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKhLMPMedknow_reprints@wolterskluwer.com
Submitted: 02-Aug-2020 Revised: 23-Aug-2020 Accepted: 16-Sep-2020
Published: 20-Apr-2021

How to cite this article: Jamali N, Adib-Hajbaghery M, Soleimani A. The effect of Curcumin ointment on the quality of life of older adults with knee osteoarthritis: A randomized placebo clinical trial. Nurs Midwifery Stud 2021;10:79-85.
Curcumin or *Curcumin longa* is one of the herbs in traditional Iranian medicine. It is a plant of the ginger family. Dried turmeric rhizomes are used for nutritional and medicinal purposes. Curcumin is the active ingredient of turmeric and chemically called diferuloylmethane.\(^{[10,11]}\)

Curcumin is a powerful antioxidant and shows anti-cancer, anti-bacterial, antiviral, and anti-inflammatory effects. It also has shown beneficial effects in the liver, gastrointestinal, and cardiovascular disorders, and the improvement of Alzheimer’s disease, rheumatoid arthritis, and diabetes mellitus. In traditional Iranian medicine, turmeric is commonly used as a topical poultice in the treatment of strain, sprain, and joint dislocations.\(^{[10]}\)

Numerous studies are available on the beneficial effects of curcumin on diabetes, hyperlipidemia,\(^{[12]}\) gastrointestinal disorders,\(^{[13]}\) liver failure, premenstrual syndrome,\(^{[14]}\) skin disorders\(^{[15]}\) and episiotomy wound healing.\(^{[16]}\) Some studies have also reported the effect of curcumin on the improvement of osteoarthritis in animal models.\(^{[17,18]}\) Two studies also examined the effect of oral curcumin in human osteoarthritis.\(^{[19,20]}\) A study also used a combination of herbs in older adults with joint pain.\(^{[21]}\) However, none of the studies examined the impact of curcumin on the QOL of older adults with KO. In addition, citing the low bioavailability of oral forms of curcumin, a number of studies suggested the necessity of studying the effect of nonedible curcumin methods.\(^{[20,22,23]}\)

Considering the lack of studies on its effect on the patients’ QOL, this study aimed to investigate the effect of curcumin ointment on the QOL in older adults with KO.

**Methods**

This study is a double-blind randomized, placebo trial performed from February 20 to June 22, 2019, on 72 older adults with KO aged 60 years and over. The study was conducted in 2019 on patients referring to the office of a physician in Kashan, Iran. Due to the lack of an earlier study on the effect of curcumin on the QOL of older adults, the sample size was estimated using the results of a pilot study in which we used the curcumin ointment on eight older adults with Knee OA. The mean baseline QOL was 58.48 ± 8.37 and changed to 64.52 ± 7.89 after six weeks of use. Therefore, considering the alpha of 0.05 and a power of 0.80, the sample size was estimated to be 29 per group. However, considering a probable dropout of 20%, we recruited 36 participants in each group.

\[
\frac{\left(1 + \frac{z^2}{\alpha^2} + \frac{z^2 + z_\beta^2}{\sigma^2}\right)}{\left(1 + \frac{1}{n} + \frac{1}{2n}\right)}\left(\frac{1}{\alpha^2} + \frac{1}{\sigma^2}\right) = 20
\]

Inclusion criteria were age 60 years and over, lack of known allergy to the ginger family, lack of a known cognitive disorder, complete consciousness and ability to answer the questionnaire items, having a medical diagnosis of KO, and willingness to participate in the study. Exclusion criteria included any allergic reaction to curcumin ointment, discontinuation of the ointment prior to the end of the intervention, a decision to withdraw from the study, death, hospitalization, and being unavailable due to migration.

Totally, 85 patients were assessed for eligibility, among them 72 were recruited sequentially and were randomly allocated into the study groups [Figure 1]. Prior to sampling, a list of 72 individuals was prepared and then the study supervisor assigned them randomly into 18 quadruple blocks using an online block randomization software. Then, the number and the name of the treatments for each number (curcumin or placebo) were written on small cards and put in small opaque envelopes. The researcher who gathered the data and the physician were blind to the content of the sealed envelopes. Envelopes were arranged in order and provided to the physician. As each participant entered the study, the physician picked and unpacked an envelope and prescribed the predetermined treatment. Thus, the participants were assigned to one of the intervention or placebo groups.

![Figure 1: The study flow diagram](image-url)
Data collection instruments
A two-part instrument was used for data collection. The first part included demographic characteristics such as age, sex, education level, duration of illness, weight (kg), height (cm), body mass index, regular physical activity (yes/no), and the use of prescribed and over-the-counter analgesics, sedatives, and remedies. In addition, there were two questions on perceived pain intensity and perceived knee stiffness that requested the patients to describe the severity of their knee pain and knee stiffness as mild, moderate, severe, or very severe.

The second part included the Osteoarthritis Knee and Hip Quality of Life questionnaire developed by Rat et al. This scale included 43 items in five domains namely physical activity (16 items), mental health (13 items), pain (4 items), social support (4 items), and social performance (3 items). Moreover, there were three independent items on personal relationships, sexual activity, and professional life. Each item is rated on a visual analog scale from 0 (worst condition) to 100 (best condition). To calculate the score for each domain as well as the total score, the sum of scores is divided by the number of questions. Higher scores indicate better QOL.

The Persian translation of this scale has been validated by Saffari et al. who examined the construct validity of the translated scale, through simultaneous administration of this scale and SF12 questionnaire on a sample of 434 patients and calculated the correlation coefficient of the subscales of the two instruments between 0.34 and 0.69. The Cronbach’s alpha for its various domains has also been reported between 0.74 and 0.89 and its kappa agreement coefficient was 0.85. As some of the participants were illiterate or low-illiterate, the researcher read them the items and documented their answers into the scale.

Curcumin ointment preparation
For the preparation of curcumin ointment, 100 g of Vaseline and 5 g of the powdered extract of 90% curcumin (purchased from Barij Essence company, Kashan, Iran) were compounded by a pharmacist to make 5% curcumin ointment. Then, the ointment was prepared in 100 g cans similar – in shape and color – to the placebo (Vaseline).

Intervention
Initially, each patient was examined by the physician for inclusion criteria. The patient was then introduced to the first researcher to complete the study instruments through a structured interview. Then, the patient was referred back to the doctor and he picked and unpacked an envelope, read the card inside it, and gave him/her a can containing the predetermined treatment, and then referred them to the researcher (who was present in the office) to be trained on how to apply it. Patients in the intervention group received curcumin ointment and those in the placebo group received Vaseline ointment, which was prepared in 100-g containers of similar size and color (yellow) and identified by special codes. The use of both substances was similar in both groups. After curcumin ointment or Vaseline ointment was given to patients, the method of administration was individually taught to them. For the first time, the ointment was applied by the researcher on the patient’s knee. First, the researcher washed the area with lukewarm water, dried it, and using a special cup took 1.5 mL of the ointment and applied it on and around the knee, and then, wrap the area with a clean nonpenetrating cloth to prevent contamination of the patient’s clothing. Then, the patient was asked to repeat the procedure on the other knee to ensuring both the researcher and the patient of the correct use. Patients were instructed to do so for 6 weeks, twice daily, once in the morning and once at night, before bed. A checklist was provided to each patient to mark it after each use.

All patients were instructed to report any allergic reaction, redness, or itching around the knee and to avoid any other topical remedies on their knees during the study. A telephone number was obtained from each patient, and the researcher followed the treatment process weekly by telephone. Then, at the end of the 4th and 6th weeks, when the patient was referred to the physician’s office for follow-up, the QOL scale was again completed for them by a research assistant who was unaware of the type of medication they were receiving.

Ethical considerations
This study was reviewed and approved by the Research Ethics Committee of Kashan University of Medical Sciences (Code of Ethics: IRKAUMS.NUHEPM.REC.1397.049, Project number 97157). Moreover, the study was registered in the Iranian Registry of Clinical Trials (code: IRCT20100403003618N6). All patients were informed that they would be contacted several times to evaluate the efficacy of the treatment. However, they did not know which group they were in. All patients were informed about voluntary participation, the right to withdraw at any time, confidential data management, and that the study would not cost them. All patients signed a written informed consent form and their rights were respected in accordance with the Helsinki declaration.

Data analysis
Data were entered into SPSS software version 16 (SPSS, Inc., Chicago, IL, USA), and descriptive methods such as frequency, percentage, mean and standard
deviation (SD) were used to describe the data. The normality of quantitative variables was assessed using the Kolmogorov–Smirnov test, and the normal distribution was confirmed. Chi-square and Fisher’s exact tests were used to compare the two groups in terms of nominal and categorical variables, and independent samples t-test and analysis of variance with Tukey’s post hoc test were used to compare the quantitative data. Friedman test was used to examine the changes in perceived knee pain and stiffness over time. Furthermore, repeated-measures analysis was used to compare changes in the QOL scores during the three measurement time points. The Greenhouse–Geisser estimation was also used to correct the degree of freedom. The level of significance was set at < 0.05 in all tests.

RESULTS

Of the 72 patients who were recruited, two people of the intervention group and three ones from the placebo group withdrew after the 1st week. Of the total sample, 43 (64.2%) were women, 49 (73.1%) were illiterate or low-literate, and 18 (26.9%) were taking analgesics before starting the study. The mean ± SD age of the patients was 68.21 ± 6.12 years in the intervention group and 67.02 ± 6.41 years in the placebo group (P = 0.439). The two groups were not significantly different in terms of their individual baseline characteristics, the perceived QOL, knee pain, and knee stiffness [Tables 1 and 2]. The Friedman test also showed that both perceived knee pain and perceived knee stiffness has improved overtime (P < 0.001 for both variables and the both group).

Repeated-measures analysis was performed to compare changes in the QOL scores over the three consecutive measurements. Mauchly’s test showed that sphericity was not assumed (χ²[2] = 65.75, P = 0.001). Therefore, the degrees of freedom were corrected using the Greenhouse–Geisser test. The results showed that over time, the use of curcumin ointment could statistically significantly increase the mean QOL score in the intervention group (F = 50.20, df = 1.240, and P = 0.001).

Given the significant interaction between the measurement time and the type of intervention (group) (F = 38.859, df = 1.252, and P = 0.001), the t-test was used to conduct pair-wise comparisons between the two groups at the three measurement time points. The results illustrated that the mean QOL was significantly different between the two groups only at the third measurement (P = 0.006) [Table 3].

Figure 2 shows that the mean overall QOL scores in the intervention group increased over time but after the second measurement, it did not change significantly in the placebo group.

DISCUSSION

At the beginning of the stay, no significant difference was found between the mean QOL scores of the two groups so that both groups possessed about half of the possible score. This finding can be attributed to the fact that most patients in both groups had moderate-to-severe knee pain and stiffness at the beginning of the study. Earlier studies have also shown that chronic pain from KO adversely affects on the older adults’ QOL.[26] A study in Brazil also reported that about 65% of patients with KO experience degrees of dependence in life affairs and a decrease in QOL.[27] Another study has also shown that KO reduces the patients’ QOL so that people with bilateral KO perceive a lower QOL than those with a unilateral disorder.[28] It seems that knee pain resulted from KO can significantly decrease the older adults’ QOL. This conclusion is consistent with previous studies that showed an inverse relationship between pain – especially chronic pain – and QOL.[29,30] Through appropriate patient care and education, nurses can play

Table 1: Between-group comparisons of the patients’ individual and clinical characteristics

| Variables                                    | Placebo          | Intervention      | P   |
|----------------------------------------------|------------------|-------------------|-----|
| Age, mean ± SD                               | 67.02 ± 6.41     | 68.21 ± 6.12      | 0.439a|
| Weight (kg), mean ± SD                       | 75.01 ± 11.23    | 76.02 ± 12.62     | 0.647a|
| Height (cm), mean ± SD                       | 165.24 ± 6.45    | 165.63 ± 7.04     | 0.833a|
| BMI, mean ± SD                               | 27.48 ± 3.88     | 27.52 ± 3.40      | 0.964a|
| Disease duration, year, mean ± SD            | 6.12 ± 4.02      | 7.11 ± 4.33       | 0.336a|
| Gender, n (%)                                |                  |                   |     |
| Female                                       | 22 (66.7)        | 21 (61.8)         | 0.87b |
| Male                                         | 11 (33.3)        | 13 (38.2)         |     |
| Education level, n (%)                       |                  |                   |     |
| Illiterate or low-literate                   | 23 (69.7)        | 26 (76.5)         | 0.72b |
| Secondary school and higher                  | 10 (30.3)        | 8 (23.5)          | 0.54b |
| Regular physical activity, n (%)             |                  |                   |     |
| Yes                                          | 16 (48.5)        | 13 (38.2)         | 0.54b |
| No                                           | 17 (51.5)        | 21 (61.8)         |     |
| Analgesic use (before the study), n (%)      |                  |                   |     |
| Yes                                          | 8 (24.2)         | 10 (29.4)         | 0.84b |
| No                                           | 25 (75.8)        | 24 (70.6)         |     |
| Use of hypnotics, n (%)                      |                  |                   |     |
| Yes                                          | 13 (39.4)        | 6 (17.6)          | 0.08b |
| No                                           | 20 (60.6)        | 28 (82.4)         |     |

*T-test, *Chi-square test. BMI: Body mass index, SD: Standard deviation
Jamali, et al.: Effect of Curcumin ointment on quality of life in osteoarthritis

The Australian Department of Health emphasized the role of nurses in enhancing the QOL of patients with osteoarthritis, including the role of nurses in helping patients to set realistic short-term and long-term goals; educating patients and the community about osteoarthritis and methods of prevention and treatment; prevention and reduction of adverse drug reactions; follow-up of the treatment and care recommendations; introduction and recommendation of complementary pain relief therapies appropriate to the patient’s condition such as heat therapy, local remedies, sports and appropriate exercises, mind and body therapies, diet and weight loss; use of auxiliary equipment and protective footwear; and introduction of patients to arthritis support groups.

The present study showed that the QOL scores of both groups increased slightly in the 4th week, although the increase in the intervention group was more than the placebo group. However, after the 4th week, the mean QOL in the placebo group did not change significantly, whereas in the intervention group, it continued to increase by more than six points. Thus, while the QOL score in the placebo group increased only 1.51 from the beginning to the end of the study, the amount of increase was 9.85 in the intervention group. It seems that the topical application of curcumin ointment can gradually increase the QOL in older adults with KO. This effect might be attributable to the gradual effect of curcumin ointment in decreasing knee inflammation and pain. Curcumin is an antioxidant, anti-inflammatory, and anti-swelling agent. Its short-term anti-inflammatory effect is reported to be equal to hydrocortisone and phenylbutazone. It seems that the gradual reduction of inflammation, pain, and swelling of the knee, reduced an important role in the improvement of knee pain in older adults with KO, which consequently improves their QOL.

Table 2: Comparison of the perceived knee pain and stiffness between the intervention and placebo groups at the three measurements

| Time               | Perceived knee pain, n (%) | Perceived knee stiffness, n (%) |
|--------------------|----------------------------|---------------------------------|
|                    | Mild 16 (48.5)              | 1 (3.0)                         |
|                    | Moderate 9 (27.3)           | 6 (18.2)                        |
|                    | Very severe 6 (18.2)        | 2 (6.0)                         |

Table 3: Comparisons of the mean quality of life scores at three measurement time points

| Time               | Intervention | Placebo | P | The effect of group | P, (RM ANOVA) |
|--------------------|--------------|---------|---|---------------------|---------------|
| Start of the study | 55.9 ± 8.12  | 58.7 ± 7.86 | 0.160 | 0.001               |
| After 4 weeks      | 59.2 ± 7.98  | 60.1 ± 8.23 | 0.687 |                       |
| After 6 weeks      | 65.8 ± 8.81  | 60.2 ± 7.25 | 0.006 |                       |

The present study showed that the QOL scores of both groups increased slightly in the 4th week, although the increase in the intervention group was more than the placebo group. However, after the 4th week, the mean QOL in the placebo group did not change significantly, whereas in the intervention group, it continued to increase by more than six points. Thus, while the QOL score in the placebo group increased only 1.51 from the beginning to the end of the study, the amount of increase was 9.85 in the intervention group. It seems that the topical application of curcumin ointment can gradually increase the QOL in older adults with KO. This effect might be attributable to the gradual effect of curcumin ointment in decreasing knee inflammation and pain. Curcumin is an antioxidant, anti-inflammatory, and anti-swelling agent. Its short-term anti-inflammatory effect is reported to be equal to hydrocortisone and phenylbutazone. It seems that the gradual reduction of inflammation, pain, and swelling of the knee, reduced an important role in the improvement of knee pain in older adults with KO, which consequently improves their QOL.

Figure 2: Variations of the overall quality of life at three measurements in the two groups
its stiffness and improved patients’ mobility which consequently improved the QOL of the intervention group.

In the present study, a noticeable change in the QOL of the intervention group began after the 4th week. This can be attributed to the fact that QOL is a mental perception that develops gradually over time and it takes several weeks to observe tangible changes in it. For this reason, QOL studies often question one’s QOL over the past few weeks. On the other hand, the delayed changes in the QOL can be attributed to a gradual decrease in patients’ perceived knee pain and stiffness. A study of 55 older adults showed that >96% and 64% of them had hip and KO, respectively, and possessed only 55% of the QOL score.[34]

Pain and decreased QOL compel patients with osteoarthritis to try different methods along with medical treatments to alleviate these problems. A review of 29 studies has shown that these patients use a variety of methods such as acupuncture, tai chi, yoga, and massage therapy.[35] Some studies have also reported the effects of turmeric[20] or its extract on pain and other symptoms of arthritis[36] however; they did not focus on the QOL of these patients. A study also examined the effects of a combination of glucosamine sulfate, methyl sulfonyl methane, willow bark extract, ginger, boswellic acid, turmeric root extract, hyaluronic acid and cayenne on pain, joint stiffness, QOL, and physical functioning in middle-aged and older adults with osteoarthritis. This compound was effective in reducing the pain severity and improving the physical functioning but had no significant effect on the patients’ QOL.[21] However, the present study showed that topical use of curcumin ointment for 6 weeks could significantly increase the QOL of the intervention group.

This is one of the few studies on the effect of curcumin on knee pain in patients with KO. However, we only studied the patients who referred to a physician’s office. Therefore, further multicenter studies with larger samples are recommended. We only followed the patients for 6 weeks, therefore, longer follow-ups are suggested to assess the duration of the effects of curcumin. Although the researcher emphasized to the patients not to disclose their treatment to others, this issue cannot be fully guaranteed.

**Conclusion**

The present study showed that topical administration of 5% curcumin ointment can significantly improves the QOL in older adults with KO. Therefore, the use of this ointment in the treatment of older adults with KO is suggested. Given the side effects of the synthetic drugs used in these patients, curcumin ointment may possibly be used as a supplement to conventional medications to help reduce the dose of painkillers and anti-inflammatory drugs and improve their pain and QOL.

This study was performed on a small sample of older adults. Given the scarcity of studies on the effect of topical administration of curcumin on QOL, it is recommended to repeat the same studies on larger samples with longer follow-up.

**Acknowledgment**

This manuscript resulted from the thesis of Mrs. Neda Jamali for the fulfillment of a Master’s degree in geriatric nursing. The authors are deeply thankful to the patients who participated in this study.

**Financial support and sponsorship**

This study supported by the research deputy of Kashan University of Medical Sciences (grant number: 97157).

**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. Kim I, Kim HA, Seo YI, Song YW, Jeong JY, Kim DH. The prevalence of knee osteoarthritis in elderly community residents in Korea. J Korean Med Sci 2010;25:293-8.
2. Akbarnejad N, Shahlbalaghi F, Khange H. The effect of acupuncture on physical function of knee among elderly patients with osteoarthritis: A randomized clinical trial. Nurs J Vulnerable 2016;2:1-14.
3. Hwang J, Lee S, Kim Y. Effects of thermotherapy combined with aromatherapy on pain, flexibility, sleep, and depression in elderly women with osteoarthritis. J Muscle Joint Health 2011;18:192-202.
4. Mehrabian H, Shojaedin S, Baratii A, Ghasemi M. Effects of aquatic exercise on the pain, symptoms, motor performance and quality of life of elderly women with knee osteoarthritis. Res Rehab Sci 2012;8:337-45.
5. Taghipour D, Hosseini S, Kia K, Abbaspour M, Ghadimil R. Prevalence of musculoskeletal pain and it’s correlation to functional disability in elderly. Knowl Health 2013;8:76-82.
6. Bahramian H, Heydarian K. Effects of three types of orthoses on pain in patients with knee Osteoarthritis. Iran J Agein 2010;4:59-65.
7. Fraga MJ, Cader SA, Ferreira MA, Giani TS, Dantas EH. Aerobic resistance, functional autonomy and quality of life (QOL) of elderly women impacted by a recreation and walking program. Arch Gerontol Geriatr 2011;52:e40-3.
8. Triantafyllou K, Vlachogiannakos J, Ladas SD. Gastrointestinal and liver side effects of drugs in elderly patients. Best Pract Res Clin Gastroenterol 2010;24:203-15.
9. Fong S, Guo X, Wong L, Ng YM, Chung JW. Novel aquatic physiotherapy programme for elderly Chinese adults with osteoarthritis of the knee: A randomised controlled trial. J Lancet 2017;390:s33.
10. Mashaiekhi K, Zare Marzouni H. Curcumin (extracted from turmeric) and its therapeutic effects. Jorjani Biomed J 2017;4:1-20.
11. Fallah Huseini H, Zahmatkash M, Haghighi M. A review on pharmacological effects of curcuma longa turmeric. J Med Plants 2010;1:1-15.
12. Qin S, Huang L, Gong J, Shen S, Huang J, Ren H, et al. Efficacy and safety of turmeric and curcumin in lowering blood lipid levels in patients with cardiovascular risk factors: A meta-analysis of randomized controlled trials. Nutr J 2017;16:68.

13. Thavorn K, Mamdani MM, Straus SE. Efficacy of turmeric in the treatment of digestive disorders: A systematic review and meta-analysis protocol. Syst Rev 2014;3:71.

14. Wong LP. Prenatal stress and dysmenorrhea: Urban-rural and multietnic differences in perception, impacts, and treatment seeking. J Pediatr Adolesc Gynecol 2011;24:272-7.

15. Nguyen TA, Friedman AJ. Curcumin: A novel treatment for skin-related disorders. J Drugs Dermatol 2013;12:1131-7.

16. Golmakani N, Rabici Motlagh E, Tara F, Assili J, Shakeri MT. The effects of turmeric (Curcuma longa L) ointment on healing of episiotomy site in primiparous women. Iran J Obstet, Gynecol Reprod Med 2008;11:29-39.

17. Murugan S, Bethapudi B, Purusothaman D, Chandrasekaran PR, Velusami CC. Antiarthritic effect of polar extract of curcuma longa on monosodium iodoacetate induced osteoarthritis in rats. Antiinflamm Agents Med Chem 2017;16:193-202.

18. Bethapudi B, Murugan S, Illuri R, Mundkinajeddu D, Velusami CC. Bioactive Turmerosaccharides from Curcuma longa extract (NR-INF-02): Potential ameliorating effect on osteoarthritis pain. Pharmacog Mag 2017;13:S623-7.

19. De Breucker S, Rouvière H, Mélot C, Appelboom T. Flexofytol® (a belgian curcumin extract) for the treatment of aged patients with osteoarthritis and comorbidity. Open J Rheumatol Autoimmune Dis 2017;7:167-77.

20. Haroyan A, Mukuchyan V, Mkrtchyan N, Minasyan N, Gasparyan S, Sargsyan A, et al. Efficacy and safety of curcumin and its combination with boswellic acid in osteoarthritis: A comparative, randomized, double-blind, placebo-controlled study. BMC Complement Altern Med 2018;18:7.

21. Nieman DC, Shanely RA, Luo B, Dew D, Meaney MP, Sha W. A commercialized dietary supplement alleviates joint pain in community adults: A double-blind, placebo-controlled community trial. Nutr J 2013;12:154.

22. Nelson K, Dahlin J, Bisson J, Graham J, Pauli GF, Walters MA. The essential medicinal chemistry of curcumin: Miniperspective. J Med Chem 2017;60:1620-37.

23. Gemmell HA, Jacobson BH, Hayes BM. Effect of a topical herbal cream on osteoarthritis of the hand and knee: A pilot study. J Manipulative Physiol Ther 2003;26:e15.

24. Rat AC, Coste J, Pouchot J, Baumann M, Spitz E, Retel-Rude N, et al. OAKHQL: A new instrument to measure quality of life in knee and hip osteoarthritis. J Clin Epidemiol 2005;58:47-55.

25. Saffari M, Emami Meybodi MK, Koenig HG, Pakpour AH, Rshidi Jahan H. Psychometric examination of the Persian version of Osteoarthritis Knee and Hip Quality of Life questionnaire. Int J Rheum Dis 2017;20:1648-57.

26. Alkan BM, Fidan F, Tosun A, Arıçğolu O. Quality of life and self-reported disability in patients with knee osteoarthritis. Mod Rheumatol 2014;24:166-71.

27. Araujo IL, Castro MO, Daltro C, Matos MA. Quality of life and functional independence in patients with osteoarthritis of the knee. Knee Surg Relat Res 2016;28:219-24.

28. Bindawas SM, Vennu V, Al Shih S. Differences in health-related quality of life among subjects with frequent bilateral or unilateral knee pain: Data from the Osteoarthritis Initiative study. J Orthop Sports Phys Ther 2015;45:128-36.

29. McCarberg BH, Nicholson BD, Todd KH, Palmer T, Penles L. The impact of pain on quality of life and the unmet needs of pain management: Results from pain sufferers and physicians participating in an Internet survey. Am J Ther 2008;15:312-20.

30. Dueñas M, Ojeda B, Salazar A, Mico JA, Failde I. A review of chronic pain impact on patients, their social environment and the health care system. J Pain Res 2016;9:457-67.

31. Rosemann T, Wensing M, Joest K, Backenstrass M, Mahler C, Szczesny J. Problems and needs for improving primary care of osteoarthritis patients: The views of patients, general practitioners and practice nurses. BMC Musculoskeletal Disord 2006;7:48.

32. Australian Government Department of Health. Osteoarthritis Nurse Clinics: A Resource for Primary Health Care Nurses. Available from: https://www.arthritis.org.au/health-professionals/health-professional-resources/Osteoarthritis_Nurse_Clinics_Resource_FINAL.pdf [Last Accessed on 2021 Jan 3].

33. Chandra D, Gupta SS. Anti-inflammatory and antiarthritic activity of volatile oil of Curcuma longa (Haldi). Ind J Med Res 1972;60:138-42.

34. Mahmoudi S, Khalil E, Mariem B, Gaddour M, Jenni S, Khachnaoui F. Quality of life for patient with knee osteoarthritis. Ann Phys Rehabil Med 2016;59:158-9.

35. Shengelia R, Parker SJ, Ballin M, George T, Reid MC. Complementary therapies for osteoarthritis: Are they effective? Pain Manag Nurs 2013;14:e274-e288.

36. Daily JW, Yang M, Park S. Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: A systematic review and meta-analysis of randomized clinical trials. J Med Food 2016;19:717-29.