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REVIEW ARTICLE

Effectiveness of Argan Oil Consumption on Knee Osteoarthritis Symptoms: A Randomized Controlled Clinical Trial

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Abstract: ***Background*:** Knee osteoarthritis (KOA) is a common chronic degenerative disorder. It causes joint pain, walking difficulties and a decline in general physical function. Many pain drugs and treatment modalities can be prescribed for KOA. Among traditional medicines in Morocco, Argan oil has been used in the treatment of knee osteoarthritis to reduce pain and improve physical activity, though there have been no medical-based evidence for such treatment. Argan oil is known to have anti-oxidant and lipid modulatory properties due to its content of many substances, such as tocopherols, phytosterols, saturated and unsaturated fatty acids.

***Objectives*:** This study was undertaken in order to investigate the effect of daily consumption of culinary argan oil on KOA symptoms.

***Patients and Methods*:** We conducted a randomized controlled clinical trial on patients with KOA according to the American College of Rheumatology (ACR) criteria. Patients were divided into 2 groups: argan oil group who received argan oil to be consumed every morning (30 ml per day) for 8 weeks and control group with no treatment. Clinical assessment before and after 8 weeks study was performed by several tests such as the visual analogue scale (VAS) for pain, walking perimeter, the Western Ontario and McMaster Universities osteoarthritis index (WOMAC), and the Lequesne index.

***Results*:** The study included 100 patients. 51 patients were randomly assigned to argan oilgroup while 49 patients were randomly assigned to control group with no treatment. Mean age of our patients was 58.24 ± 7.2 years, with a majority of women (93%). Following 8 weeks of argan oil consumption, argan oil group had a very significant decrease of VAS for pain ($p< 0.0001$), with a significant decrease in WOMAC pain index ($p < 0.0001$), and improvement of WOMAC function index ($p < 0.0001$). Lequesne index ($p < 0.0001$) as well as walking distance ($p =0,002$) significantly improved. When data of argan oil group were compared to those of control group, we found statistically significant differences in all the above measured parameters : VAS of pain (P=0,02), WOMAC pain (p<0,0001), WOMAC function (p<0,0001), walking distance (p=0,001) and lequesne index (p<0,0001).

***Conclusion*:** Patient's consumption of argan oil seems to be safe and efficacious in improving clinical symptoms of KOA.

Keywords: Argan oil, knee osteoarthritis, pain, function.

1. INTRODUCTION

Osteoarthritis is the most prevalent and costly joint disease in our society that constitutes a leading cause of disability and pain in the adult population. The knee is the most affected joint [1, 2].

Knee osteoarthritis (KOA) is a chronic condition characterized by a complex and multifactorial nature which explain the variability in symptoms presentation and response to treatment. Thus, it constitutes a challenging condition for therapeutic management [1, 3]. Optimal management involves non-drug and drug approaches that focus on relieving pain and improving function [1, 4]. Conventional medications are often effective for symptom relief, but they can also

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cause significant side effects, especially in elderly population. Several natural substances have been shown to be at least as effective as non-steroïdal anti-inflammatory drugs at relieving the symptoms of KOA and preliminary evidence suggests some of these compounds may exert a favorable influence on the course of the disease [5].

Among traditional medicines in Morocco, argan oil has been used in the treatment of knee osteoarthritis to reduce pain and improve physical activity, though there has been no medical-based evidence for such treatment. Virgin argan oil is a product obtained from roasted seeds of the fruit of the argan tree (Argania spinosa L. Skeels), only endemic in south western (SW) Morocco. It is the most remarkable species in North Africa, due to its botanical and bioecologic interest as well as its social value [6-8]. This oil has been used by the Amazigh population for centuries due to its sensorial and health-giving properties [7, 8]. It is principally composed of mono-unsaturated (up to 80%) and saturated (up to 20%) fatty acids. As minor components, it contains polyphenols, tocopherols, sterols, squalene, and triterpene alcohols. Together with the mono-unsaturated fatty acids, these minor components are likely to be responsible for its beneficial effects [8-10].

Several studies have reported its cardioprotection effect, an anti- proliferative effect on human prostate cancer cell lines and antioxidant properties [11, 12].

The present study, to our knowledge, is the first one to show the potential efficacy of Argan oil consumption on clinical parameters of knee osteoarthritis.

2. PATIENTS AND METHODS

2.1. Study Design and Participants

We conducted a randomized clinical trial in the rheumatology department of Hassan II University Hospital. The patients included in the study have knee osteoarthritis according to the American College of Rheumatology (ACR) criteria [13]. All patients underwent an X Ray of both knees. Exclusion criteria were: osteoarthritis due to inflammatory arthritis, microcrystalline etiology, patient who had knee surgery, people with malignancy and stage IV of Kellgren and Lawrence (K/L) score [14].

Patients enrolled in the clinical trial were randomly divided into two groups: argan oil treatment group and control group with no treatment. We used the function random of excel to classify the two randomized groups.

Argan oil group received argan oil and consumed every morning (30 ml per day= two tablespoons) for 8 weeks. Argan oil was purchased from a women cooperative production unit with high quality standards and with known oil chemical composition [8-15]. The control group did not receive anything because there was no product of oily nature that can be safe and make a placebo.

Patients of both groups were asked to continue their regular daily diet and especially to continue their usual pharmacological treatment for knee osteoarthritis (analgesics, NSAIDs or chondroprotective agents). No therapeutic changes were made during the study and three months before the inclusion.

The study protocol was approved by a local ethical committee of the faculty of medicine, Sidi Mohamed Ben Abdellah University. Patients signed up a written consent to participate in the study.

2.2. Socio-demographic Characteristics

Each subject answered a survey to mention age, gender, history of previous medical or surgical disease, medication history and disease duration.

All subjects underwent a medical interview and a thorough medical examination. The height and weight of each patient were obtained with them wearing indoor clothing and without shoes. Body Mass Index (BMI) was then calculated as weight (kg) divided by the square of height (m).

2.3. Knee Osteoarthritis Characteristics

Self-rated pain intensity at the moment of the evaluation was measured on a 10-cm horizontal visual-analogue scale (VAS), with 0 cm labeled as “no pain” and 10cm labeled as “worst pain I have ever had”. The Western Ontario and McMaster Universities (WOMAC) index, a self-assessment multidimensional instrument that evaluates 17 functional activities (WOMAC function: WF), 5 pain-related activities (WOMAC pain: WP) and 2 joint stiffness categories in 3 different subscales (WOMAC stiffness: WS) was used to measure dysfunction and pain. Lequesne Algo-Functional index in KOA has been developed as an interview format and is based on of three aspects: pain, maximum distance walked and activities of daily living. Walking distance (WD) on meters was also assessed [13, 16].

This clinical assessment was done in each group at the inclusion and after 8 weeks study.

2.4. Statistical Analysis

The statistical analysis was performed with SPSS version 20. All data are presented as the mean ± standard deviation (SD) for quantitative variables and as percentages for qualitative variables. Two tails paired student t-test was used as a statistical analysis method to compare data in each group before and after argan oil consumption. The statistical significance was set as $p \leq 0,05$.

3. RESULTS

3.1. Socio-demographic Data and KOA Characteristics

A total of 100 patients were randomized into two groups: Argan oil group (n=51) and control group (n=49).Mean age of our patients was 58.24 ± 7.2 years, with a majority of women (93%). Demographic and clinical characteristics of the patients at baseline were well balanced among groups, and are summarized in Table **1**. 49% of control group patients had stage 3 of K/L while 51% of argan oil group patients had stage 2 of K/L. The percentage of the use of analgesics, Non-steroidal anti-inflammatory drugs (NSAIDs), and chondroprotective agents was almost similar in both groups (Table **2**).

Table 1. Demographic data and knee osteoarthritis symptoms in Argan oil group and control group.

	Argan Oil Group	Control Group	p value
Age(years)	58,24± 8.8	58,85± 5.6	0,61
Sex(F/M)	51/4	49/3	-
Body mass index (Kg/m^2)	32± 5.0	32 ± 3.6	0,45
Disease duration (years)	4,47±3,04	4,76 ±2,45	0,69
Pain VAS (mm)	47,25± 15,24	48±15	0,82
WOMAC pain	6,55± 4,17	5,2±3	0,07
WOMAC stiffness	3,86± 2,5	3,82±2,21	0,92
WOMAC function	15,73± 7,62	14± 6,41	0,24
WOMAC index	26,25 ±12,67	23±9,75	0,16
WD(m)	855,88± 357,86	1112,24±239,65	0,09
Lequesne index	5,50± 2,834	5,84±2,6	0,54

WD : Walking distance. VAS : visual analogue scale.

Table 2. Radiological and therapeutic characteristics of both groups.

	Control Group n=49		Argan Oil Group n=51	
	Number	**Percentage %**	**Number**	**Percentage %**
Stage 2 of K/L	21	43	26	51
Stage 3 ofK/L	24	49	18	35
Analgesics	45	92	45	88
NSAIDs	15	31	17	33
Chondroprotective agents	42	86	45	88

NSAIDs : nonsteroidal anti-inflammatory drugs. **K/L**: Kellgren and Lawrence.

3.2. Changes within Argan Oil Group and Between-goup Differences

Upon 8 weeks of study, clinical parameters of KOA of patients who consumed argan oil were modified toward better trends (Table **3**). Indeed, all clinical parameters were significantly improved after the consumption of argan oil, except the WOMAC stiffness, which decreased slightly, but not significantly. The pain VAS was significantly lower after 8 weeks (p<0,001), as well as the WOMAC index (p<0,001) and Lequesne index (p<0,001). The walking distance has become less limited (p=0,002).

Interestingly, when compared to control group, the consumption of argan oil during 8 weeks resulted in a very significant improvement in clinical parameters of KOA, namely the pain VAS (=0,02), WOMAC index (p<0,001), WD (p=0,001), and Lequesne index (P<0,001) (Table **3**).

No side effects related to Argan oil consumption were registered during the treatment and all patients completed the treatment and performed the post-treatment assessment.

4. DISCUSSION

The efficacy of Argan oil consumption on pain relief and functional recovery in patients with knee osteoarthritis were tested in the present study. To our knowledge, this study is the first to show the efficacy of Argan oil consumption on clinical parameters of knee osteoarthritis.

Osteoarthritis is a disease with metabolic, age and injury related phenotypes. The concept of metabolic osteoarthritis is approved by epidemiological and biological studies [17-19].

It has long been thought that obesity contributes to primary osteoarthritis of the knee through static and dynamic loads on the cartilage leading to chronic cartilage degeneration [20]. However this does not explain the increased incidence in the non weight-bearing joints of obese patients [21], then the role of metabolic disorders has been recognized [18]. Furthermore, Abourazzak FE *et al*. demonstrated a significant association between individual metabolic factors and pain and functional impairment in KOA Moroccan women [17]. They found that diabetes, dyslipidemia and hyperten-

Table 3. Clinical parameters of KOA at baseline and after the 8 weeks period study of Argan oil consumption. P* refers to comparison of the data evolution between the two groups.

	Argan Oil Group			Control Group			Between-Group Differences P*
	Baseline	8 Weeks	p value	Baseline	8 Weeks	p value	
Pain VAS (mm)	47,25±15,24	32,35±13,94	<0,001	48±15	50,2±16,9	0,2	0,02
WOMAC Pain	6,55± 4,17	4,86±3,93	<0,001	5,2±3	5,84±3	0,01	<0,0001
WOMAC Stiffness	3,86±2,5	3,69±3,46	0,6	3,82±2,21	4,45±2	0,02	0,1
WOMAC Function	15,73±7,62	11,71±6,33	<0,001	14±6,41	16,2±6,2	0,003	<0,0001
WOMAC index	26,25 ±12,67	20,24±12,61	<0,001	23±9,75	26,5±9,4	<0,001	<0,0001
WD (m)	855,88± 357,86	972,35± 416,15	0,002	1112,24±239,65	1028,37±138,63	0,08	0,001
Lequesne index	5,50±2,834	4,49±2,18	<0,001	5,84±2,6	6,1±2,8	0,06	<0,0001

sion may independently increase Knee OA symptoms even in the absence of obesity.

Osteoarthritis and the metabolic syndrome have both a relation with a number of mediators induced by pro-inflammatory cytokines, like oxidative stress agents, oxidized low-density lipoproteins, adipokines, pro-inflammatory lipid mediators and nitric oxide [22, 23]. The acceleration of aging and cell senescence can be due to chronic low grade inflammation, leading to oxidative stress. The term "inflammaging" designates this combination of aging and inflammation [24].

Obesity increased mass and joint load and altered pro-inflammatory factor adipokines secretion, leading to the chronic low grade inflammatory status in joint tissues [25]. Additionally, cholesterol accumulation in the cartilage can impair the efflux function of cartilage inducing OA [26]. Oxidized LDL can activate synovial cells such as macrophages, endothelial cells, and synovial fibroblasts, resulting in release of growth factors, MMP and pro-inflammatory cytokines, causing cartilage destruction and bone deformations [27]. Furthermore, dyslipidemia with increased free fatty acid and decreased high density lipoprotein and adiponectin are associated with OA development by decreased vascular reactivity and endothelial dysfunction [28]. It has been suggested that the damage caused by hyperglycemia is both direct and indirect via its effect on chondrocyte metabolism imbalance and sensitivity to matrix metalloproteinase promoting cartilage matrix degeneration and apoptosis [18, 29].

In the light of these data, the treatment of metabolic disorders has been suggested as a possible avenue to retard the progression of osteoarthritic degeneration [30]. Our results suggest that argan oil can be an interesting therapeutic alternative of KOA. Indeed, argan oil consumption can improve parameters of metabolic syndrome and plasma lipid atherogenic indices in patients with knee osteoarthritis [31].

Interestingly, the unsaponifiable fraction of this oil is essentially rich in antioxidant compounds such as tocopherols, which are present in a higher proportion compared to olive oil (637 mg/kg versus 258 mg/kg, respectively) and particularly in its γ-isoform (75%) [32]. Argan oil was found to increase the molar ratio of α-tocopherol/total cholesterol and α-tocopherol concentration as well as paraoxonase activities and vitamin E concentration in healthy men [33]. Tocopherols (vitamin E) are the most potent lipid-soluble antioxidants in blood, breaking free-radical chain reactions of lipid peroxidation [34]. γ-tocopherol may be a more potent antioxidant and anti-inflammatory agent than α-tocopherol in some situations [35].

Tocopherols may mediate the osteoarthritis process by interfering with inflammation, which is increasingly recognized as an important process in osteoarthritis [36]. In addition, they may help stabilize lysosomal membranes, thereby inhibiting the release of enzymes is believed to play a role in the pathogenesis of osteoarthritic joint damage [37].

To summarize, argan oil consumption can relieve knee osteoarthritis pain via two possible ways, directly due to tocopherols, or indirectly via improvement of metabolic syndrome, which is often associated with pain and functional impairment in KOA.

CONCLUSION

New approaches are needed, both to increase the safety and efficacy of symptomatic treatment and to exert a favorable influence on the course of knee osteoarthritis.

Argan oil consumption showed a beneficial and safe effect on clinical parameters of this disease, which should encourage other studies to consolidate the results obtained.

LIST OF ABBREVIATIONS

KOA = Knee Osteoarthritis

SW = South Western

OA = Osteoarthritis

MMP = Metalloproteinase

AUTHORS CONTRIBUTION

Author JE handled patients and gathered the data. FEA and TH handled patients and designed the study. NB partici-

pated in statistical data analysis. ME designed the study and coordinated the study.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are base of this research.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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