Hyper oxygenated olive oil in symptomatic treatment of knee osteoarthritis : a double blind placebo-controlled trial.

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Keywords : Hyperoxygenated olive oil, pain, knee osteoarthritis, complementary medicine, alternative medicine.

Abstract :

Knee osteoarthritis is responsible for an important medicamentous consumption, which can be deleterious especially in elderly population. In these cases, the use of non medicamentous treatments is particularly interesting.

The objective of this study is to compare the antalgic effect of hyper oxygenated olive oil and conventional olive oil.

We conducted a monocentric, a double blind placebo-controlled trial which included 30 patients, who complained from gonalgia attributed to stage I or II knee osteoarthritis.

For the same patient, we considered that the case group was the knee treated by hyper oxygenated olive oil. The control group was represented by the knee treated by conventional olive oil. A massotherapy protocol was performed on each knee by a physiotherapist.

For each knee of each patient, we noted the VAS (Visual Analog Scale) to measure the pain, and the level of satisfaction.

For the case group, VAS was significantly reduced after massotherapy, dropping from 5,7 to 1,8 ($p<0,05$); 20 patients were very satisfied (66,7%), 10 patients were moderately satisfied (33,3%).

Many authors demonstrated the anti inflammatory, antalgic and chondroprotective effects of olive oil.

Hyper oxygenated olive oil is obtained by an ozonisation reaction of conventional olive oil, producing oxygenated derivatives, which anti inflammatory and immunomodulation effects have been demonstrated, notably by Maritza et al.

The use of hyper oxygenated olive oil in symptomatic treatment of knee osteoarthritis is reliable and interesting alternative, especially in fragile, elderly population, highly at risk of medicamentous side effects.

Introduction

Knee osteoarthritis can be considered as a public health problem, especially in Tunisia.

Its increasing frequency linked to the increase in life expectancy, as well as the functional impact for which it is responsible, make this pathology a health and economic issue.

Its management calls primarily for symptomatic drug treatment, especially in the early stages. It implies a significant consumption of analgesics and anti-inflammatory drugs, with the consequence of an increase in the risk of adverse effects, in fragile and elderly patients, thus posing a therapeutic problem. The use of non-drug alternatives then has all its interest, and is a topical subject.

In this context, the external use of olive oil as an adjunct to analgesic massage therapy has demonstrated its beneficial effects in numerous studies (1–7).

No study has, according to the literature, studied the analgesic effect of hyper-oxygenated olive oil on knee pain in relation to knee osteoarthritis.

The objective of this prospective, randomized double-blind study is to compare the analgesic effect of hyper-oxygenated olive oil and that of conventional olive oil.

Materials and methods

1. Type of study

We conducted a single-center, prospective, randomized, double-blind, controlled trial type study. We made sure, beforehand, of the approval of the ethics committee. In accordance with the Helsinki Declaration, we obtained the informed consent, duly written and signed, from each patient.

2. Patients

We selected **30 patients** (60 knees) from the outpatient department of orthopedic surgery and rheumatology, including all patients consulting for bilateral gonalgia related to Ahlbäck stage I or II knee osteoarthritis.

The exclusion criteria were as follows:

- patients with knee surgery,
- allergy to the products tested or to their excipients,
- any patient refusing to participate in the study.

We estimated the minimum number of subjects needed for the study based on a pilot study including 10 patients. We estimated the analgesic effect of conventional olive oil (placebo) and hyperoxygenated olive oil based on the VAS (visual analog scale) before (VAS-pre) and after massage therapy (VAS-post) by the two aforementioned products. We then compared the difference "VAS-pre - VAS-post" for the control group and the test group (the VAS fell by 1.4 points with conventional olive oil, and by 4 points with hyper oxygenated olive oil).

Based on these values, using a 95% confidence interval and a power of 0.9, we estimated the common standard deviation to be 1.494. Thus, we were able to calculate the minimum number of subjects required for the study: 12 patients (six patients for each group).

3. Products tested

- The placebo used was conventional extra virgin olive oil.
- The product tested was extra virgin olive oil which had undergone a process of hyper-oxygenation by physical method.
- Both products had the same consistency and the same scent.

4. Randomization

For the same patient, we considered that **the experimental group** corresponded to the knee treated with hyperoxygenated olive oil, **the control group (control)** corresponded to the contralateral knee, treated with placebo (conventional olive oil) .

- We have a blue bottle (for hyperoxygenated olive oil) and a red bottle (for the placebo: conventional olive oil); the contents of the two bottles having the same texture and the same fragrance, the two bottles being perfectly opaque. For the same patient, a nurse is asked to choose which knee will be treated with the blue bottle, and which will be treated with the red bottle.
- A second nurse was responsible for listing epidemiological, functional and clinical data.

Neither the nurses, nor the physiotherapist, nor the patient, know which bottle corresponds to the product tested or to the placebo.

5. Intervention

For each of the knees tested, the physiotherapist performed a ten-minute analgesic massage therapy for each of the two knees. The affected area extended over four fingers on either side of the knee joint, on its different faces.

The techniques implemented were: deep transverse massage (DTM), kneading of the quadriceps muscle, and gentle mobilization of the patella.

6. Data

All of the following data were collected for all of our patients: age, sex, history, concept of self-medication, quantification of drug consumption. We noted: the visual analogue scale (VAS), preceding the massage therapy session (VAS-pre) and following the massage therapy session (VAS-post), as well as the degree of satisfaction with massage therapy (not satisfied, moderately satisfied , very satisfied) for each of the two knees.

Ahlbäck's radiological stage was noted for each of the two knees.

7. Statistical analysis:

All the data were entered and analyzed using SPSS version 25 software by a physician who was not included in the study. The various tests performed included the chi-square test, and the t-test

for equality of means. The significance level of p was set at 0.05, a value below which the result was considered significant.

Results

1. Epidemiological data:

The mean age of our patients was 62.73 years, ranging from 47 to 80 years.

We noted a female predominance in our series, with 19 women (63.3%) and 11 men (36.7%).

For the use of paracetamol, NSAIDs and analgesics to remedy 2, we have summarized our results in Table 1.

We found the notion of self-medication in 16 patients, i.e. 53.3% of cases.

2. Functional results:

For the knee treated with hyper-oxygenated olive oil, VAS was significantly reduced after massage therapy, from an average of 5.7 versus 1.8, with a significant difference ($p < 0.05$).

For the knee treated with conventional olive oil (placebo), the mean VAS was reduced with no significant difference between the pre-VAS (4.37) and the post-VAS (3.37).

For the knee treated with hyper-oxygenated olive oil, 20 patients were very satisfied (66.7%), 10 patients were moderately satisfied (33.3%), no patient was "not satisfied".

For the knee treated with placebo, 18 (60%) patients were “not satisfied”, 12 patients (40%) were moderately satisfied and no patient was very satisfied.

3. Adverse effects

No adverse effects were noted during our study.

Discussion

Knee osteoarthritis is a condition affecting more than 50% of patients over 65 years of age (4), the main clinical expression of which is pain. It is responsible for a significant functional and psychological impact, giving rise to excess drug consumption in patients who are often polymedicated, then increasing the risk of adverse effects and drug interactions.

The use of alternative treatments then takes on all its interest. In this context, the external use of extra virgin olive oil as an adjunct to analgesic massage therapy has shown its beneficial effects in numerous studies (1–7).

Many authors have studied the mode of action of olive oil, finding its anti-inflammatory and analgesic role in the short term, and its chondroprotective effect to the medium and long term. (7) Biologically, the anti-inflammatory role of olive oil can be explained by a competition of molecules from olive oil extracts with pro-inflammatory lipopolysaccharides (LPS) (8). Mevel et al. demonstrated that extracts of extra virgin olive oil were responsible for a decrease in the chondrocyte expression of cyclooxygenase-2 (COX-2), nitric oxide (NO) and prostaglandin E2, involved in the inflammatory response (9). The presence of oleocanthal, which is a polyphenol found in extra virgin olive oil, would have an anti-inflammatory effect by reducing the expression of inflammation proteins such as interleukin 1-ß, TNF alpha (10). The hydroxytyrosol contained in olive oil is thought to intervene through an anti-oxidative action (11).

Hyper-oxygenation of olive oil is obtained through an ozonization reaction (12): a solution of extra virgin olive oil is introduced into an ozone reactor operating at room temperature. The reaction produced involves ozone molecules and the double carbon chains of unsaturated fatty acids found in olive oil, with the production of oxygenated derivatives (hydroperoxides, polyperoxides, diperoxides). These derivatives would be involved in the stimulation of the production of intra-cellular antioxidant enzymes, and would be responsible for a modulation of the local inflammatory reaction, by an action on interferon c, TNF alpha, interleukin 8 and CD11b (13).

Our study is the first, to our knowledge, to focus on the effectiveness of hyper-oxygenated olive oil on gonalgias linked to early knee osteoarthritis. Through our study, we demonstrated that there was a significant reduction in pain after massage therapy using hyperoxygenated olive oil, compared to the use of placebo ($p < 0.05$).

Conclusion:

The use of hyper-oxygenated olive oil in the symptomatic treatment of early knee osteoarthritis is an interesting and reliable alternative, especially in polymedicated patients, in whom the risk of adverse drug reactions is high.

It would nevertheless be interesting to include a larger number of patients and to study the effect of this product over a longer term.

Conflicts of interest: None

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	Use of paracetamol	Use of NSAIDs	Use of analgesics level 2

Never	1 (3,3%)	2 (6,7%)	14 (46,7%)
Less than 3 times a week	10 (33,3%)	18 (60%)	14 (46,7%)
More than three times a week	15 (50%)	6 (20%)	2 (6,6%)
Every day	4 (13,3%)	4 (13,3%)	0 (0%)

Table I : Use of analgesics