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Comparing Analgesic Effects of a Topical Herbal Mixed Medicine with Salicylate in Patients with Knee Osteoarthritis

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Abstract: Knee osteoarthritis is the most common cause of disability among people and it is a common disease of joints that can lead to cartilage damage. In this study the analgesic effects of a herbal ointment containing cinnamon, ginger, mastic (Saghez) and sesame oil is compared with Salicylate ointment in patients suffering from knee osteoarthritis. It was a double-blind randomized controlled trial study. Patients with diagnosed arthritis were involved in the study and they were divided in two groups via block randomization method. For six weeks, twice a day, intervention group applied herbal ointment and control group used Salicylate ointment. The severity of pain, morning stiffness and limited motion were measured using Visual Analog Pain Scale. In order to analyze the trends of these three indexes, repeated measurement test was used. Ninety two participates with the mean age of 52.2 (± 12.4) years and with the mean disease period of 30.45 (± 30.3) months were involved in the study. There was no significant difference between two groups regarding the distribution of sex, weight, height, BMI and the duration of illness. No statistical difference was observed between two groups regarding pain relief, morning stiffness and limited motion; nevertheless in repeated measurements during second, fourth and sixth weeks in both groups the decreasing trend of these three indexes had been statistically significant ($p < 0.0001$). It seems that using this herbal combination is clinically effective for patients suffering from knee osteoarthritis in order to decrease their pain, morning stiffness and limited motion; its effect is comparable with Salicylate ointment.

Key words: Osteoarthritis, herbal medicine, randomized controlled trial

INTRODUCTION

Osteoarthritis is one of the most common debilitating diseases which usually involves joints and damages cartilage (Felson, 1993; Creamer *et al.*, 1998; Gemmell *et al.*, 2003; Martel-Pelletier *et al.*, 2008). It influences knees more than any other joints and about 80% of people older than 65 years old are usually affected by the disease (Creamer and Hochberg, 1997; Gemmell *et al.*, 2003). The symptoms of knee osteoarthritis are pain, morning stiffness and knee limited motion (Hochberg *et al.*, 1995). In the past few years there has not been much progress in treating the disease and it has been limited to some analgesic anti-inflammatory drugs (Hungin and Kean, 2001; Petrella *et al.*, 2002). There are various curing methods including oral medicines, topical drugs, intra-joint drugs, complementary drugs and surgery (Buffum and Buffum, 2000; Miller *et al.*, 2005; Ameye and Chee, 2006; Altman, 2009) nonetheless nonsteroidal anti-inflammatory drugs are extensively used for treatment (Buffum and Buffum, 2000; Hungin and Kean, 2001). It has been recommended to use the topical

form of these medicines as they do not have the side effects of systemic drugs (Roth and Shainhouse, 2004; Altman, 2009). Salicylate ointment is a common topical medicine prescribed for this disease however one of the problems in using this ointment is that it cannot deeply penetrate skin (Hungin and Kean, 2001; Altman, 2009).

Herbal medicines could be used to relief pain (WHO, 1998) and there have been some new researches about applying herbal medicines for treating osteoarthritis (Teekachunhatean *et al.*, 2004). Some studies showed that using herbal combinations could be effective and could have fewer side effects; these drugs are very prevalent and popular in some countries (Teekachunhatean *et al.*, 2004). Cinnamon essence which has analgesic and anti-rheumatic effects could inhibit IL-1 beta and IL-6 (Montes-Belmont and Carvajal, 1998; Chao *et al.*, 2005). Ginger is one of the most famous herbal drugs and is traditionally prescribed for headaches and rheumatic pains (Haghighi *et al.*, 2003). It seems that ginger could have pharmacologic effects similar to nonsteroidal anti-inflammatory drugs and it could prevent generating prostaglandin via controlling cyclooxygenase 1 and 2

(Grzanna *et al.*, 2005; Shen *et al.*, 2005). Some other studies showed that mastic is another strong analgesic material as well (Gulcin *et al.*, 2003).

As effective herbal medicine are cheaper and less harmful they more accepted by patients and finding efficient analgesic herbs could be greatly beneficial in medicine. This study investigated the analgesic effects of an herbal combination of ginger, mastic and sesame oil as a topical medicine compared with Salicylate in patients affected by knee osteoarthritis.

MATERIALS AND METHODS

This is a double-blind randomized controlled trial study conducted among patients with osteoarthritis in knee joints. Considering confidence limits of 95%, power of 80% and trying to achieve the least significant statistical difference equal to 15 mm of pain relief (± 22) based of Visual analog scale (VAS), the sample size was calculated as 39 people for each group; in our study 46 people were included. Patients signed printed consent forms and collected data were kept confidential. Patients were allowed to take acetaminophen in case of severe pain.

The participants were divided into two groups of placebo and intervention group via block randomization.

Inclusion criteria were diagnosing osteoarthritis by a orthopedic specialist, pain score higher than 30 mm and stability in taking medication within two last weeks. Exclusion criteria were applying any topical medicine for knee within last month, wounds in knee, intra-joint injection or taking corticosteroid drugs within three last months, surgery on knee, having knee problem other than osteoarthritis and physiotherapy within last month or during the study. If both knees were involved, the knee with more pain have had been assessed and in case of equal pain, the knee of dominant leg have had been considered. Randomization was done by a trained nurse. Totally 115 people were assessed from which 23 persons did not fulfilled inclusion criteria. Nobody left the study within initial four weeks, however during fourth to sixth week, one person in placebo group and three persons in intervention group were excluded; from those who left, two persons did not referred back on time even after follow-up and one other person stopped taking the drug during the study (Fig. 1).

Patients took two grams (a knuckle) of topical ointment three times a day and massaged it over the knee for one minute for six weeks. Patients got no recommendation about changing their sport habits or limited motion but they were advised to prevent over-pressures on knees. Pain severity, morning stiffness

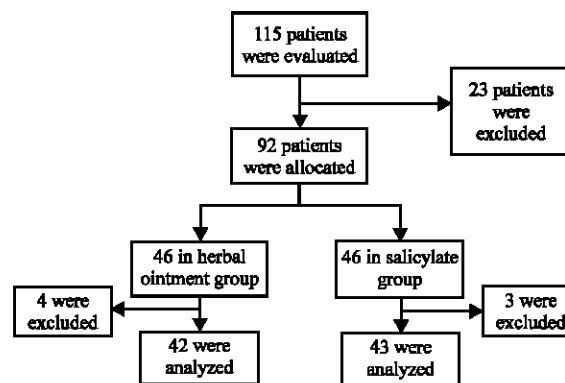


Fig. 1: State of randomization of participants in the study

and nightly pains were measured by VAS with a 100 mm scale, starting from zero (without pain or without morning stiffness, or without limited motion) and ending to 100 (maximum pain, maximum morning stiffness, or maximum limited motion); patients were trained about VAS before answering the questions. In each referral, patients were asked about the amount of pain while walking during last 24 h.

Changing trends of pain, morning stiffness and limited motion were assessed using repeated measurement and taking sedatives and disease length were considered as covariates. Then, once sphericity assumption was rejected, their average p-values were reported through adjusting degree of freedom by correction coefficients of Greenhouse-Geisser and Huynh-Feldt. SPSS 11.5 was used for statistical analysis.

RESULTS

In this study, 92 people were assessed and 46 people were in each group; after sixth week, three persons in Salicylate group and 4 persons in herbal pomade did not referred back. Both groups were similar in sex and side of affected knee. Age mean of all participants was 52.2 (± 12.4) years and there was no significant difference between two groups. The mean duration of illness, height, weight and BMI were 30.45 (± 30.3) years, 159.3 (± 7.1) centimeters, 71.2 (± 12) kg and 28.1 (± 4.6) Kg m⁻² and there was no significant statistical difference in these variables between two groups (Table 1).

In both groups of patients taking herbal and salicylate ointment after starting interventions the changing trend of pain became falling and in both groups the observed difference in pain severity in second, fourth and sixth week had significant statistical difference with the time before intervention ($p = 0.0001$). Nevertheless, the

trends of changes in two groups of patients did not have significant statistical difference after controlling variables of disease duration and taking acetaminophen analgesics ($F_{(3,1479)} = 0.974$; $p = 0.358$; $r = 0.245$) (Table 2).

The trend of changes in morning stiffness after interventions was falling in both groups too and the observed difference between two groups in morning stiffness after and before interventions was statistically significant ($p=0.0001$). Nonetheless, the trends of changes in two groups did not have significant statistical difference after controlling variables of disease length and taking acetaminophen analgesics ($F(3, 1.649) = 0.418$; $p = 0.62$; $r = 0.35$) (Table 2).

Table 1: Comparing the characteristics of two groups receiving herbal medicine and Salicylate

Group	Salicylate	Herbal ointment	p-value
Sex			
Male	2 (4.3%)	0 (0%)	0.5
Female	44 (95.7%)	46 (100%)	
Side of knee			
Left	18 (39.1%)	22 (47.8%)	0.53
Right	28 (60.9%)	24 (52.2%)	
Taking sedatives before intervention			
Yes	17 (37%)	10 (21.7%)	0.1
No	29 (63%)	36 (78.3%)	
Regular usage of prescribed pomade			
Always	34 (79.1%)	31 (73.8%)	0.57
Most of the time	9 (20.9%)	11 (26.2%)	
Taking sedative in first and second weeks			
Never	11 (23.9%)	8 (17.4%)	0.7
Sometimes	11 (23.9%)	10 (21.7%)	
One per day	7 (15.2%)	11 (23.9%)	
Two or three per day	17 (37%)	17 (37%)	
Taking sedative in third and fourth weeks			
Never	7 (15.2%)	8 (17.4%)	0.88
Sometimes	13 (28.4%)	14 (30.4%)	
One per day	10 (21.7%)	7 (15.2%)	
Two or three per day	16 (34.8%)	17 (37%)	
Taking sedative in fifth and sixth weeks			
Never	8 (18.6%)	5 (11.9%)	0.78
Sometimes	11 (25.6%)	14 (33.3%)	
One per day	7 (16.3%)	7 (16.7%)	
Two or three per day	17 (39.5%)	16 (38.1%)	
Age (year)	52.7 (± 14)	51.7 (± 10.6)	0.71
Disease length (month)	30.2 (± 33.1)	30.7 (± 27.5)	0.31
BMI	28 (± 4.7)	28.2 (± 4.4)	0.66

Data was analyzed using chi square

In addition, changes in limited motion during second, fourth and sixth weeks were falling in both groups too and the observed difference between two groups in limited motion after and before interventions was statistically significant ($p = 0.0001$). The trend of changes in two groups of patients did not have significant statistical difference after controlling variables of disease length and taking acetaminophen analgesics ($F(3, 1.583) = 1.037$; $p = 0.343$; $r = 0.51$) (Table 2).

DISCUSSION

In this study, the mean of age, the duration of disease, height, weight, BMI, gender distribution, type of knee and daily sedative dosage were similar in both groups. Based on the results, morning stiffness, pain and limited motion had more reduction in herbal ointment group in second, fourth and sixth week, however this difference was not statistically significant. While analyzing the trends of changes, the reduction of these treatment indexes in repeated measures in second, fourth and sixth week was statistically significant in both groups. Therefore we can say the herbal ointment could have an outcome at least equal to Salicylate in management of the symptoms of knee osteoarthritis.

The effects of Nonsteroidal anti-inflammatory drugs in management of osteoarthritis are still controversial (Lin *et al.*, 2004) and unfortunately there are few studies about salicylate ointment. likely reasons for inefficacy of salicylate ointment in some studies could have originated from various variables, number of times it had been used and slight penetration of medicine into skin (Shackel *et al.*, 1997; Cross *et al.*, 1998).

Though few studies are conducted about herbs that are effective in management of osteoarthritis, ginger is the most well known herb which its effects on osteoarthritis had been studied and had been used for management of osteoarthritis and arthritis rheumatoid. Probably, because of inhibiting Cyclooxygenases (COX) and Lipoxigenase, ginger had anti-inflammatory effects (Gregory *et al.*, 2008). In Altman and Marcussen (2001) after six weeks pain in knee had reduced 24.5 mm in oral ginger group and 16.4 mm in placebo group; the difference was significant

Table 2: Mean and standard deviation of pain, morning stiffness and limited motion (visual analog scale) during the study in the two groups

Variables	Time of investigation				p-value
	Baseline	2nd week	4th week	6th week	
Pain					
Herbal ointment	70.00 \pm 14.23	56.60 \pm 15.59	49.45 \pm 18.04	45.24 \pm 19.06	0.358
Salicylate	65.58 \pm 16.3	52.44 \pm 20.74	46.21 \pm 23.08	43.65 \pm 23.32	
Morning stiffness					
Herbal ointment	56.43 \pm 26.9	46.60 \pm 25.99	41.48 \pm 24.91	39.76 \pm 25.06	0.62
Salicylate	50.47 \pm 29.4	41.98 \pm 27.8	37.72 \pm 28.42	35.14 \pm 28.96	
Limited motion					
herbal ointment	60.95 \pm 22.77	50.40 \pm 22.62	45.17 \pm 23.57	40.71 \pm 24.36	0.343
Salicylate	55.35 \pm 24.87	44.07 \pm 25.83	39.70 \pm 26.38	37.58 \pm 26.21	

and no side effects had been observed. However in Bliddal *et al.* (2000) ginger had temporary analgesic effect. Haghghi *et al.* (2005) showed that ginger was as effective as ibuprofen in relieving knee pain in osteoarthritis and it could decrease pain as much as 30 mm but it did not reduced limited motion.

Cinnamon essence could alleviate pain and it could have anti-rheumatoid effects as well (Montes-Belmont and Carvajal, 1998). Joshi *et al.* (2010) proposed the likely anti-inflammatory effects of cinnamon and suggested to conduct further researches about it. The anti-inflammatory effects of cinnamon may be due to controlling IL-6 and IL-1 beta (Chao *et al.*, 2005). In this study, mastic and sesame oil were used as a base for this herbal ointment; nonetheless, sesame oil could have great effects on joints because it excessively contains oleic acid, linolenic acid and arachidonic acid and some anti oxidants (Kremer *et al.*, 1990; Linos *et al.*, 1999).

Van Haselen and Fisher (2000) showed that homeopathic herbal ointment is as effective as none-steroidal anti-inflammatory ointment in decreasing osteoarthritis pain. There are still controversial and contrasting results about the effects of herbal medicines for management osteoarthritis and it is necessary to do further researches. One of the problems with these ointment is their weak penetration into skin and joints; it is essential to add some ingredients to increase penetrative capacity of ointment into joints. Another method is to increase the effective herbal ingredients to make ointment with high concentration.

It is suggested to do further researches with larger sample sizes and using higher doses of this herbal medicine. It may be helpful to add ingredients which increase ointment penetrative power. Also it is suggested to use effective components of this herbal medicine to make ointment. If possible, it would be a good idea to take some further researches about oral form of the drug.

CONCLUSION

Based on the results of this study, taking this herbal combination could have valuable clinical effects for pain relief, limited motion and especially morning stiffness among patients affected by osteoarthritis; in order to decrease the side effects of chemical ointments this herbal ointment can be utilized.

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