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Research Article

CLINICAL EVALUATION OF MAJOON YAHYA BIN KHALID AND LOCAL APPLICATION OF ROGHAN DARCHINI IN MANAGEMENT OF PRIMARY KNEE OSTEOARTHRITIS

Mohd Khalid ^{1*}, MA Siddiqui ², Danish Mand ¹, Mohd Jafar ¹

¹P G Scholar, Department of Moalajat (medicine), National Institute of Unani Medicine, Bengaluru, Karnataka, India

²Professor, Department of Moalajat (medicine), National Institute of Unani Medicine, Bengaluru, Karnataka, India

*Corresponding Author Email: khalidhameedkhan@gmail.com

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ABSTRACT

Primary knee osteoarthritis is an extremely common cause of disability of lower extremities which results due to breakdown and destruction of joint tissues. The present study was designed to evaluate the efficacy of Majoon Yahya bin Khalid and local application of Roghan Darchini in management of Primary Knee Osteoarthritis. It was an open label evaluation study for the duration of 30 days carried out on 30 patients aged between 35 to 60 years at NIUM hospital, Bengaluru, from April 2014 to Feb 2015. After taking written voluntary informed consent, test drugs Majoon Yahya bin Khalid was given 9 gm orally twice a day, and Roghan Darchini 2-3 ml for local application on the affected knee joints once a day. Subjective as well as objective parameters were evaluated at baseline, 15th and 30th day. The results were analyzed using paired proportion and paired student t tests. Significant improvement was observed in subjective parameters of joint pain and restriction of movements with $p < 0.001$. All the five subscales of objective parameter (Knee Osteoarthritis Outcome Score) were found to be highly significant with $p < 0.001$. The study revealed that the test drugs are effective and safe in management of primary knee osteoarthritis.

Keywords: Osteoarthritis; Waja-ul-Mafasil; Majoon Yahya bin Khalid; Roghan Darchini; Unani; KOOS

INTRODUCTION

Primary knee osteoarthritis is characterized by joint pain, limitation of joint movements, crepitus, occasional effusion, and variable degrees of local inflammation without having any systemic effect ¹. According to WHO, osteoarthritis is the second commonest musculoskeletal problem in the world population (30%) after back pain (50%) ². In India, the prevalence of osteoarthritis is about 5.78 % ². Among elderly, knee osteoarthritis is much common as compared to other form of arthritis ^{2, 3}; hence WHO projected it as the 4th most important cause of disability in women and 8th in men ⁴. Osteoarthritis is a normal part of aging, and usually results from mechanical and idiopathic factors, ⁵ and is more common in individuals performing heavy physical work, especially, if it involves kneeling, knee bending, or repetitive use of knee joints ⁶.

The pathogenesis of osteoarthritis remains very complex and controversial. About 25% patients of knee OA manifest with clinical evidence of inflammation that may be secondary to release of IL-1, as well as the normal consequence of ageing ⁷⁻⁸. The clinical picture of knee OA strongly simulates with Waja-ul-Mafasil, which has been extensively elaborated by Unani physicians. Hakim Azam Khan says that Waja-ul-Mafasil implies the pain of joints of the body ⁹⁻¹⁰. Important risk factors mentioned in Unani medicine are weaker joints, sedentary life, excess coitus, especially just after meal, heavy meals even at full stomach, and least exercise ¹¹. It occurs due to weakness of the joint involved, followed by accumulation of morbid matter into the affected joint, that may be Damvi (sanguine), Safravi (yellow bilious), Saudavi (black bilious), and Balghami (phlegmatic), or the admixture of the four humours ^{11, 12, 13}. As a result, ligaments turn

tout, tendons become tense, and the pain ensues due to least potential space in the joint.

NSAIDs, aspirin, colchicines, Cox-2 inhibitors, intra-articular steroids etc. provide merely symptomatic relief; moreover, these agents produce various adverse effects like gastrointestinal bleeding, gastritis, epigastric pain, nausea, and dyspepsia ^{1, 8, 14, 15}.

In Unani system of medicine, Waja-ul-Mafasil has been managed through a number of single and compound drugs. However, these drugs have not been scientifically explored so far for their delineated effects. Hence, the present study was drafted to evaluate the effects of Majoon Yahya bin Khalid and Roghan Darchini, as the ingredients of these formulations possess anti-arthritic, analgesic, and anti-inflammatory activities ¹⁶⁻¹⁷.

MATERIALS & METHODS

The trial was conducted at NIUM Hospital, Bengaluru, from April, 2014 to February, 2015. After obtaining approval from Institutional Ethical Committee, the patients with the diagnosis of knee OA clinically and/or radiologically and fulfilling the inclusion criteria, were enrolled in the study. Inclusion criteria was 35 – 60 years of either gender, clinically and/or radiologically diagnosed patients, patients who have agreed to sign the informed consent form and follow -up the protocol (Fig No. 1). Exclusion criteria included age less below 35 years and above 60 years, pregnancy and lactation, severe systemic illness, diabetes mellitus, hypertension, and patients who fail to follow up. After complete history and physical examination, patients fulfilling the inclusion and exclusion criteria were subjected to haematological and radiological investigations. A written voluntary informed

consent was obtained for the trial, and the drug was advised to the patients. In case of acute pain, patients were advised to take simple analgesic “paracetamol” orally. Routine investigations were performed before and after treatment such as Hb %, TLC, DLC, ESR, Random blood sugar, Blood urea, S. Creatinine, S. Billirubin, SGOT, SGPT, Serum calcium, Serum Uric acid, CRP & RA Factor, X-Rays: Knee Joints, and ECG.

Trial Formulations

Majoon Yahya bin Khalid: The ingredients Asaroon (*Valeriana wallichii*) 7g; Zanjabeel (*Ziniber officinale*) 7g; Zeera Kirmani (*Carum carvi*) 7g; Filfil Daraz (*Piper longum*) 7g; Sana Makki (*Cassia angustifolia*) 17.5g; Suranjan Shireen (*Cholchicum luteum*) 35g, and Asl Asli (Honey) 3 times the weight of rest ingredients.

Majoon was given in the dosage of 9 gm twice a day orally, 1 hour after meal with lukewarm water for 30 days. The drug was prepared by NIUM pharmacy accomplishing established preparation method of Majoon as per Unani literature, and proper scrutiny of every ingredient by the concerned department.

Roghan Darchini: It was procured by the concerned department from the market and was given to the patients in the dose of 2-3 ml for local application once a day on the affected joint/s.

Assessment of Efficacy

Subjective parameters were joint pain (0= Nil; 1= barely perceptible; 2= Mild; can carry out daily activities with some trouble; 3= Moderate; cannot carry out daily activities easily; 4= Severe; bed ridden), stiffness in joints after inactivity (0= Nil; 1= barely perceptible; 2= Mild; can carry out daily activities with some trouble; 3= Moderate; cannot carry out daily activities easily; 4= Severe; bed ridden), and restriction of joint movements (0= Nil; 1= Barely Perceptible; 2= Mild; can carry out daily activities with some trouble; 3= Moderate; cannot carry out daily activities easily; 4= Severe; bed ridden). Objective parameters

were Knee osteoarthritis outcome score (KOOS) consists of 5 subscales; pain, other symptoms, activities of daily living (ADL), sport and recreation (sports/recreation) and knee-related quality of life (QoL). KOOS subscale scores were aggregated and averaged as the primary outcome. The five individual KOOS subscale scores were considered as secondary outcomes to enable clinical interpretation.

Follow up was on 15th & 30th day from the onset of treatment. In case of any adverse effect or reaction, the same was duly recorded in the case report form. Two patients each complained of gastric irritation, and bulla formation at the site of oil application, and quit the trial. They were managed with appropriate medicines accordingly.

Statistical Methods

Results on continuous measurements were presented on Mean $\pm$ SD (Min-Max) and results on categorical measurements were presented in number (%). Significance was assessed at 5% level of significance. Student *t* test (one tailed, dependent) was used to find the significance of study. Paired proportion test was used to find the significance of proportion in paired data.

RESULTS

The baseline demographic data has been given in Table 1. Significant improvement was noted in subjective parameters of joint pain and restriction of movements with $p < 0.001$, given in Table 2, 3, & 4 respectively. All the five subscales of objective parameter (Knee Osteoarthritis Outcome Score) were found to be highly significant with $p < 0.001$, detailed in Table 5. Effect of trial formulations on RA factor, ASO, and CRP were insignificant (Table 6, 7, & 8). Effect on X-ray knees has been illustrated in Table No. 9. Safety parameters were in their normal range (Table 10).

Figure 1: Flow chart of patients studied

Table 1: Demographics of study population

Age	No of patients	Percentage	Mean $\pm$ SD: 50.63 $\pm$ 7.41
31-40	3	10.0	
41-50	12	40.0	
51-60	15	50.0	Mean $\pm$ SD: 28.96 $\pm$ 4.78
Gender			
Female	18	60.0	
Male	12	40.0	
BMI (kg/m²)			
<18.5	0	0.0	
18.5-23	2	6.7	
23-25	4	13.3	
25-30	11	36.7	
>30	13	43.3	
Socio-economic Status			
Lower middle	15	50.0	
Upper lower	2	6.7	
Upper middle	9	30.0	
Upper	4	13.3	
Occupation			
Service	6	20	
House wife	15	50.0	
Farmer	1	3.33	
Own Business	2	6.67	
Skilled worker	3	10	
Unskilled	3	10	
Diet pattern			
Mixed diet	23	76.67	
Veg	7	23.33	
Pattern of knee involvement			
Unilateral	9	30	
Bilateral	21	70	

Table 2: Joint Pain: An evaluation before and after treatment

Joint pain	Baseline	15 th day	30 th day	% change
0	0(0%)	0(0%)	2(3.9%)	3.9%
1	0(0%)	13(25.5%)	30(58.8%)	58.8%
2	21(41.2%)	33(64.7%)	17(33.3%)	-7.9%
3	29(56.9%)	5(9.8%)	2(3.9%)	-53.0%
4	1(2%)	0(0%)	0(0%)	-2.0%
Total	51(100%)	51(100%)	51(100%)	-

62.7% improvement is significant with P<0.001**, paired Proportion test

Table 3: Stiffness in joint after inactivity: An evaluation before and after treatment

Stiffness	Baseline	15 th day	30 th day	% change
0	0(0%)	0(0%)	2(3.9%)	3.9%
1	5(9.8%)	15(29.4%)	32(62.7%)	52.9%
2	24(47.1%)	34(66.7%)	17(33.3%)	-13.8%
3	22(43.1%)	2(3.9%)	0(0%)	-43.1%
Total	51(100%)	51(100%)	51(100%)	-

56.8% (3.9+52.9%) improvement is significant with paired Proportion test

Table 4: Restriction of movement: An evaluation before and after treatment

Rest move	Baseline	15 th day	30 th day	% change
0	25(49%)	25(49%)	31(60.8%)	11.8%
1	17(33.3%)	23(45.1%)	20(39.2%)	5.9%
2	9(17.6%)	3(5.9%)	0(0%)	-17.6%
Total	51(100%)	51(100%)	51(100%)	-

17.6% is statistically significant P=0.0015**, Paired Proportion test

Table 5: An Evaluation of Symptoms score, Pain score, ADL score, Sports/Recreation and Quality of Life scores at baseline, 15th day and 30th day evaluation

Subscales	Baseline	15 th day	30 th day	P value		
				Baseline-15 th day	Baseline-30 th day	15 th day-30 th day
Symptoms	62.57 $\pm$ 16.08	68.94 $\pm$ 13.18	74.16 $\pm$ 10.66	0.006**	<0.001**	0.007**
Pain	50.60 $\pm$ 17.64	59.04 $\pm$ 15.74	65.59 $\pm$ 11.42	0.002**	<0.001**	0.007**
ADL	52.84 $\pm$ 14.58	62.04 $\pm$ 14.44	67.71 $\pm$ 10.61	<0.001**	<0.001**	0.014*
Recreation	9.31 $\pm$ 7.55	1.98 $\pm$ 1.82	12.65 $\pm$ 11.06	<0.001**	<0.001**	<0.001**
QoL	12.87 $\pm$ 10.80	31.97 $\pm$ 7.87	43.03 $\pm$ 8.41	<0.001**	<0.001**	<0.001**

Student *t* test (Paired) has been used to find the significance (n= 51)

Table 6: R A Factor: An evaluation before and after treatment

R A Factor	BT	AT	% change
Negative	30(100%)	30(100%)	0.0%
Positive	0(0%)	0(0%)	0.0%
Total	30(100%)	30(100%)	-

P=1.000, Not significant, paired Proportion test

Table 7: ASO: An evaluation before and after treatment

ASO	BT	AT	% change
Negative	25(83.3%)	22(73.3%)	-10.0%
Positive	5(16.7%)	8(26.7%)	10.0%
Total	30(100%)	30(100%)	-

P=0.333, Not significant, paired Proportion test

Table 8: CRP: An evaluation before and after treatment

CRP	BT	AT	% change
Negative	27(90%)	27(90%)	0.0%
Positive	3(10%)	3(10%)	0.0%
Total	30(100%)	30(100%)	-

P=1.000, Not significant, paired Proportion test

Table 9: X-ray Knee/s: An evaluation before and after treatment (KL grading)

X-ray Knee/s	BT	AT	% change
Normal	5(16.7%)	4(13.3%)	-3.3%
Grade I	9(30.0%)	9(30.0%)	0.0
Grade II	8(26.7%)	7(23.3%)	-3.3%
Grade III	8(26.7%)	10(33.3%)	+6.6%
Total	30(100%)	30(100%)	-

P=0.321, Not significant, paired Proportion test (n= 51)

Table 10: An evaluation of safety parameters before and after treatment

	Before treatment	After treatment	Difference	t value	P value
Hemoglobin	13.98±1.31	13.96±1.45	0.02	0.163	0.872
TLC	8710.00±1863.51	8190.00±1879.35	520.00	1.799	0.083+
Neutrophils	57.27±9.44	54.27±8.97	3.00	2.006	0.054+
Lymphocytes	34.80±8.45	38.07±9.06	3.26	2.623	0.014*
Monocytes	3.33±1.42	3.23±1.28	0.10	0.260	0.761
Eosinophils	4.67±2.11	4.43±1.14	0.23	0.535	0.597
ESR	37.50±21.13	30.97±20.82	6.53	1.932	0.063+
RBS	110.40±22.14	124.87±38.43	14.47	2.138	0.041*
Blood Urea	28.50±6.61	29.30±5.53	0.80	0.456	0.652
Serum Creatinine	0.88±0.12	0.86±0.14	0.017	0.579	0.567
Serum Uric Acid	5.41±0.92	5.53±0.97	0.11	0.847	0.404
SGOT	23.07±9.11	25.37±11.75	2.30	1.293	0.206
SGPT	30.10±14.72	32.83±18.57	2.73	1.192	0.243
S. Alk. Phosphatase	105.43±21.19	104.77±12.74	0.67	0.182	0.857
Total Bilirubin	0.72±0.36	0.61±0.26	0.11	1.920	0.085+
Serum Calcium	9.46±0.43	9.50±0.33	0.04	0.402	0.691

Student t test (Paired)

+ Suggestive significance (P value: 0.05<P<0.10); * Moderately significant (P value: 0.01<P ≤ 0.05); ** Strongly significant (P value: P≤0.01)

DISCUSSION

The study was conducted to evaluate the efficacy of Majoon Yahya bin Khalid and local application of Roghan Darchini in management of Primary Knee Osteoarthritis. Out of 30 patients, 15 were from the age group of 51-60 years, and 12 patients were in the age group of 41-50 years (Table 1). It infers that number of patients with Knee OA increased with the increase of age which may be corroborated with the advancement of age resulting in greater chances of morbidity,¹⁸ coincided with that of NHANES III,¹⁹ the Johnston County Osteoarthritis Project,²⁰ and Ziad et al²¹⁻²². Out of 30 patients, 18 were female and 12 were male (Table 1) which is in conformity with Framingham OA study,²³ and Barbara et al²⁴ that the burden of OA is highest among women, and incidence of OA rises faster in women than in men after the age of 50 years²⁵.

Out of 30 patients, BMI of 13 patients was > 30, and 11 patients were in the 25-30 range (Table No. 1). The observed data was consistent with numerous previous trials including Cimmino et al²⁶ who found a significant relationship between BMI ≥30 kg/m² and OA in weight-bearing joints, especially knee²⁷. Regarding socio-economic status, 15 patients were from lower middle class, and 9 from upper middle class (Table No.1). This data is in conformity with the reports of Ajit NE et al²⁸ and Salve et al²⁹ that Knee OA was higher in low socioeconomic class as compared to middle class³⁰.

15 patients were housewives (Table 1), and the data coincides with the findings of Shadab,¹⁸ Nobi *et al*,³⁰ Nayab,³¹ and Dahaghin *et al*,³² as physical demands of caring for home and family put housewives at greater risk of developing Knee OA²¹ irrespective of the participant's age, sex, and BMI³².

23 patients were of mixed dietary pattern, and only 7 patients were vegan (Table 1). The data favours the relation of non-vegetarian foods in the causation of osteoarthritis which is in conformity with Majusi,¹² Ibn Sina,¹³ and Razi³³ who have advised the restriction of non-vegetarian diets in Waja-ul-Mafasil, as these are not easily digestible and lead to weakness of Quwwat-e-Hazima (digestive faculty) by producing Akhlat-e-Fasida (vicious humours)^{18, 21, 31}. This association has been observed in very few studies where the role of Reactive Oxygen Species (ROS) intensifying the aging processes including of the joints, and oxidants has been identified³⁴.

Out of 30 patients, 9 patients had unilateral Knee OA, and 21 patients were of bilateral Knee OA (Table 1), and the data is coincided with a previous study of 2 year follow-up, where 34% patients with unilateral disease subsequently developed disease in the contra-lateral knee,²⁷ and the shift from unilateral to bilateral knee osteoarthritis becomes much more common as the disease severity increases³⁵. The probable argument may be that contra-lateral knee is not necessarily free of disease in patients with unilateral radiographic disease³⁶.

There was highly significant reduction in the pain ($p < 0.001$) from the baseline score; 56.8% of mildly significant reduction in stiffness was observed from the baseline score, and highly significant ($P = 0.0015$) improvement was noted in restriction of joint movements. All the five subscales of objective parameter (Knee Osteoarthritis Outcome Score) were found to be highly significant with $p < 0.001$.

The observed efficacy of test drugs on the symptoms may be due the properties of the ingredients which are present in the formulations. All the drugs are Haar Yabis (hot and dry) in 2nd or 3rd grade, have Muhallil (resolvent), Mufat'teh (deobstruent), Mus'hil (purgative), Qabiz (astringent), and Dafa'y-e-Barid Ma'dda (evacuator of cold substances). Suranjan (*Colchicum luteum*), drug of choice for Waja-ul-Mafasil, has two important Jauhar: at first its Latif (light) and Mus'hil (purgative) Jauhar (constituent) is released which evacuates the accumulated matter of joints layer by layer by actions of Tahlil (resolution) and Jazb (absorption),^{10-11, 37-39} and then Qa'abiz Jauhar is released which acts as an astringent of organs as well as their passages; thus they become strong enough to not let the morbidic matter redeposited in the joints^{10-11, 37-39}. Suranjan has been shown to afford symptomatic relief in arthritis in a 90-day trial,⁴⁰ and the most probable mechanism suggested was the inhibition of pro-inflammatory cells⁴¹⁻⁴². *Colchicine* is the most important anti-inflammatory compound which inhibits microtubules in pro-inflammatory cells including macrophages in arthritis⁴².

Zanjabeel (*Zingiber officinale*) evacuates Balghami morbidic matter, and thus is very beneficial in treatment of Waja-ul-Mafasil elevating the arthritis pain, associated stiffness and restricted movements³⁷. It has been shown to decrease pain and swelling in arthritis,⁴³ decreased stiffness, and inhibition of prostaglandin, leukotrienes bio-synthesis, and anti-knee osteoarthritis activities⁴⁴. Filfil Daraz (*Piper longum*) does Tahlil-e-Waram (resolution of swelling), reduces pain of Barid Mizaj (cold temperament) origin, and is used to treat arthritic pain³⁷. *Piper longum* is reported to be used as a remedy for treating arthritic conditions, as piper extracts and piperine possess inhibitory activities on prostaglandin and leukotrienes COX-I inhibitory effect, as well as on NF- κ B activation, thus exhibit anti-inflammatory activity⁴⁵⁻⁴⁶. Moreover, piperine possesses anti-inflammatory and anti-arthritic effects⁴⁷.

By virtue of its Quwwat-e-Harat (hotness), Asarun (*Valeriana wallichii*) possesses highly potent Muhallil and Mufat'teh

actions, provides Taskheen (calefaction) in Barid Mizaj organs, relieves pain by resolving deep seated Waram (swelling), and renders Ghaliz Ma'dda (thick matter) into Latif (light). Based on these properties, the morbidic matter accumulated in the affected joints is easily evacuated³⁷. *Valeriana wallichii* has been reported for analgesic,⁴⁸ anti-inflammatory,⁴⁹⁻⁵⁰ and antioxidant actions⁵¹.

Sana Makki (*Cassia angustifolia*) acts through evacuation of Balghami Ma'dda (phlegmatic matter), as Sana Makki is claimed to penetrate into the deepest parts of the body, and evacuates accumulated morbidic matter by the mechanism of purgation, which is the accepted and established part of management plan in Waja-ul-Mafasil³⁷. *Cassia angustifolia* has flavonoids which show anti-microbial, antioxidant, and anti-inflammatory activities⁵²⁻⁵³.

Carum carvi is effective in relieving pain and inflammation in patients suffering from lumbar pains and rheumatism due to its anti-inflammatory agent carry one which inhibits 5-lipoxegenase and cyclooxygenase activity, and thus pain and inflammatory changes are reduced.⁵⁴ This drug has been added to reduce the side effect of Suranjan as it induces gastric irritation and Zo'af-e-Me'da (stomach weakness)³⁸.

Regarding Darchini (*Cinnamomum officinalis*), Buqrat mentioned that Kasrat-e-Latafat (higher degree of lightness) has accentuated it to a potent Muhallil, Jazib, and Mufat'teh activities. It dries up the accumulated morbidic matter by the process of Tahlil. *Cinnamomum officinalis* contains Cinnamic acid, Cinnamaldehyde, Eugenol, and essential oils, and it has been reported for anti-inflammatory and anti-oxidant effect which is useful in reducing pain and inflammation associated with arthritis.⁵⁵

CONCLUSION

The study inferred that the trial formulations are effective in reducing joint pain, stiffness, and restriction of joint movements. The limitation of this study was smaller sample size and short duration of therapy. Hence, controlled clinical trials with large sample size are required to further prove the efficacy and safety of this treatment regimen in comparison to other prevalent treatment options.

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