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Research Article

EVALUATION OF THE EFFECT OF *HIJAMA BI'L SHART IN WAJA-UL-MAFASIL* (KNEE OSTEOARTHRITIS): AN OPEN LABELLED RANDOMIZED CONTROLLED COMPARATIVE CLINICAL STUDY

Abrar Mohd Khan [1]*, M.D.A. Bhat [2], Peer Abdul Waahid [3], Abdul Hafeez [1]

[1]P.G. Scholar Dept. of Moalajat National Institute of Unani Medicine Bengaluru Karnataka, India

[2]Lecturer Dept. of Moalajat National Institute of Unani Medicine Bengaluru Karnataka, India

[3]P.G. Scholar Dept. of Kulliyat National Institute of Unani Medicine Bengaluru Karnataka, India

*Corresponding Author Email: abrar.nium@gmail.com

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ABSTRACT

Waja-ul-Mafasil is a type of arthralgia which involves several joints. It is a chronic degenerative disease of joints and is progressive in character, occurring in middle and later life. Aim of the study was to evaluate the effect of *Hijama bi'l Shart* (wet cupping) as an alternate treatment option in the management of *Waja-ul-Mafasil* (Osteoarthritis knee). A randomized open labelled controlled comparative clinical trial was carried out at department of Moalajat, National Institute of Unani Medicine hospital, Bengaluru for the duration of 30 days. 40 diagnosed patients of *Waja-ul-Mafasil* were randomly allocated to two groups i.e; group-A and group-B, each comprising of 20 patients. In group-A *Hijama bi'l Shart* was performed over the affected knee(s) on each visit at interval of 10 days for 30 days. The group-B patients received *Majoon Suranjan* 5gm twice daily for 30 days along with *Hijama bi'l Shart*. Subjective parameters i.e. Pain, Morning Stiffness, Difficulty in Movement and objective parameters VAS and KOOS were statistically analysed to assess the effect of intervention. There was no significant difference between the two groups concerning baseline characteristics ($P>0.05$). Both group-A & group-B exhibited statistically significant difference in objective parameters. In intragroup comparison VAS and KOOS showed statistically significant difference in both group-A and group-B ($p<0.001$). On intergroup comparison group-B showed better response on VAS with $p<0.05$ in both right & left knee. *Hijama bi'l Shart* can effectively alleviate the *Waja-ul-Mafasil* (knee osteoarthritis) without any side effects. The study revealed that *Hijama bi'l Shart* has potent analgesic & anti-inflammatory effect.

Key words: *Waja-ul-Mafasil*; Knee osteoarthritis; *Hijama-bi'l-Shart*; Wet Cupping; *Majoon Suranjan*; VAS; KOOS

INTRODUCTION

The term osteoarthritis implies an inflammatory disease of the joints. It is a chronic degenerative disease of the joints and is progressive in character, occurring in middle and later life. The most frequently affected joints are knees, hips, certain joints of hands and spinal appophyseal joints. The reported prevalence of OA in rural India is 5.8%[1].

Osteoarthritis is classified in to two types namely primary and secondary OA. Exact aetiology of primary knee OA is unknown but there are some risk factors. Major risk factors associated with knee OA are age, female sex, obesity, trauma, heredity, physical activity etc[2]. While as in secondary OA exact aetiology is known and may occur due to some diseases like diabetes mellitus, hyperparathyroidism, hemochoromatosis etc. Management of this disease can be done by non-pharmacological, pharmacological & surgical interventions. Non-pharmacological measure like patient education and joint protection measures, such as avoidance of poor posture and limitation of excess joint loading are helpful. The pharmacological measures are use of NSAIDs, COX-2 inhibitors, Opioid analgesic and intra articular injection. The surgical intervention includes lavage, joint debridement, osteotomy, joint arthroplasty etc[3,4].

According to *Unani* medical terminological anthology, *Waja-ul-Mafasil* is a type of arthralgia which involves several joints. It is classified in to two groups on the basis of aetiology likely *Waja-ul-Mafasil Sāda* and *Waja-ul-Mafasil Māddī*. *Waja-ul-Mafasil Sāda* is further classified in to three types namely *Sū-e-mizaj Hārr, Bārid & Yābis*. *Waja-ul-Mafasil Māddī* is further classified as *Waja-ul-Mafasil Balghamī* (Phlegmatic), *Damwī* (sanguineous), *Safrāwī* (bilious or choleric), *Saudāwī* (Melancholic), *Rīhī* (gaseous) *& Murakkab* (Compound). The most common cause of *Waja-ul-Mafasil* is *Khilt-e-Balghamī* followed by *Khilt-e-Damwī*[5,6,7]. Usually *Waja-ul-Mafasil* occurs due to *Mādda* (Potential matter or active substance). The basic pathology of the disease is the accumulation of morbid matter due to weakness of joint. The weakness of particular joint is either primarily due to *Sū-e-mizaj* (dystemperament) or secondary to injury or heavy work[8]. In *Unani* system of medicine general principle of management is *Tādil-e-mizaj*, evacuation of *Mādda* and *Taqwiyat*. *Majoon Suranjan* has specific action in the treatment of *Waja-ul-Mafasil* and recommended in its all types. For the treatment of *Waja-ul-Mafasil*, a number of regimes such as venesection, cupping, massage and exercise etc are also recommended[5,7].

In view of high prevalence, possible joint failure and severe adverse effects of drugs in conventional medicine and in *Unani* system of medicine, the regimes and drugs have not been scientifically explored for their delineated effects and to provide safe and effective treatment of knee OA.

MATERIAL & METHODS

Study entitled "Evaluation of the effect of *Hijama bi'l Shart in Waja-ul-Mafasil (Osteoarthritis Knee)* - An Open labelled randomized controlled comparative clinical study" was designed for the duration of 30 days and was carried out on 40 patients consisting of two groups (group-A and group-B) *Hijama bi'l Shart* was done in patients enrolled in group-A and Group-B patients received *Majoon Suranjan* 5gm twice a day along with *Hijama bi'l Shart*. *Hijama bi'l Shart* was performed at every visit interval of 10th day. The trial was conducted at National Institute of Unani Medicine and Hospital, Bengaluru, from April, 2015 to February, 2016. After obtaining approval from Institutional Ethical Committee of National Institute of Unani Medicine vide NO. NIUM /IEC / 2013-14 / 007/ Moal/ 07, Dated 24.04.2014, the patients with the diagnosis of knee OA ACR criteria (clinical and radiographic) were used. The inclusion criteria, patients of both gender, age group of 38-60years and ACR criteria, patients who have agreed to sign the informed consent form and follow -up the protocol. Exclusion criteria included ages below 38 years and above 60 years, Pregnancy and lactation, Patient with systemic and metabolic diseases, Patients of osteoarthritis other than Knee osteoarthritis, Patients with the history of trauma and accidents. 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; Routine investigations such as Hb %, TLC, DLC, ESR, Blood urea, S. Creatinine, S. Bilirubin, SGOT, SGPT, Serum Uric acid were performed before and after the treatment. For diagnostic and safety purposes some investigations like X- ray knee joints, CRP, RA factor, Random blood sugar, CT, BT, HbsAg, and HIV were done before the trial. The GCP was adhered to and regular monitoring was made. An over view of study show in figure 1.

Technique of *Hijama bi'l Shart*: Under all aseptic precautions patients were subjected to *Hijama bi`l Shart* near *"Al Rakba"* (lateral and medial aspects of Knee Joint). Two (02) sterile manual suction cups were applied near knee joint around the distal end of femur over lateral and medial sides, to lift the tissue beneath the cups and to increase blood circulation locally. After 5 minutes[9,10] suction cups were removed followed by multiple incisions about 4 mm long & 2 mm deep, around 10-15[10] in number over the cupped area using sterile surgical blade (No. 12). Again, the manual suction cups were applied over the incised area to draw blood into the cups for 5-10 minutes[9,11]. In total 20-30 ml[9] of blood was drawn from both the cups applied near the knee joint; amount of blood was measured by Swab weighing method (1gm=1ml)[12]. Surgical incisions were treated with antiseptic dressing.

Dosage and route of administration of drug: The control drug *Majoon Suranjan* was procured from the market manufactured by Hamdard laboratory Delhi and 5gm was administered orally twice daily to patients in group-B along with *Hijama bi'l Shart*. No concomitant treatment was allowed during entire protocol therapy.

Assessment & Follow up: After fulfilling the inclusion criteria, the baseline scores were noted and patients were subjected to either group-A or group-B. Patients were asked to follow up after 10th, 20th and 30th day. The subjective and objective parameters were recorded on each visit. The scores were recorded in case record form; the patients were also enquired for any adverse effects during the trial periods.

Efficacy measures: Subjective parameters were assessed using an arbitrary scale as knee 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), Morning stiffness in knee joints (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 difficulty in movement in knee joint (0= Nil; 1= Barely Perceptible; 2= Mild; can carry out daily activities with some trouble; 3= Moderate; cannot carry out daily activities easily;). Objective parameters were VAS and KOOS. VAS is a 10 cm numerical Likert scale. Pain intensity was evaluated according to the NRS-11, and measured along a 0–10 scale, where 0 is no pain, 1–3 is mild pain, 4–6 is moderate pain, and 7–10 is severe pain.[13] 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). Each question has been assigned a score from 0 to 4. A normalized score (100 indicating no symptom and 0 indicating extreme symptom) is calculated. KOOS subscale scores are aggregated and averaged as the primary outcome. The five individual KOOS subscale scores are then be considered as secondary outcomes to enable clinical interpretation[14].

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of data.

Data analysis: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. And student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

RESULT

The baseline demographic data has been given in Table 1. In subjective parameters it was observed that after treatment, Joint pain, morning stiffness and difficulty of movement were significantly reduced in both the groups. Joint pain reduced by 60% (Right knee) and 85% (Left knee) in group-A while 75% (Right knee) and 85% (Left knee) reduction was observed in group-B. Morning stiffness reduced by 35% (Right knee) and 30% (Left knee) in group-A, were as 55% reduction (Both knee) was observed in group-B patients. Difficulty of joint movement got reduced by 35% (Right knee) and 65% (Left knee) in group-A, whereas this reduction was 50% (Right knee) and 75% (Left knee) in group-B. Subjective parameters are shown in Table no. 2, 3 & 4. In objective parameters it was observed that after treatment VAS score got significantly reduced and KOOS also improved significantly. VAS score reduced from 6.35±1.46 to 2.95±0.89 (Right knee) and 5.70±1.03 to 2.40±0.82 (Left knee) in group-A while in group-B it reduced from 6.17±1.47 to 2.22±1.06 (Right knee) and from 5.68±1.00 to 1.79±0.63 (Left knee). Similarly, VAS score reduced significantly ($p<0.001$) in both the groups after treatment. On intergroup analysis group-B showed significant reduction in VAS score with $p<0.05$. This reduction might be due to known effect of *Majoon Suranjan*. VAS score is show in table 5. Assessment of symptoms, i.e;

pain, ADL, sports/Recreation and quality of life were done by using KOOS and showed significant improvement. Symptoms improved significantly from 59.30±21.96 to 76.25±14.42 (Right knee) and 67.60±16.56 to 81.80±9.17 (Left knee) in group-A, where as in group-B patients, this improvement was from 59.50±19.78 to 79.22±13.58 (Right knee) and 68.95±14.89 to 82.68±9.12 (Left knee). Improvement in pain from 35.20±17.96 to 59.15±10.48 (Right knee) and 44.65±13.30 to 64.50±6.95 (Left knee) in group-A was observed, whereas improvement from 37.33±15.77 to 62.94±9.26 (Right knee) and 44.16±12.16 to 67.53±2.27 (Left knee) was observed in group-B. ADL improved significantly from 40.05±19.92 to 65.60±10.75 (Right knee) and 50.20±14.38 to 71.85±5.80 (Left knee) in group-A, while as in group-B it improved from 41.61±17.04 to 69.78±10.52 (Right knee) and 49.79±12.76 to 74.11±0.74 (Left knee). Sports/Recreation functions improved significantly from 31.32±17.55 to 57.75±13.33 (Right knee) and 41.75±15.15 to 62.00±11.52 (Left knee) in group-A, where as it improved from 32.06±15.01 to 60.28±13.11 (Right knee) and from 41.26±14.17 to 63.58±8.95 (Left knee) in group-B. Quality of life improved significantly from 35.1±5.37 to 45.5±3.30 (Both knee) in group-A, and from 37±6.55 to 47.3±3.06 (Both knee) in group-B. There was significant improvement (P<0.001) in KOOS in both the groups while comparing before and after the treatment. On intergroup comparison, there was no statistically significant difference between the group-A & group-B (p>0.05). KOOS is shown in table 6-10.

Table 1: Distribution of patients according to demographic data and patient characteristics

Age in years	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
40-50	25 (62.5)	14	70.0	11	55.0	P=0.608 Chi-Square test
51-60	15 (37.5)	6	30.0	9	45.0	
Total	40 (100)	20	100.0	20	100.0	
Mean ± SD		49.10±6.50		50.15±6.33		
Gender	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
Female	33 (82.5)	15	75.0	18	90.0	P=0.407 Chi-Square test
Male	7 (17.5)	5	25.0	2	10.0	
Total	40 (100)	20	100.0	20	100.0	
Diet	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
Mixed	28(70)	13	65.0	15	75.0	P=0.490 Chi-Square test
Veg	12 (30)	7	35.0	5	25.0	
Total	40 (100)	20	100.0	20	100.0	
BMI (kg/m^2)	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
<18.5	2 (5)	1	5.0	1	5.0	P=0.842 Fisher Exact test
18.5-25	28 (70)	15	75.0	13	65.0	
25-30	10 (25)	4	20.0	6	30.0	
Mean±SD		23.26±2.577		23.425±2.619		
Lifestyle	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
Sedentary	22 (55)	11	55.0	11	55.0	P=0.068 Fisher Exact test
Average	9 (22.5)	2	10.0	7	35.0	
Laborer	9 (22.5)	7	35.0	2	10.0	
Total	40 (100)	20	100.0	20	100.0	
SES	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
UL	16 (40)	5	25.0	11	55.0	P=0.173 Fisher Exact test
LM	12 (30)	8	40.0	4	20.0	
UM	11 (27.5)	6	30.0	5	25.0	
U	1 (2.5)	1	5.0	0	0.0	
Total	40 (100)	20	100.0	20	100.0	
Mizaj	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
Bal	30 (75)	14	70.0	16	80.0	P=0.465 Chi-Square test
Dam	10 (25)	6	30.0	4	20.0	
Joint Involved	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
Both Knee	37 (92.5)	20	100.0	17	85.0	P=0.231 Fisher Exact test
Left Knee	2 (5)	0	0.0	2	10.0	
Right Knee	1 (2.5)	0	0.0	1	5.0	
Total	40 (100)	20	100.0	20	100.0	
Worst A. Joint (Symptomatically)	**Total No (%)**	**Group A**		**Group B**		**P value**
		No	**%**	**No**	**%**	
Left Knee	7 (17.5)	0	00.0	7	35.0	P=0.144 Chi-Square test
Right Knee	33 (82.5)	20	100.0	13	65.0	
Total	40 (100)	20	100.0	20	100.0	

Table 2: Comparative Assessment before and after treatment in Subjective parameter

Joint Pain in Right knee (Subjective Parameter)						Joint Pain in Left knee (Subjective Parameter)					
Group A(n=20)	**BT**	**F1**	**F2**	**AT**	**% change**	**Group A(n=20)**	**BT**	**F1**	**F2**	**AT**	**% change**
0	0(0%)	0(0%)	1(5%)	0(0%)	0.0%	0	0(0%)	1(5%)	0(0%)	0(0%)	0.0%
1	3(15%)	4(20%)	8(40%)	15(75%)	60.0%	1	2(10%)	4(20%)	17(85%)	19(95%)	85.0%
2	8(40%)	10(50%)	11(55%)	5(25%)	-15.0%	2	15(75%)	15(75%)	3(15%)	1(5%)	-70.0%
3	9(45%)	6(30%)	0(0%)	0(0%)	-45.0%	3	3(15%)	0(0%)	0(0%)	0(0%)	-15.0%
NA	0(0%)	0(0%)	0(0%)	0(0%)	0.0%	NA	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
Group B (n=20)	**BT**	**F1**	**F2**	**AT**	**% change**	**Group B (n=20)**	**BT**	**F1**	**F2**	**AT**	**% change**
0	0(0%)	0(0%)	1(5%)	1(5%)	5.0%	0	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
1	2(10%)	6(30%)	10(50%)	16(80%)	70.0%	1	2(10%)	5(25%)	16(80%)	19(95%)	85.0%
2	10(50%)	9(45%)	7(35%)	1(5%)	-45.0%	2	14(70%)	13(65%)	3(15%)	0(0%)	-70.0%
3	6(30%)	3(15%)	0(0%)	0(0%)	-30.0%	3	3(15%)	1(5%)	0(0%)	0(0%)	-15.0%
NA	2(10%)	2(10%)	2(10%)	2(10%)	0.0%	NA	1(5%)	1(5%)	1(5%)	1(5%)	0.0%
P value	0.479	0.401	0.515	0.100	-	P value	1.000	0.780	1.000	1.000	-
Chi-Square test/Fisher Exact test											

Table 3: Comparative Assessment before and after treatment in Subjective parameter

Morning Stiffness Right in Right knee (Subjective Parameter)						Morning Stiffness in Left knee (Subjective Parameter)					
Group A(n=20)	**BT**	**F1**	**F2**	**AT**	**% change**	**Group A(n=20)**	**BT**	**F1**	**F2**	**AT**	**% change**
0	3(15%)	4(20%)	8(40%)	8(40%)	25.0%	0	3(15%)	6(30%)	8(40%)	9(45%)	30.0%
1	10(50%)	11(55%)	10(50%)	12(60%)	10.0%	1	12(60%)	12(60%)	10(50%)	11(55%)	-5.0%
2	5(25%)	5(25%)	2(10%)	0(0%)	-25.0%	2	3(15%)	2(10%)	2(10%)	0(0%)	-15.0%
3	2(10%)	0(0%)	0(0%)	0(0%)	-10.0%	3	2(10%)	0(0%)	0(0%)	0(0%)	-10.0%
NA	0(0%)	0(0%)	0(0%)	0(0%)	0.0%	NA	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
Group B (n=20)	**BT**	**F1**	**F2**	**AT**	**% change**	**Group B (n=20)**	**BT**	**F1**	**F2**	**AT**	**% change**
0	1(5%)	4(20%)	8(40%)	12(60%)	55.0%	0	2(10%)	7(35%)	10(50%)	13(65%)	55.0%
1	11(55%)	11(55%)	10(50%)	6(30%)	-25.0%	1	14(70%)	11(55%)	9(45%)	6(30%)	-40.0%
2	5(25%)	3(15%)	0(0%)	0(0%)	-25.0%	2	3(15%)	1(5%)	0(0%)	0(0%)	-15.0%
3	1(5%)	0(0%)	0(0%)	0(0%)	-5.0%	3	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
NA	2(10%)	2(10%)	2(10%)	2(10%)	0.0%	NA	1(5%)	1(5%)	1(5%)	1(5%)	0.0%
P value	0.637	0.647	0.351	0.069	-	P value	0.690	1.000	0.521	0.200	-
Chi-Square test/Fisher Exact test											

Table 4: Comparative Assessment before and after treatment in Subjective parameter

Difficulty in Movements Right knee (Subjective Parameter)						Difficulty in Movements Left knee (Subjective Parameter)					
Group A(n=20)	**BT**	**F1**	**F2**	**AT**	**% change**	**Group A(n=20)**	**BT**	**F1**	**F2**	**AT**	**% change**
0	3(15%)	4(20%)	8(40%)	8(40%)	25.0%	0	0(0%)	1(5%)	2(10%)	1(5%)	5.0%
1	10(50%)	11(55%)	10(50%)	12(60%)	10.0%	1	7(35%)	7(35%)	14(70%)	19(95%)	60.0%
2	5(25%)	5(25%)	2(10%)	0(0%)	-25.0%	2	13(65%)	12(60%)	4(20%)	0(0%)	-65.0%
3	2(10%)	0(0%)	0(0%)	0(0%)	-10.0%	3	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
NA	0(0%)	0(0%)	0(0%)	0(0%)	0.0%	NA	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
Group B (n=20)	**BT**	**F1**	**F2**	**AT**	**% change**	**Group B (n=20)**	**BT**	**F1**	**F2**	**AT**	**% change**
0	2(10%)	7(35%)	10(50%)	12(60%)	50.0%	0	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
1	13(65%)	10(50%)	8(40%)	6(30%)	-35.0%	1	4(20%)	6(30%)	17(85%)	19(95%)	75.0%
2	3(15%)	1(5%)	0(0%)	0(0%)	-15.0%	2	13(65%)	12(60%)	2(10%)	0(0%)	-65.0%
3	0(0%)	0(0%)	0(0%)	0(0%)	0.0%	3	2(10%)	1(5%)	0(0%)	0(0%)	-10.0%
NA	2(10%)	2(10%)	2(10%)	2(10%)	0.0%	NA	1(5%)	1(5%)	1(5%)	1(5%)	0.0%
P value	0.278	0.136	0.217	0.090	-	P value	0.314	1.000	0.284	1.000	-
Chi-Square test/Fisher Exact test											

Table 5: Comparative Assessment before and after treatment in VAS

Pain Intensity in Right knee (VAS)				Pain Intensity in Left knee (VAS)			
Result	Group A	Group B	P value	Result	Group A	Group B	P value
BT	6.35±1.46	6.17±1.47	0.702	BT	5.70±1.03	5.68±1.00	0.962
F1	5.10±1.12	4.61±1.33	0.228	F1	4.47±0.84	3.95±0.97	0.082
F2	3.90±1.37	3.11±1.32	0.080	F2	3.30±0.86	2.74±0.73	0.035*
AT	2.95±0.89	2.22±1.06	0.002*	AT	2.40±0.82	1.79±0.63	0.013*
Difference from BT				Difference from BT			
F1	1.395	1.556	-	F1	1.368	1.737	-
F2	2.737	3.056	-	F2	2.400	2.947	-
AT	3.400	3.944	-	AT	3.300	3.895	-
P value from BT				P value from BT			

F1	<0.001**	<0.001**	-	F1	<0.001**	<0.001**	-
F2	<0.001**	<0.001**	-	F2	<0.001**	<0.001**	-
AT	<0.001**	<0.001**	-	AT	<0.001**	<0.001**	-
Between group: Student t test (Independent), Within group: Student t test(Paired)							

Table 6: Comparative Assessment before and after treatment in KOOS

Symptoms in Right knee (KOOS)				**Symptoms in Left knee (KOOS)**			
Result	Group A	Group B	P value	Result	Group A	Group B	P value
BT	59.30±21.96	59.50±19.78	0.977	BT	67.60±16.56	68.95±14.89	0.791
F1	62.75±21.26	66.72±19.81	0.556	F1	71.65±14.44	74.00±13.26	0.600
F2	72.50±17.13	75.44±15.69	0.585	F2	79.15±10.99	80.00±11.12	0.812
AT	76.25±14.42	79.22±13.58	0.518	AT	81.80±9.17	82.68±9.12	0.764
Difference from BT				Difference from BT			
F1	-3.450	-7.222	-	F1	-4.050	-5.053	-
F2	-13.200	-15.944	-	F2	-11.550	-11.053	-
AT	-16.950	-19.722	-	AT	-14.200	-13.737	-
P value from BT				P value from BT			
F1	0.002**	<0.001**	-	F1	<0.001**	<0.001**	-
F2	<0.001**	<0.001**	-	F2	<0.001**	<0.001**	-
AT	<0.001**	<0.001**	-	AT	<0.001**	<0.001**	-
Between group: Student t test (Independent), Within group: Student t test(Paired)							

Table 7: Comparative Assessment before and after treatment in KOOS							
Pain in Right knee (KOOS)				**Pain in Left knee (KOOS)**			
Result	Group A	Group B	P value	Result	Group A	Group B	P value
BT	35.20±17.96	37.33±15.77	0.701	BT	44.65±13.30	44.16±12.16	0.905
F1	41.55±15.37	44.44±16.06	0.574	F1	52.10±12.37	50.68±10.45	0.702
F2	54.45±14.24	57.22±12.67	0.532	F2	61.85±9.04	64.11±6.33	0.375
AT	59.15±10.48	62.94±9.26	0.247	AT	64.50±6.95	67.53±2.27	0.079
Difference from BT				Difference from BT			
F1	-6.350	-7.111	-	F1	-7.450	-6.526	-
F2	-19.250	-19.889	-	F2	-17.200	-19.947	-
AT	-23.950	-25.611	-	AT	-19.850	-23.368	-
P value from BT				P value from BT			
F1	<0.001**	0.004**	-	F1	<0.001**	0.003**	-
F2	<0.001**	<0.001**	-	F2	<0.001**	<0.001**	-
AT	<0.001**	<0.001**	-	AT	<0.001**	<0.001**	-
Between group: Student t test (Independent), Within group: Student t test(Paired)							

Table 8: Comparative Assessment before and after treatment in KOOS

ADL in Right knee (KOOS)				**ADL in Left knee (KOOS)**			
Result	Group A	Group B	P value	Result	Group A	Group B	P value
BT	40.05±19.92	41.61±17.04	0.798	BT	50.20±14.38	49.79±12.76	0.926
F1	46.15±15.79	49.67±17.61	0.520	F1	57.30±12.81	56.16±11.45	0.771
F2	60.55±12.34	62.89±12.45	0.565	F2	67.95±8.93	71.05±7.29	0.244
AT	65.60±10.75	69.78±10.52	0.235	AT	71.85±5.80	74.11±0.74	0.101
Difference from BT				Difference from BT			
F1	-6.100	-8.056	-	F1	-7.100	-6.368	-
F2	-20.500	-21.278	-	F2	-17.750	-21.263	-
AT	-25.550	-28.167	-	AT	-21.650	-24.316	-
P value from BT				P value from BT			
F1	0.001**	0.004**	-	F1	0.001**	0.005**	-
F2	<0.001**	<0.001**	-	F2	<0.001**	<0.001**	-
AT	<0.001**	<0.001**	-	AT	<0.001**	<0.001**	-
Between group: Student t test (Independent), Within group: Student t test(Paired)							

Table 9: Comparative Assessment before and after treatment in KOOS

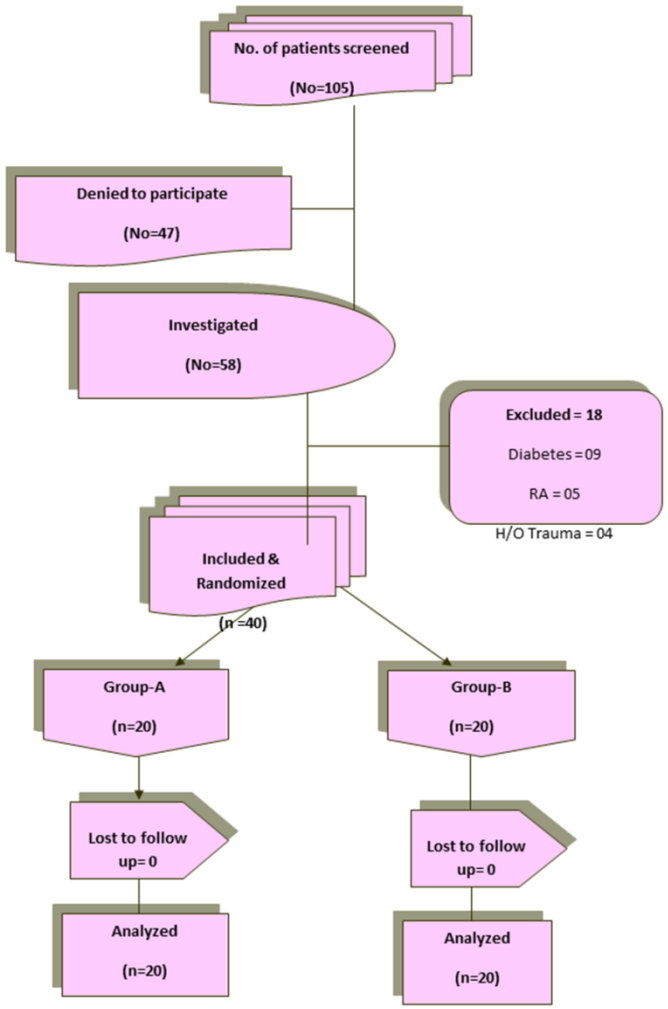
Sports/Recreation Right in knee (KOOS)				**Sports/Recreation Left in knee (KOOS)**			
Result	Group A	Group B	P value	Result	Group A	Group B	P value
BT	31.32±17.55	32.06±15.01	0.893	BT	41.75±15.15	41.26±14.17	0.918
F1	35.75±19.49	36.78±18.26	0.868	F1	50.00±15.73	49.74±13.07	0.955
F2	48.50±16.63	53.61±14.93	0.328	F2	57.25±13.33	61.00±10.78	0.342
AT	57.75±13.33	60.28±13.11	0.560	AT	62.00±11.52	63.58±8.95	0.637
Difference from BT				Difference from BT			
F1	-5.789	-6.294	-	F1	-8.250	-8.474	-
F2	-18.421	-22.647	-	F2	-15.500	-19.737	-
AT	-26.842	-29.706	-	AT	-20.250	-22.316	-
P value from BT				P value from BT			
F1	0.020*	0.020*	-	F1	0.002**	0.001**	-

F2	<0.001**	<0.001**	-	F2	<0.001**	<0.001**	-
AT	<0.001**	<0.001**	-	AT	<0.001**	<0.001**	-
Between group: Student t test (Independent), Within group: Student t test(Paired)							

Table 10: Comparative Assessment before and after treatment in KOOS

Quality of Life (KOOS)			
Result	Group A	Group B	P value
BT	35.1±5.37	37±6.55	0.365
F1	39.75±4.96	41.25±5.38	0.365
F2	42.15±5.69	44±3.89	0.237
AT	45.5±3.30	47.3±3.06	0.081
Difference from BT			
F1	-4.650	-4.250	-
F2	-7.050	-7.000	-
AT	-10.400	-10.300	-
P value from BT			
F1	<0.001**	<0.001**	-
F2	<0.001**	<0.001**	-
AT	<0.001**	<0.001**	-
Between group: Student t test (Independent), Within group: Student t test(Paired)			

Figure: An over view of study



DISCUSSION

The study was conducted to "Evaluation of the effect of *Hijama bi'l Shart in Waja-ul-Mafasil* (Osteoarthritis Knee) - An open labelled randomized controlled comparative clinical study". Out of 40 patients, 25 (62.5%) patients in the study were in the age group of 41-50 years and 15 (37.5%) patients were in the age group of 51-60 years. Number of studies have reported that knee OA is a disease of 4th to 5th decade of life and the advanced age group [15,16,17] because, cartilage gets thinner as the age advance, which may increase the laxity of joint, making the joint prone to injury and the cartilage susceptibility to shear stress is increased at the basal levels where cartilages attach to bone[2,18,19]. Although knee OA is a disease of advanced age even then, in this study its incidence was more in age group ranging from 40-50 years which was similar to the study conducted by Seitzman RL et al[20]. Out of 40 patients, 33 (82.5%) patients were female and 07 (17.5%) patients were male. Studies have reported that knee OA is more common in women as compared to men[16,17,21], because women have a possess a greater proportion of total body fat and relatively higher levels of adipose derived systemic leptin concentration as compared to men which may partially account for the gender disparity in OA[4]. The present study is consistent with the studies reported by Wang L et al.[22] Srinivas P et al.[23] and Ali AK et al.[24] all of which have mentioned that knee OA is more common in women. Out of 40 patients, 28 (70%) patients were taking mixed diet and 12 (30%) patients were used to take veg. diet. In *Unani* system of medicine, *Waja-ul-Mafasil* is thought to be caused due to abnormal digestion *(Sū-e-Hazm)*[5,25] Mixed diet may lead to slow the process of digestion resulting in production of *Ghayr Tabayī Akhlāt,* that's why eminent *Unani* physicians have advised the restriction of non-vegetarian diets in *Waja-ul-Mafasil*. This study result was consistent with Srinivas P et al.[23] and Khalid M et al.[26] Out of 40 patients, 2 (5%) patients were underweight, 28 (70%) patients were of normal BMI & 10 (25%) patients were found to be overweight. But epidemiological data supports that overall obese persons are more affected in knee OA[27,28,29]. In the present study incidence was more in normal BMI patients which was similar to Muraki S et al.[30] Zhang Q et al.[31] Vishal AA et al.[32] & Radha MS et al.[33] Out of 40 patients 22 (55%) patients were having sedentary lifestyle, 9 (22.5%) patients were having average lifestyle and 9 (22.5%) patients were laborers. Eminent Unani physicians have stated that excessive rest and lack of exercise may cause *Waja-ul-Mafasil*[5,8,34]. In this study incidence was more in patients with sedentary life style which was in consistence with Pal CP et al.[16] and Ganvir SD et al.[35] out of 40patients, 16 (40%) patients were belonging to upper lower class, 12 (30%) patients were belonging to lower middle class, 11 (27.5%) patients were belonging to upper middle class and 1 (2.5%) patient was from upper class. This study is consistent with Robbel L et al.[36] Ajit NE et al.[37] Out of 40 patients, both knees were involved in 37 (92.5%) patients, in 2 (5%) patients only the left knee was involved and in 1(2.5%) patient only right knee was involved. Studies have reported that knee OA is more in bilateral knee[28,38,39]. This study is in consistence with the studies carried out by Hawamdeh ZM et al.[40] Dar AK et al.[41] and Gunther KP et al.[28] Out of 40 patients, in 7 (17.5%) patients the left knee & in 33 (82.5%) patients the right knee was worst affected. Sernert N et al reported that KT1000 arthrometer revealed a significant increase in laxity measurements in right knees compared to left knee[42]. In the present study, right knee joint was worst affected & is consistent with Hawamdeh ZM et al.[40]

In subjective parameters both groups showed highly significant difference in intragroup analysis but, no significant difference was observed in intergroup assessment, as shown in table no. 2, 3 & 4. In VAS score, both groups showed highly significant difference in intragroup analysis where as on intergroup comparison using unpaired t-test, the results indicate that group-B showed significant reduction in VAS score ($p<0.05$) as shown in table no. 6. In KOOS, both groups showed highly significant difference in intragroup analysis but, no significant difference was observed in intergroup assessment, as shown in table 6-10.

The overall effect of *Hijama bi'l* Shart on *Waja-ul-Mafasil* (Knee OA) in pain, stiffness, and difficulty in knee movement may be due to the evacuation of morbid matter supposed to be the causative agent[43]. In modern system of medicine, the exact mechanism of wet cupping is still unknown[10].

Knee Pain: The observed effect of *Hijama bi'l Shart* on the knee pain may be put in the way, that when skin is punctured through scarification, it leads to release of β-endorphin (endogenous analgesic Opioid) and adrenocortical hormones into the circulation[44,45,46]. Both β-endorphin and adrenocortical hormones could be helpful in blocking inflammation in OA[45,47,48]. Upon skin injury the normal skin keratinocytes synthesize endothelin-1 which is a pain mediator and acts on endothelin-A receptors. Also by acting on endothelin-B receptors resulting in release of β-endorphin from keratinocytes and activation of G-protein-coupled potassium channels linked to opioid receptors on pain receptors, the endothelin-1 can produce analgesia. Also, β-endorphins are mainly produced from the outer root sheath of the anagen hair follicles of skin and dermal fibroblasts[47,49]. *Hijama bi'l Shart* may be beneficial through the effects of cortisol, which reduces stress, and dopamine which acts on the reward pathway in the brain[45,47,49] and may also increase the levels of natural antioxidants in the body[50].

Stiffness: Morning stiffness is due to spasm of the synovial membrane and related tendons as a result of lack of oxygen and tissue nourishment[2,4]. This spasm may be due to periarticular damages and capillary thickening[51]. According to eminent Unani physicians, spasm is due to accumulation of *Ghayr Tabayī Mādda* (morbid matter) and cold temperament[34,52,53,54]. *Hijama bi'l Shart* reduces the stiffness through detoxification of the body[11,45,47,55,56] and increases oxygenation in tissues and muscles by developing hyperaemia[11,43,45,47].

Difficulty in joint movement: Difficulty of movement is directly related to pain and swelling and patient feels difficulty in joint movement due to synovitis, effusion or periarticular soft tissue contractures[1,2]. Swelling in the joint is due *Sū-e-mizaj Māddī* (dystemperament due to accumulation of morbid matter). *Hijama bi'l Shart* reduces the swelling by evacuation of *Mādda* (morbid matter)[57,58]. While in modern system of medicine, the effect of *Hijama bi'l Shart* on joint movement is still unknown. The effect on joint movement may be due to reduction of pro-inflammatory chemical mediators[43,47]. Cupping also boosts the immune system by increasing number of macrophage cells[45,47,59] which also help in improving the joint movement.

ADL and Sports/Recreation: *Hijama Bi'l Shart* might improve ADL and Sports/Recreation function through reduction of inflammation in tissues & cells[60,61] and boost the immune system by increasing the number of macrophages[45,47].

Quality of life: *Hijama Bi'l Shart* improves the quality of life in *Waja-ul-Mafasil* by reducing the symptoms and by increasing the levels of body's natural antioxidants[47].

Efficacy of *Majoon Suranjan* is established[62,63,64]. This compound formulation contains a number of ingredients which

have anti-inflammatory, analgesic[65,66], muscle relaxant[62,64,67] and antioxidant properties, because of which this compound formulation possess antioxidant and immunomodulatory activity[65,66,68], That's why group-B shows more significant effect clinically.

All safety parameters were within normal limits in both the groups. Assessed on before and after completion of protocol therapy with P value>0.05.

CONCLUSION

The study concludes that *Hijama bi'l Shart* alone and in combination with *Majoon Suranjan* is effective in the treatment of *Waja-ul-Mafasil* (Knee Osteoarthritis). Efficacy of *Hijama bi'l Shart* alone and in combination with *Majoon Suranjan* was confirmed by KOOS and VAS score. *Hijama bi'l Shart* alone and in combination with *Majoon Suranjan* showed statistically significant reduction in pain on VAS and improvement in KOOS with $p<0.01$. In intergroup comparison, the combined effect of *Hijama bi'l Shart* with *Majoon Suranjan* in pain on VAS score was statistically significant than *Hijama bi'l Shart* alone with $p<0.05$. Safety profiles were within normal range, ascertaining the safety of *Hijama bi'l Shart* and *Majoon Suranjan*. The effect of *Hijama bi'l Shart* on *Waja-ul-Mafasil* may be attributed to its property of evacuation of morbid material, release of β-endorphin, cortisol, dopamine and natural antioxidants. From the above observation we can conclude that *Hijama bi'l Shart* in the present study is safe and effective in managing *Waja-ul-Mafasil* (Knee Osteoarthritis) and that NSAIDs, COX-2 inhibitor or surgical intervention should no longer be the only treatment option available to patients with *Waja-ul-Mafasil* (Knee Osteoarthritis). Further studies are imperative to confirm these results and to shed light on the mechanism(s) of action of *Hijama bi'l Shart*.

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