The Pharma Innovation Journal 2023; SP-12(10): 1020-1025

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2023; SP-12(10): 1020-1025

www.thepharmajournal.com
Received: 20-07-2023
Accepted: 26-08-2023

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Clinical study on effect of Hijama-bila-shurt (Dry cupping) in the management of fibromyalgia syndrome

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Abstract
This study intended to evaluate the effect of Hijama-Bila-Shurt (Dry cupping) alone and Hijama-Bila-Shurt with Habbe Asgand as a part of multimodal approach in the management of Fibromyalgia (FM) by using NRS scale and a functional improvement in FM related symptoms in Fibromyalgia Syndrome(FMS) by using FIQR. The study was designed as open, randomized and controlled clinical trial carried out on total 60 patients in which they were divided into 3 groups, Test Group 'A' & 'B' and Control Group 'C' containing 20 patients in each group. Group A received only Hijama-Bila-Shurt (Dry Cupping), Group B received Hijama-Bila-Shurt & Habbe Asgand and Group C received Amitriptyline as standard drug. The improvement in Group A, at the end of study was statistically not significant at $p>0.05$. In Group B and C it was found statistically significant $p<0.05$ for both NRS and FIQR which cinclude that Hijama-Bila-Shurt along with *Habbe-Asgandh* is found as effective as the control drug Amitriptyline in the management of Fibromyalgia related syndrome.

Keywords: Hijama, fibromyalgia syndrome (FMS), Habbe Asgand, cupping therapy, unani medicine

Introduction
Fibromyalgia is the most common cause of generalized regional pain and disability often characterized by chronic widespread pain at multiple tender points, joint stiffness, cognitive dysfunction, and insomnia [1-5]. It is also associated with fatigue and sometimes severe depressive episodes [6]. Commonly associated disorders with FMS are anxiety, somatisation, Dysthymia, Panic disorders, Post traumatic stress and overall Depression [7-11].
The exact etiology and pathophysiology of the fibromyalgia is still on known [12]. Recent research indicate that FMS, is a multi symptomatic disorder characterized by dysfunctions incentral pain processing [13-15].
In Unani system of medicine, there is no proper description of Fibromyalgia, such kind of ailments are considered as *Amraz-e-Ghair Mudawwina*, Various disorders having long standing widespread pain and psychological symptomatology such as IBS and *Waja-ul-badan* are considered as "*Araz-e-Nafsai.*" [16-18] As Unani Medicine is concern with the non pharmacological approach to manage the FMS. There are various non pharmacological modalities which are influenced to treat various kinds of pain disorders such as, *Hijama* (cupping), *Fasad* (venesection / Phlebotomy), *Dalak* (Massage), *Nutool* (Irrigation), *Inkebab* (Hot fomentation), *Abzan* (sitzbath) and *Takmeed* (Diathermy) etc [19]. Among them *Hijama* therapy is one of the important regimen which is being practiced since long time for the management of pain in various musculo-skeletal disorders [19].
Furthermore, *Habb-e-Asgandh*, a polyherbal Unani compound formulation (Table 1), used in musco-skeletal disorders. The chief ingredient is *Withania somnifera* (Asgandh/Ashwaghandha) which have shown to possess, anti-depressant, anti-stress, analgesic, cartilage protective, actions [20]. Due to its Anti-inflammatory, Analgesic and *Musakkin* effect, the herb is reported to be effective in the treatment of chronic pain and musculoskeletal disorders [21].
Given the reported effect and the common practice of physicians with *Habb-e-Asgandh* in the management of pain related conditions, it was included in the regimen proposed for Fibromyalgia in the present study.
Keeping in view of the above idea a Randomized, standard controlled clinical study was designed on the topic "Clinical evaluation of effects o*f Hijama- Bila- Shurt* (Dry Cupping) as a part of multimodal approach in the management of Fibromyalgia syndrome."

Methodology

Ethical clearance & Trial Registry

The institutional ethics Committee, Ajmal Khan Tibbiya College, Faculty of Unani Medicine AMU, has approved the protocol for study (Ref no: 321/FUM dated: 23/12/20). The trial has been registered under The Clinical Trials Registry-India (CTRI/2022/10/046928).

Study population and participant Eligibility inclusion criteria

- Clinically Diagnosed patient of FMS based on 2016 revision of American College of Rheumatology (ACR) Diagnostic Criteria of 2011/2010.
- Patients of either gender between age group of 20-60 years, who are able to give written informed consent and follow the protocol of study.

Exclusion Criteria

- Patients below 20 years and above 60 years
- Primary generalized polyarthritis, poly myalgia rheumatica, rheumatoid arthritis, diabetic neuropathy and hypothyroidism
- Pregnant and Lactating women
- Patients with un controlled Diabetes Mellitus and severe hypertension
- Patient taking medicine for any other psycho-somatic disorders
- History of trauma
- Patients having anaemia (Hb less than 9 gm %)
- Patients unable to give informed written consent

Withdrawal criteria

- If the subject is not willing to continue
- The cases in which adverse reactions are noticed
- Any acute systemic illness during the therapy
- Drug/Therapy intolerance
- Noncompliance with the study protocol
- Exacerbation of the disease

Informed Consent

Patients, who fulfilled the prior declared inclusion criteria, were invited to receive detailed written information about the procedure of clinical trial before obtaining their written informed consent.

Method of Collection of Data

The patients were selected from the OPD and IPD of Ajmal Khan Tibbiya College and Pain clinic Jawaharlal Nehru Medical College, AMU, Aligarh. On the basis of clinical presentation, history, examination and on following inclusion and exclusion criteria.

Study Design: Open randomized standard controlled clinical trial was performed on 60eligible patients of FMS from January 2020 to December 2021 allocate into three groups after using computer generated randomization table. The duration of protocol was 28 days with weekly screening.

Sample size: Sample size was fixed as 60 patients. 20 in each group (Consort diagram, figure 1).

Allocation of the patients

Test Group A: 20 patients were included in Group A, in this intervention group, patients receive weekly session of Dry Cupping (*Hijamah- Bila- Shurt*) on tender points over the body surface for 10 minutes for total of 4 weeks.

Test Group B: 20 patients were included in this intervention group, patients receive intervention of Group A plus 2 tablets (650 mg each) of *Habb-e-Asgandh* orally twice daily an hour after meals for 4 weeks.

Control Group C: 20 patients were allocated in this control group and prescribed to take one tablet (10 mg) of Amitriptyline orally once daily at bed time for 4weeks.

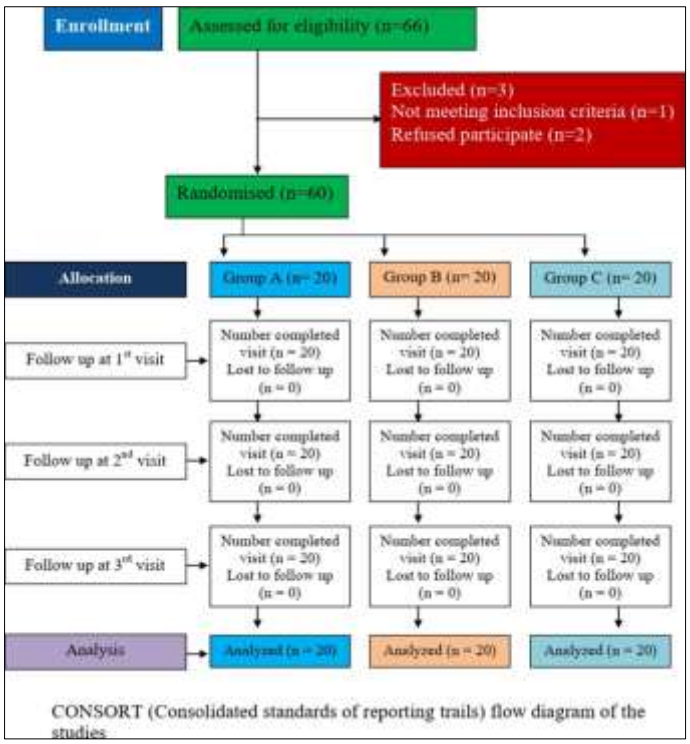

Fig 1: Test Drug ingredients of [21]

Table 1: Habbe Asgandh

S.No	Ingredients	Botanical Name	Quantity
1	Asgandh	*Withania Somnifera*	40 gm
2	Ajwaindesi	*Trachyspermum ammi*	20 gm
3	Bidhara	*Argyreia nervosa*	40 gm
4	Peeplamol	*Piper longum* (root)	20 gm
5	Peepalkalan	*Piper longum* (fruit)	20gm
6	Satawar	*Asparagus racemosus*	40 gm
7	Zanjabeel	*Zingiber officinale*	40 gm
8	Muslisiyah	*Curculigo orchioides*	20 gm

Outcome measures (Objective parameters)

1. NRS (Numerating Rate scale) [22]
2. FIQR (Revised Fibromyalgia Impacted Questionnaire) [23]

Following investigations were done to exclude the patients of other co-morbidities as well as to assess safety of the test drug: Haemogram (including Hb %, TLC, DLC, ESR), LFT (includes total serum bilirubin, Direct bilirubin and Indirect bilirubin) and KFT (includes Serum Creatinine, Urea)

After the completion of treatment, the pre and post treatment values or scores of different parameters (subjective and objective) were assessed and subjected to comparison and statistical analysis to evaluate the efficacy of the test intervention and to compare with standard control group.

Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Paired Proportion test has been used to find the significance of proportion in paired data. The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and MS Word and Excel have been used to generate graphs, tables etc. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance of the study is assessed at 5% level of significance.

Results & Discussions

The results of all three groups were statistically evaluated to determine the efficacy. The majority of the cases i.e. 22 (36.7%) were found in the age group of 30-40 years, showing higher incidence in 3rd decade. The total 32 (53.3%) patients were female while 28 (46.7%) were males, showing higher incidence in females. 20 patients were belongs to the upper middle class (II) and 20 patients were found in the category of lower middle class (III), while 11 patients were found in lower class (V), 6 patients were found in upper lower class and only 3 patients were found in upper class, showing lower incidence in upper class (I). The maximum number of patients i.e.22 (36.6%) were found of *Damvi mizaj*, 17(28.4) patients were of *Safravi mizaj*, 15(25) patients were of *Balghami mizaj* while only 6(10) patients were of *Saudavi mizaj*, showing higher incidence in *Damvi mizaj* patients.

As evident by Table No.11, in Group A, the mean of NRS for pain was 6.4 with S.D ± 1.729 before the intervention and it was 6.25 with S.D ± 1.682 at the end of intervention. In Group B, the mean was 6.8 with S.D ± 1.908 before the treatment while the mean was 4.6 with S.D ± 1.789 at the end of treatment. In Group C the mean of NRS was 6.950 with S.D ± 1.669 and it was 3.050 with S.D ± 2.038 at the end of the treatment. The intergroup data were analyzed by unpaired t test, on comparing between Groups A&B, value of $p<0.001$, which is significant statistically. Similarly on comparison between Group B & C, value of p=0.003, which is also significant statistically. On comparison between the Groups A& C, the value of $p<0.0001$, which is highly significant statistically.

The Changes in the NRS was statistically significant in Group B and Group C at $p<0.05$ while in Group A the changes in NRS were not significant statistically. Hence, multi modal approach found effective in the management of FMS in Group B. The effect on the NRS scale may be due to the cumulative effect of Hijama-Bila-Shurt and *Habbe- Asgandh*. As the most of the ingredients of *Habb-e-Asgandh*, possess adaptogenic [20, 24], anti-inflammatory [24, 20], sedative [24, 20], Anti-depressant [20, 24], Anti-stress [25, 26], Analgesic [25-29] Furthermore, in certain preliminary studies Hijama-Bila-shurt was found effective in relieving pain in various musculoskeletal disorders [30-31]. Therefore, the findings of the study are in consonance with the previous studies.

As evident by Table No.12, the mean of FIQR in Group A was 41.61 with S.D ± 6.874 before the intervention and it was 38.74 with S.D 8.088 at the end of intervention. In Group B the mean was 44.30 with S.D ± 14.89 and it was 31.24 with S.D±12.19 at the end of treatment. In Group C, the mean was 45.09 with S.D 6.356 and it was 32.68 with S.D ± 5.607 at the end of treatment.

The Changes in the mean of FIQR of Group A is not significant statistically while the changes in the mean of Group B as well as Group C are significant statistically (at $p<0.05$). Since FIQR is based on 3 domains in which the reare several symptoms like morning stiffness, anxiety, depression, generalize body ache and fatigue etc. Multimodal approach of the treatment is significantly effective in all domains of FIQR. These effect may be due to amelioration of symptoms of Fibromyalgia ie. Anxiety, depression, fatigue and wide spread pain. The improvement in these symptoms may be due to diverse pharmacological properties of ingredients of *Habbe-Asgandh* i.e. *Asgandh* (*Withania somnifera*), *Ajwain* (*Trachyspermum ammi*), *Bidhara* (*Argyreia nervosa*), *Muslisiyah* (*Curculigo orchioides*), *Satawar* (*Asparagus racemosus*), *Zanjabeel* (*Zingiber officinale*), *Peeplamool* (*Piper longum* root) and *Pipal kalan* (*Piper longum* fruit). Some recent studies revealed that these ingredients also possess various pharmacological properties like Antioxidant [20] Anxiolytic [20], Anti-inflammatory [20, 24] and Analgesics [25-27] properties.

The improvement in symptoms of anxiety is due to anxiolytic effect of *Asgandh*, *Ajwain*, *Peeplamool*, *Bidhara* and *Satawar*. The reduction in the symptoms of depression may be dueto anti-depressant effect of *Asgandh*, *Peepalkalan*, *Satawar* and *Mulisiyah*. The relief in the pain may be due to the analgesic, anti-inflammatory and anti-nociceptive actions

of the *Asgandh*, *Ajwain*, *Peeplamool*, *Pipalkalan*, *Bidhara*, *Zanjabeel* and *Muslisiyah*. Furthermore, some ingredients of *Habbe-Asgandh* possess immunomodulator and anti-oxidant properties which may be helpful in the improving body immune system. Since the perception of pain is increased in the patients with FMS because of decrease immunity, therefore the adaptogenic, immunomodulator and anti-oxidant properties may be helpful in the improving of immune system and thereby helpful in the reduction of sensitivity of the pain in the patients of FMS.

In Unani system of medicine *Hijama-Bila- shurt*is practiced for the management of various musculoskeletal disorders including pain alleviation. Some recent studied have shown promising result in relieving pain and it associated symptoms because cupping can induce comfort and relaxation on a systemic level and the resulting increase in endogenous opioid production in the brain leads to improved pain control [33, 34]. Other researchers proposed that the main action of cupping therapy is to enhance the circulation of blood and to remove toxins and waste from the body. That could be achieved through improving microcirculation, promoting capillary endothelial cell repair, accelerating granulation and angiogenesis in the regional tissues, thus helping normalize the patient's functional state and progressive muscle relaxation [35, 36]. Cupping also removes noxious materials from skin micro circulation and interstitial compartment which benefit the patient [37].

Effects on safety Parameters

The safety studies were also conducted in the study. It was found that safety parameters i.e. Haemogram, LFT and KFT was remain within normal limits before and after the treatment and no adverse effect was reported during the study.

Table 2: Effects of interventions on Haemoglobin percentage

Groups	Assessment		t &p value Intra group
	Before Treatment (Mean ± S.D)	After Treatment (Mean ± S.D)	
Group A	12.54±1.43	12.44±1.281	t=1.090, p=0.2895
Group B	13.07±1.856	13.10±1.714	t=.2104, p=0.8356
Group C	13.30±1.746	12.90±2.254	t=1.126, p=0.2743

Table 3: Effects of interventions on Total Leucocytes Count

Groups	Assessment		t&p value Intragroup
	Before Treatment (Mean ± S.D)	After Treatment (Mean ± S.D)	
Group A	6.435±1.874	6.265±1.503	t=0.6323, p=0.5347
Group B	6.358±2.138	6.343±1.574	t=.06580, p=0.9482
Group C	5.925±1.734	5.865±1.734	t=1.928, p=0.0689

Table 4: Effects of interventions on Neutrophils Count

Groups	Assessment		t&p value Intra group
	Before Treatment (Mean ± S.D)	After Treatment (Mean ± S.D)	
Group A	67.85±4.428	67.10±4.115	t=0.8902, p=0.03845
Group B	63.45±9.012	61.95±8.721	t=1.279, p=0.2164
Group C	64.30±5.895	64.50±5.781	t=0.1564, p=0.8773

Table 5: Effects of interventions on Lymphocytes

Groups	Assessment		t&p value Intra group
	Before Treatment (Mean ± S.D)	After Treatment (Mean ± S.D)	
Group A	26.85±4.522	27.15±3.498	t=0.3320, p=0.7435
Group B	30.50±9.627	31.15±8.780	t=0.5879, p=0.5635
Group C	29.80±6.510	28.95±5.671	t=0.7333, p=0.4723

Table 6: Effect of interventions on ESR

Groups	Assessment		t&p value Intra group
	Before Treatment (Mean ± S.D)	After Treatment (Mean ± S.D)	
Group A	34.45±17.21	34.15±16.66	t=1.143, p=0.2674
Group B	30.15±14.54	29.70±14.19	t=2.015, p=0.0583
Group C	27.35±19.88	27.00±19.50	t=1.789, p=0.0896

Table 7: Effects of Interventions on Serum Creatinine

Groups	Assessment		t&p value Intra group
	Before Treatment (Mean ± S.D)	After Treatment (Mean ± S.D)	
Group A	0.7655±0.2029	1.162±1.856	t=0.9653, p=0.3465
Group B	0.8920±0.3082	0.8780±0.3030	t=2.088, p=0.0505
Group C	0.93650.2733	0.92700.2606	t=1.843, p=0.0810

Table 8: Effects Of interventions on blood Urea

Groups	Assessment		t&p value Intragroup
	Before Treatment (Mean ± S.D)	After Treatment (Mean ± S.D)	
Group A	21.09±15.63	20.94±15.61	t=0.5046, p=0.6196
Group B	19.05±6.653	18.90±6.711	t=1.1831, p=0.0828
Group C	24.44±4.576	23.72±4.464	t=1.751, p=0.0960

Table 9: Effects of interventions on Total Serum Bilirubin

Groups	Assessment		t&p value Intra group
	Before Treatment (Mean ± S.D)	After Treatment (Mean ± S.D)	
Group A	0.5040±0.1145	0.5000±0.1157	t=1.798, p=0.0880
Group B	0.4735±0.1008	0.4715±0.1025	t=1.165, p=0.2585
Group C	0.9365±0.2733	0.9270±0.2606	t=1.843, p=0.0810

As per the above-mentioned data there is no statistically significant change in the safety parameters during the study.

Table 10: Effects of interventions on Demographic data

Demographic data						Total
Age	**20-30 Yrs**	**30-40 Yrs**		**40-50 Yrs**	**50-60 Yrs**	**60**
	15	**22**		**11**	**12**	
Gender	Male			Female		60
	28			32		
M.Status	Married			Unmarried		60
	40			20		
Religion	Muslim			Non-muslim		60
	43			17		
Occupation	Worker	Student	Hw	Ue	Professional	60
	14	09	19	13	05	
Pasthis.	Significant			Non-significant		60
	08			52		
Familyhis.	Significant			Non-significant		60
	15			45		
Ses	Upper class(I)	UMC (II)	LMC (III)	ULC (IV)	Lower class (V)	60
	03	20	20	06	11	
Mizaj	Damvi	Balghami		Safravi	Saudavi	60
	22	15		17	06	

Table 11: Effects of Interventions on NRS Scale

Effect of interventions on NRS			
Groups	**Assessment**		**t & p value Intra group**
	Before Treatment (Mean ± S.D)	**After Treatment (Mean ± S.D)**	
Group A	6.4±1.729	6.25±1.682	t=1.143, p=0.2674
Group B	6.8±1.908	4.6±1.789	t=10.34, *p*<0.0001
Group C	6.950±1.669	3.050±2.038	t=9.671, *p*<0.0001
p value Inter group A& B			<0.0001
p value Inter group A & C			<0.0001
p value Inter group B& C			0.0003

Table 12: Effects of interventions on FIQR Score

Effect of interventions on FIQR			
Groups	**Assessment**		**t&p value Intra group**
	Before Treatment (Mean ± S.D)	**After Treatment (Mean ± S.D)**	
Group A	41.61±6.874	38.74±8.088	t=1.850, p=0.08
Group B	44.30±14.89	31.24±12.19	t=10.14, *p*<0.0001
Group C	45.09±6.356	32.68±5.607	t=12.88, *p*<0.0001
p value Inter group A&Bs	0.0244		
Pvalue Inter group A&C	0.0383		
P value Inter group B & C	0.4988		

Conclusion
On the basis of the above findings, it can be said that intervention of Hijama therapy along with oral administration of Habbe Asgandh can be safely used for the management of FMS as an alternative treatment.

Acknowledgement
Authors are thankful to the Chairman and all the staff of Department of Ilaj Bit Tadbeer AKTCH and Consultant In-charge of pain clinic JNMCH, AMU, Aligarh.

Limitation of study
Although, this study was conducted on a small sample size and for limited period of time. Therefore, it is suggested that the study may be conducted on a large sample size and including Phase III clinical trial to arrive at a better result.

Source of funding
As part of M.D Ilaj Bit Tadbeer Dissertation, funded by AMU Aligarh.

Conflict of Interest None

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