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CLINICAL EVALUATION OF CODED DRUGS UNIM-304 & UNIM-312 ALONG WITH MUNZIJ (UNIM-308), MUSHIL (UNIM-309) AND TABREED (UNIM-310) THERAPY IN WAJA-UL-MAFASIL (RHEUMATOID ARTHRITIS)

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ABSTRACT

Each participant was well informed about the trial and written consent was obtained before initiation of the study. Demographic data and information on the present disease condition, concomitant disease and therapy was recorded. Thorough general physical and systemic clinical examination was carried out. Signs and Symptoms pertaining to Rheumatoid arthritis were recorded in CRF. The vital parameters like blood pressure, heart rate, temperature and respiratory rate were also recorded. X-Ray of affected joints was conducted and blood samples were collected for the evaluation of laboratory parameters like Haemogram, C-Reactive proteins and Rheumatoid factor to establish and confirm inclusion criteria and other laboratory test like complete blood picture, kidney function test, liver function test and routine and microscopic examination of urine were done. All clinical and laboratory follow-up were done at every 4 weeks.

KEYWORDS: Waja-ul-mafasil, UNIM, Rheumatoid arthritis, Unani medicine, Remission.

The study was carried out in a total number of 64 patients of Waja-ul-Mafasil of either sex satisfying the criteria of American Rheumatism association. All the patients received treatment with coded Unani drugs UNIM-312 along-with local application of UNIM-304 for a period of 90 days after complete therapy of Munzij (UNIM-308), Mushil (UNIM-309) and Tabreed (UNIM-310). Out of 64 cases 55 patients completed the study, 36 patients were sero-positive, out of 55 subjects 21 patients got complete remission, 25 patients got partially

remission, 09 patients showed no relief and 09 patients dropped out. No hepatotoxic and nephrotoxic side effects noticed during the course of study. The clinical and laboratory findings after treatment have shown that coded drugs possessed efficacy in the treatment of Waja-ul-Mafasil.

INTRODUCTION

The term Waja'al-Mafāsil consists of two words, "Waja'"means pain and "Mafāsil" means joints, hence Waja'al-Mafāsil means pain in joints. In the classical Unani texts, Waja'al-Mafāsil is broadly explained and its clinical findings closely resemble the findings of Rheumatoid arthritis (RA) mentioned in modern system of medicine. Waja'al-Mafāsil is also known as Gathiya (Arzānī, 1931; Majūsī, 2010) and this is one of the hereditary diseases (Ibn Sīnā, 2007). Buqrāt (Hippocrates), Jālīnūs (Galen), Rāzī (Rhazes), Ibn Sīna (Avicenna) and other Unani physicians described the painful joints of hands and feet under the term Waja'al-Mafāsil. Involvement of other joints like hip, heel, back and toes are called sequentially in the name of Waja'al-Khāsira, Waja'al-'Aqib, Waja'al-Qatan and Niqris (Ibn Sīnā, 2007).

Unani System of Medicine is based on the theory of humours (Akhlat) and it is generally considered by Unani physicians that diseases are caused by morbid matter (Maddah-e-Ghair Tabai) mostly. Waja –ul- Mafasil (Waja- means pain and Mafasil- means joints) also known as Gathia and is a disease in which joints become painful and swollen with reduction of their normal activity. On the basis of causative factors sue-mizaj saada and sue Mizaj Maaddi, it is of two types. Waja-ul-mafasil occurs due to sue-mizaj Saada (Derangement of temperament) are hot, cold, wet and dry. Waja-ul-mafasil that occur due to humoural disturbances like Balghami, Safravi, Saudavi and Damvi or may occur by conglomeration of two or more humours. (Khan, 2003)

It is characterized by pain, swelling, tenderness and morning stiffness in the joints of hands, feet, knee and ankle joints. When causative substance (maddah) causing disease enters into the joints and it neither absorbed due to lack of power of absorption (Qawwat-e-Jazibah) nor expels from them due to weak power of expulsion (Quawwat-e-dafia) in the joints tends to retained in the joints. (Majoosi, 1889).

Waja-ul-mafasil depending upon the maddah affecting the joints usually, Balgham (Phlegm) predominate while Dam (Sanguine), Safra (Yellow bile) and Sauda (Black bile) may also involved. In some cases more than one humour is involved. (Arzani, Hussain).

On the basis of humour involvement four types of the disease have been described in the literature and can be diagnosed by their clinical features like

(i) Damvi: Redness and swelling of the skin over the affected joints are visibly marked and the pain is severe. Other symptoms of blood dominance (Ghalba-e-dam) are also present.

(ii) Safravi: There is a slight yellow discoloration of the skin. Swelling is less than that of damvi type. Pain and burning sensation along with other symptoms of bile dominance (Galba-e-safra) are also found.

(iii)Balghami: Besides other symptoms of phlegm dominance (Ghalba-e-balgham), skin color over the affected joint is whitish and swelling is less. The pain is deep seated and the patients are often obese.

(iv)Saudavi: There is a hard swelling and dryness over the joint and the colour of overlying skin is blackish blue. Other symptoms of black bile dominance (Ghalba-e-sauda) are also present.

When causative substance is retained in the joints for a long period, its viscosity (Ghilazat) and viscidity (Lazoojat) are increased and it becomes hard, ankylosing of joints starts (Tahajjur-e- mafasil) and the condition become incurable (Jurjani, 1903).

Rheumatoid arthritis is a systemic disease of unknown etiology characterized by a chronic proliferative and inflammatory reaction in the synovial membrane which eventually results in erosion and destruction of joints cartilage and supporting structure. Usually the pattern of joint involvement is characteristically symmetrical and its cause typically prolonged with the symptoms occasionally, however a typical, asymmetrical and incomplete forms do occur, confusing the diagnosis. It has a worldwide distribution and affects approximately 3% of population, mostly occurs above 30 years of age. Females are affected three times as frequently than males. Arthritis occurs throughout the world in all climates and among all ethnic groups; almost 16% of female and 5% of male population is affected. The disease commences most commonly in the third and fourth decades but no age group is exempted. Prevalence is higher in twins and first degree relatives but not in spouses, suggesting a weak genetic predisposition (Boon *et al.*, 2006).

In majority of patients, the onset of the disease is insidious with pain, Stiffness and symmetrical swelling of a number of small joints as well as major joints. Initially pain is experienced only on moving the affected joints. As the disease advances, pain, muscle spasm and progressive joint destruction results in the limitation of joint movements, joints stability

and deformities. At first the deformities are correctable, but later permanent contracture develops and the joints may become completely disorganized (Harvey *et al.*, 1976).

MATERIAL AND METHODS

Type of trial: An open level clinical trial.

Research Methodology: Each participant was well informed about the trial and written consent was obtained before initiation of the study. Demographic data and information on the present disease condition, concomitant disease and therapy was recorded. Thorough general physical and systemic clinical examination was carried out. Signs and Symptoms pertaining to Rheumatoid arthritis were recorded in CRF. The vital parameters like blood pressure, heart rate, temperature and respiratory rate were also recorded. X-Ray of affected joints was conducted and blood samples were collected for the evaluation of laboratory parameters like Haemogram, C-Reactive proteins and Rheumatoid factor to establish and confirm inclusion criteria and other laboratory test like complete blood picture, kidney function test, liver function test and routine and microscopic examination of urine were done. All clinical and laboratory follow-up were done at every 4 weeks.

Selection criteria

Inclusion criteria

- Patients of either sex.
- Patients in the age group of 15-70 years
- Systematically healthy individuals
- Patients with Signs and symptoms of Rheumatoid arthritis (pain, swelling, tenderness, morning stiffness, restricted or loss of function).
- Patients fulfilling the ACR-EULAR criteria.

Exclusion criteria

- Patients below 15 and above 70 years
- Persons having gout/Osteo-arthritis
- Persons having Rheumatoid nodules or deformity
- Obese persons
- Pregnant/lactating women
- Hypertension and other cardiovascular diseases
- Diabetes and other metabolic disorders

- Tuberculosis and other respiratory diseases
- Gastrointestinal disorders
- Renal/hepatic impairment
- Presence of malignancy
- History of alcohol and drug abuse
- Epilepsy and other neurological disorders

Subject selection

The patients of Waja-ul-mafasil attending out door patients department of CRIUM, Lucknow were selected for the study. A detailed clinical history was taken and complete physical examination was carried out to make the clinical diagnosis of Waja-ul-mafasil.

Investigation: X-Ray of affected joints was conducted and blood samples were collected for the evaluation of laboratory parameters like Haemogram, C-Reactive proteins and Rheumatoid factor to establish and confirm inclusion criteria and other laboratory test like complete blood picture, kidney function test, liver function test and routine and microscopic examination of urine were done. All clinical and laboratory follow-up were done at every 4 weeks.

Treatment schedule and drugs

Munzij and Mushil Therapy

UNIM-308, Coctive (Munzij): A decoction of ten single drugs soaked in water all over night and boiled in 200 ml. water in the morning, was given orally on empty stomach up to Nuzj appears in the urine or up to maximum 20 days followed by a Mushil.

UNIM-309, purgative (Mushil): A decoction of fifteen single drugs soaked in water all over night and boiled in 250 ml. Water, was given orally on empty stomach for 03 to 05 days as purgative on alternate days followed by Tabreed.

UNIM-310 (Tabreed): 5 gm UNIM-310 was administered orally for 03 to 05 days with water alternate days with UNIM-309.

UNIM-312: Two tablets (500 mg each) administered orally with lukewarm water twice in a day for 90 days after Munzij-Mushil therapy.

UNIM-304: Oil application on affected joints twice a day for 90 days was done.

Follow up of subject: Patients were followed up at every 15 days to record change in symptoms and signs. Clinical follow up and investigations were performed at the base line,

after Munzij-Mushil therapy and every 30 days gap and at the end of study. Follow up of relieved cases were performed after every three months for one year.

Safety assessment: The safety was assessed by monitoring adverse events reported by the patients or elicited by the investigator on clinical as well as laboratory investigations before and after treatment. The laboratory tests included Haematological tests (Hb, TLC, DLC, ESR), Liver function test (Serum bilirubin, SGOT, SGPT and alkaline phosphatise) and Kidney function tests (Blood urea and serum creatinine).

Statistical data recording: Data recording was done on separate case record form for each subject at base line, after M. M. Therapy and at every 15 days up to three months. Active and passive complaints of patients were recorded in grades starting from "+" to "+++" at the time of Base line and at different follow up. Percentage in grading was calculated and results were assessed in terms of complete remission (more than 70%), partially remission (50% to 70%), Poor remission (less than 50%).

RESULTS AND DISCUSSION

Temperament and response

The data showed that out of 55 cases studied maximum 38 cases had Balghami followed by 08 cases had Saudavi, 07 Safravi and 02 Damvi temperament. As per temperament and response of the formulae concerned, it is found more effective in Balghami temperament as out of 38 cases 17 cases got complete remission, 15 cases got partially remission and 06 got poor response. In Saudavi out of 08 cases, 02 cases got complete remission, 04 cases got partially remission and 02 cases showed poor remission. In Safravi 07 cases, 01 got complete remission, 05 got partially remission and 01got poor remission and Damvi temperament 02 cases 01 got complete remission and 01 got partially remission as presented in table-1

Table 1: Response according to Temperament (Mizaj) of patients.

Mizaj (Temperament)	RESPONSE			TOTAL (%)
	Complete remission	Partially remission	Poor remission	
Balghami	17	15	06	38 (69.10)
Saudani	02	04	02	08 (14.55)
Safrani	01	05	01	07 (12.72)
Damvi	01	01	-	02 (03.63)
TOTAL (%)	21 (38.18)	25 (45.44)	09 (16.38)	55 (100.00)

Chronicity and response

Study data shows that maximum cases were having chronicity up to 02 years, out of 20 cases 07 cases got complete remission, 10 cases got partially remission and 03 cases showed poor remission followed by 10 cases having chronicity 2-4 years, 05 cases got complete remission, 04 got partially remission and 01 showed poor remission, 4-6 years, 09 cases, 6-8 years, 08 cases, 8-10 years 05 cases and above 10 years 03 cases. As chronicity and response of the formulae concerned, it is effective in the cases having chronicity up to 04 years and 03 cases having above 10 years chronicity 01 case got complete remission, 01cases got partially remission and 01 case got poor remission Table-2.

Table-2: Response according to chronicity of the disease.

Chronicity	Response			Total (%)
	Complete Remission	Partially Remission	Poor Remission	
Up to 02 year	07	10	03	20 (46.42)
02-04 year	05	04	01	10 (16.07)
04-06 year	04	03	02	09 (08.93)
06-08 year	02	05	01	08 (12.50)
08-10 year	02	02	01	05 (07.14)
Above 10 year	01	01	01	03 (08.93)
Total (%)	21 (38.18)	25 (45.44)	09 (16.38)	55 (100.00)

Sex and response

In the table-3, the study shows that this disease is three times more common in females than males as out of 55 cases studied 39 were female and only 16 cases were males. As per response concerned, drug is somewhat equally effective in both the sexes, out of 39 females cases 17 cases got complete remission, 18 cases got partially remission and 04 cases got poor remission. While in 16 males cases, 04 cases got complete remission, 07 cases got partial remission and 05 showed poor remission.

Table 3: Response according to sex of patients.

Sex	Complete Remission	Partially Remission	Poor Remission	Total (%)
Male	04	07	05	16 (29.05)
Female	17	18	04	39 (70.95)
TOTAL (%)	21 (38.18)	25 (45.44)	09 (16.38)	55 (100.00)

Dietary habits and response

Data projected from study also shows that it is common in non-vegetarian and vegetarian approximately; out of 55 cases studied 23 cases were vegetarian and 32 non-vegetarian. As

per response concerned, good response recorded in both the types of habits, out of 23 vegetarian cases 08 got complete remission, 11 cases got partial remission and 04 cases got poor remission. Likewise 32 non-vegetarian cases, 13 cases got complete remission, 14 cases got partial remission and 05 cases got poor remission as presented in table-4

Table 4: Response according to dietary habits.

	Response			
Dietary Habits	**Complete Remission**	**Partially Remission**	**Poor Remission**	**Total (%)**
Vegetarian	O8	11	04	23 (41.81)
Non-vegetarian	13	14	05	32 (58.19)
Total (%)	21 (38.18)	25 (45.46)	09 (16.36)	55 (100.00)

Social status and response

Study also shows that out of 55 cases, 31 cases from lower income group, followed by 18 cases from middle income group and only 06 cases from high income group. As per income group and response of the drug concerned, good response recorded in HIG as out of 06 cases, 03 cases got complete remission, 02 cases got partial remission and 01 case got poor remission. In MIG out 18 cases studied 07 cases got complete remission, 09 cases got partial remission and 02 cases got poor remission. In LIG group, out of 31 cases studied, 11 cases got complete remission, 14 cases got partial remission and 06 cases got poor remission Table-5.

Table 5: Response according to social status of patients.

Social Status	**Response**			**Total (%)**
	Complete Remission	**Partially Remission**	**Poor Remission**	
LIG Group	11	14	06	31 (56.36)
MIG Group	07	09	02	18 (32.73)
HIG Group	03	02	01	06 (10.91)
Total (%)	21 (38.18)	25 (45.46)	09 (16.36)	55 (100.00)

Age and Response

In the table-6, the study shows that this is very common in the age group of 21 to 40 years as out of 55 cases studied maximum 12 cases were belonging to 31-40 age, followed by 13 cases in the age group of 21-30 years. 07 cases were 51-60 years age group and 03 cases were above 60 years age. As per response is concerned, good response observed in the age group of 31-40 years as out of 12 cases belonging to this group 05 cases got complete remission, 05

cases got partial remission and 02 case got poor remission. In the age group of 21-30 years 08 cases got relived 04 cases were partial relived and 01cases showed poor response.

Table 6: Response according to age group of patients.

Age Group (In years)	Response			Total (%)
	Complete Remission	Partially Remission	Poor Remission	
Up to 20	04	05	03	12 (21.80)
21-30	08	04	01	13 (23.66)
31-40	05	05	02	12 (21.80)
41-50	01	06	01	08 (14.55)
51-60	02	04	01	07 (12.72)
Above 60	01	01	01	03 (05.47)
Total (%)	21 (38.18)	25 (45.44)	09 (16.38)	55 (100.00)

Clinical signs and symptoms

Clinical signs and symptoms treated with these formulae response in the swelling change in large amount. Tenderness showed before treatment in 54 cases and 01 case had no tenderness and after treatment 07 cases got relieved from tenderness, 48 cases had tenderness and 01 case had no tenderness at before treatment. Pain showed in 55 cases before treatment, after treatment 36 cases got relieved in pain and 19 cases were not relieved pain. Early morning stiffness reduced after treatment, walking time also showed good response (Table 7).

Table 7: Clinical signs and symptoms.

Signs and Symptoms	Unit of Measure	Statistics	Day of Examination	
			Before Treatment	After Treatment
Swelling	Inches	Mean ± SD n=55	92.75 ± 16.97	92.41 ± 16.88
Tenderness	Positive	n=55	54	48
	Negative		01	07
Pain	Present	n=55	55	19
	Absent		00	36
Early morning stiffness	Minutes	Mean ± SD n=55	70.36 ± 23.25	34.90 ± 25.00
Walking time	Seconds	Mean ± SD n=55	30.36 ± 15.08	25.09 ± 15.41

Laboratory investigations

On admission 39 patients were R.A. Factor positive and 16 cases sero-negative, in 41 cases C.R.P. was positive and 14 cases having C.R.P. negative, with raised/ normal ESR, normal renal and liver function test were registered. After treatment level of ESR showed downwards

trend and no change in R.A. Factor, slight change observed in C.R.P. positive cases, 02 cases become negative (Table 8).

Table 8: Laboratory investigations before and after treatments.

Parameters	Measurement Unit	Statistics	Before Treatment	After Treatment
Hemoglobin	gm%	Mean ± SD n=55	10.26 ± 1.35	10.43 ± 1.26
E.S.R.	mm/1st hour	Mean ± SD n=55	75.31 ± 30.48	64.57 ± 27.11
T.L.C.	/Cu mm	Mean ± SD n=55	9157.41 ± 1355.72	9248.15± 1053.78
Serum Uric Acid	mg/dl	Mean ± SD n=55	4.84 ± 1.12	5.17 ± 1.32
R.A. Factor	Positive	n=55	39	39
	Negative		16	16
C.R.P. Test	Positive		41	39
	Negative	n=55	14	16

Overall response

Overall response of patients, 55 subjects completed the study, out of 55 cases, 21 cases got complete remission, 25 cases got partially remission and 09 cases got poor remission.(Table 9).

Table 9: Showing response of the drugs.

		Response		
	Complete Remission	Partially Remission	Poor Remission	
Total (%)	21 (38.18)	25 (45.44)	09 (16.38)	55 (100%)

CONCLUSION

The study reveals that result of the Unani coded formulae effective, as out of 55 cases studied 21 cases got complete remission, 25 cases got partial remission and 09 cases got poor remission. The formulae reduced signs and symptoms like pain, tenderness, swelling, loss of functions and morning stiffness in uniform way. During the study blood investigations of each patient for haemogram, liver function test, kidney function test, Rheumatoid factor, C-reactive protein were done at base line, after Munzij- Mushil therapy, every follow up and after completion of study. We found that there was no significant effect of formulae on RA factor after completion of study, however there was slight increased in Hb% and marked decline ESR in well responded cases. No Toxicity and adverse effect of the drugs reported during the study. Blood investigations done to observe any hepatic or renal toxicity at

baseline, during follow up and after completion of study. It is observed that drug is safe and has no toxic effect on liver and kidney.

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