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CLINICAL EFFICACY OF COMPOUND UNANI FORMULATION IN *NIQRIS* (GOUT)

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ABSTRACT

Historical background: According to *Ibn-e-Habal*, *Niqris* originated from the word '*Anquroon'* which means big toe of foot, because this disease usually starts with the involvement of this particular joint and hence the disease has been named after this joint.[1,2,3] Gout comes from the Latin 'Gutta'-which means 'Drop' (Noxa) - with reference to the mediaeval "flowing down of humour". Which justify the ancient belief about disease matter i.e. humours falling down drop by drop into the joint.[4,5,6] Incidence of gout is on rise with time and the prevailed mainstream treatment is not effective that mush as required. So, this unani formulation has been decided to testify scientifically and to prove its efficacy on patients of gout; which has been claimed in classical Unani text. **Study Design**: Present study has been designed to study the efficacy of a compound Unani formulation drug in the management of *Niqris* (Gout). It is an open clinical trial. The efficacy of this drug has been evaluated on the basis of standard parameters, subjective and objective both. The study was conducted on 60 patients for duration of 60 days. **Result:** After Intervention, most of the subjective parameters improved significantly, on objective parameters, improvement is very significant. All the biochemical parameters P=0.001. This result suggesting the effect of test drug is very effective in lowering the serum uric acid. Findings of trial were recorded on a specially designed chart and inference was made by appropriate statistical analysis.

KEYWORDS: *Niqris; Gout; Hyperuremia; Temperament; Mizaj.; Joints pain; Arthritis*.

INTRODUCTION

"Gout" was coined by a monk named Randolphus of Bucking in the 13th century from the Latin word "Guuta" (which translates into "Drop").[7] Randolphus thought that gout resulted from the excess of one of the four humours that maintained health. This drop was thought to flow into the joint, causing pain. Harrison's wrote that gout is a metabolic disease most often affecting middle-aged to elderly men and postmenopausal women. It is the result of an increased by body pool of urate with hyperuricemia. It is typically characterized by episodic acute and chronic arthritis, due to deposition of monosodium urate (MSU crystals in joints and connective tissue to make tophi, and the risk for deposition of uric acid in kidney interstitium known as uric acid nephrolithiasis.[6,8]

Ali-Ibn-Abbas Majoosi have written that the pain which occurs in the joins of both legs or single leg and sometimes in wrist joint or elbow joint and mainly in the joints of great toes to be known as Niqris.[7] *Ismail Jarjani* have described that as *Mavad-e-fazooni* (morbid humours) which gets accumulate in the small joints and tendon, if it causes pain and inflammation in small joints called as *Niqris*. It occurs mainly in greater toe. Ankle joint and the joint of toes may also be involved.[9]

Pathophysiological factor of Gout is *Akhlate-e-Fuzlia* According to Ibn Sina the *Madda* of *Niqris* can be pure Dam or can be combination of *Damvi-Balghami* or *Damvi Safiravi* or *Damvi-Saudavi* or pure *Balghami* or it can be *Balgham-e-Murra*. But majority of ancient physician accepted that *Balghami-Murra* is the main cause of *Madda-e-Niqris*, and then is can be pure *Balghami*, *Dam*, *Safra* respectively. Rarely the cause of *Madda-e-Niqris* can be Sauda.[10] Prevalence of hyperuricemia varies according to the age, sex, race geographical conditions and association with other diseases.[11] Gout becomes commoner with increasing age. In men the reported prevalence ranges from <0.5% in those aged under35 to >7% in those aged over 75. It is

rare in premenopausal women but increases to 2.5 – 3.0% in those aged over 75.[12]

The Unani medicines have proven its own importance regarding its affectivity, cost and minimal side effects, the general treatment of *Niqris* in system of medicine consists of moderating the alter humours, excretion of excessive and altered *khilt*, correction of digestion and regulation of metabolism and subside the local inflammation. For this purpose, the medicines having properties like, *Mulattif, Munzij, Mudirrr-e-boul, Muqawwi-e-meda* and *Muhallil-e-auram* are used.

There is some allopathic medicine like, NSAID, allopurinol, probenecid etc. Being used as drug of choice for gout, but these drugs are failed to treat gout permanently also have many side effects. In Unani System of medicine also described many single and compound drugs are also described like, *Zanjabil, Muqil, Darchini, Badyaan, Majoon Suranjan, Habb-e-Asgandh, Majoon Chobchini, Safoof-e-Auja* etc. to treat Gout without causing any side effect but most of these drugs have not been studied on scientific parameters, so keeping the fact in mind a step will be taken evaluate efficacy and safety of compound Unani formulation prepared by *Chobchini* (*Smilax china*), *Suranjan Shirin* (*Colchicum latium*), *Sibr* (*Aloe barbadenesis*) in the management of gout.

MATERIAL AND METHODS

The present clinical study entitled as "Clinical efficacy of compound Unani formulation of *Suranjan shrin, sibr, chobchini* in cash of *Niqris*", was conducted at hospital under department of *Moalajat*. Before starting the clinical trial, the proposal was kept before ethical committee of medical college. Once the ethical clearance was sought, clinical study was started by enrolling eligible patients for open clinical trial.

In present study all 60 patients of *Niqris* were screened and selected for clinical trial and studied to asses clinical efficacy of Unani formulation comprises of *suranjan shirin, sibr* and *chobchini* in case of *Niqris.* All 60 patients of *Niqris* were selected on the basis of complete physical examinations family history, clinical symptoms and laboratory investigation, their social and dietary habits were also inquired and included in the clinical study. Details about the disease and treatment were recorder in case report form. Patients were treated with the Unani compound drug (*suranjan shirin, sibr, chobchini*).

Criteria for the selection of cases

Inclusion criteria

- Patients come to college's hospital OPD were selected.
- Both sexes of patient between age group of 20 to 60 years have been selected.
- Acute Gout
- Inter critical gout
- Clinically stable Patient

Exclusion criteria

- Gout with Diabetic Mellitus.
- Chronic tophaceous gout
- Urolithiasis
- Patient below 20 and above 60 years.
- Patient with organ failure.
- Pregnant women and lactating mother
- Patient with active cardiac diseases and major diseases of heart.
- Patient with severs neurological disorders.

Sample Size: The sample size was 60.
Study design: This is an open level phase II clinical trial
Duration of Study: The treatment period was 60days

Investigations: Following investigations where done in each and every case, before and after study; Hb%, TLC, DLC (specially Neutrophils, Lymphocytes, Eosinophils and Monocytes) and ESR. Serum uric acid, urine routine and microscopic- specially urine uric acid crystals are examined at every visit. RBS (Random Blood Sugar) was investigated before study only.

Efficacy assessment: The assessment of efficacy in the patients was based on the following two types of parameters.

1. Subjective parameters.
2. Objective parameters.

The subjective parameters include symptoms like pain, swelling etc. while objective parameters include laboratory investigations of patient suffering from *Niqris*. An arbitrary grading of subjective and objective parameters was design for appropriate assessment and statistically evaluation of various symptoms to evaluate the efficacy of test drug. Basal symptoms were recorder in case report form according to their grades. After 60 days of the treatment, the pre and post values of different parameters were analyzed grade wise and subjected to comparison and analysis statistically to evaluate the efficacy of treatment.

Subjective Parameters

1. Pain
2. Tenderness
3. Swelling
4. Redness
5. Temperature of affected joints.
6. Movement of affected joints
7. Deformity of joints.

These seven different symptoms were rated with a different grading scale in which the patient can rate some of their symptoms themselves. And the same way the clinician also rated some symptoms according to the patient's presentation. These ratings were done before

treatment (zero day); rating was also taken during the treatment on 30th day and after treatment (60 days).

Subjective parameters

1. Pain: scored by Visual Analogue scale (VAS).[13,14,15] Patient is asked to put a mark on the scale at every visit from 0-10, indicating their pain intensity. The distance between that mark and the origin is measured to obtain the patient's pain score.
2. Tenderness:
   - 0 = No tenderness
   - 1 = mild: Patient allows pressure without any resistance.
   - 2 = moderate: Patient allows pressure with little resistance
   - 3 = Severe: Patient holds hand and does not allow further pressure
3. Swelling:
   - 0 = None
   - 1 = mild-swelling
   - 2 = moderate – swelling +redness
   - 3 = severe- swelling + redness + pain
4. Redness
   - 0 = Mild
   - 1 = Moderate
   - 2 = Severe
5. Temperature of effected joint:
   - 0 = Absent
   - 1 = Present
6. Movement of effected joint:
   - 0 = Normal
   - 1 = Partial restricted
   - 2 = fully restricted
7. Deformity:
   - 0 = None
   - 1 = slightly narrowing of joint space
   - 2 = Moderate loss of sphericity of joint space
   - 3 = Severe narrowing or obliteration of the joints.

Objective Parameters: The grading was done on the basis of reports of the lab investigations of the patients before and after the treatment.

1. Hemoglobin
2. TLC
3. Neutrophils
4. Lymphocytes
5. Eosinophil
6. ESR
7. Serum uric acid
8. Urine: Routine and microscopic especially for uric acid crystals.

Criteria for the selection of drugs: For the rational and effective treatment of *Niqris* the Unani drug was required all those properties which could revert this pathologic condition towards normal to restore physiologic functions. So, by careful literature review of Unani classics the descent Unani single drugs were found out, and a compound formulation was prepared containing following *mufarrad advia*; *chobchini*, *suranjan shirin*, *sibr*.

Methods of preparing Dosage and method of administration of test drug: The compound Unani formulation authenticated, standardized and prepared by GMP certified manufacturing unit. The drug will be kept away from direct heat, sunlight in airtight jar, in the dark, dry and cool place. All the three single drugs were pounded to make fine powder. Mixture of all three powers were made in the proportion of 2:2:1 (*chobchini*, *sibr, suranjan shirin*). This mixture of powder was filled in capsule in the quantity of 500mg/capsule. A dose of two capsule in thrice a day after meal for a period of 60 days were given to all patient gout.

Ingredients
Each 100gm contains

Unani Names	Botanical names	gm.
Chobchini	*Smilex china* Linn	40
Surannashirirn	*Cholchicum luteum* Baker	40
Sibr	*Aloe Barbadenesis* Mill	20

Follow up during treatment: 60 days study was divided in to two follow ups which were made at the interval of 30 days. At every visit the patient were asked about the progression and regression of their subjective symptoms. All objective parameters(investigations) were done before and after the study.

Withdrawal criteria
Failure to follow the protocol.
Any adverse reaction or advice event.
Any Idiosyncratic reaction.
Any life-threatening systemic disorder or pregnancy is revealed during study.

Methods: GCP (Good Clinical Practice) was strictly followed throughout complete duration of study.
Statistics: Paired 't' test was applied to evaluate the efficacy of the drug.

RESULTS

Table 1: Effect on pain.

	Before Study	After Study
Mean	4.75	2.91
Std. Deviation	1.283	1.197
Std. Error	0.128	
't' Value	14.2	
'p' Value	0.001	

Table 2: Effect on Tenderness.

	Before Study	After Study
Mean	1.75	0.75
Std. Deviation	0.704	0.679
Std. Error	0.078	
"t" value	12.68	
"p" value	0.001	

Table 3: Effect on Swelling.

	Before Study	After Study
Mean	1.73	1.03
Std. Deviation	0.548	0.662
Std. Error	0.083	
"t" Value	8.397	
"p" Value	0.001	

Table 4: Effect on Redness.

	Before study	After study
Means	1.61	0.68
Std. Deviation	0.64	0.56
Std. Error	0.07	
"t" Value	13.139	
"p" Value	0.001	

Table 5: Effect on Temperature of joint affected.

	Before Study	After Study
Mean	0.86	0.3
Std. Deviation	0.342	0.462
Std. Error	0.068	
't' Value	8.14	
'p' value	0.001	

Table 6: Effect on Movement of affected joint.

	Before Study	After Study
Mean	1.25	0.65
Std. Deviation	0.654	0.577
Std. Error	0.079	
't' value	7.542	
'p' value	0.001	

Table 7: Effect on joint deformity.

	Before Study	After Study
Mean	1.61	0.41
Std. Deviation	0.696	0.555
Std. Error	0.064	
't' Value	8.16	
'p' Value	0.001	

DISCUSSION

The present study was designed to evaluate clinical efficacy of a compound Unani formulation drug in the management of *Niqris*. It is an open clinical study. The efficacy of this drug was evaluated on the basis of standard parameters which are based on subjective and objective parameters. The study was conducted on 60 patients study duration was 60 days with three visits on zero 30^{th} and 60^{th} day. The observation regarding demography and subjective and objective parameters of test were recorded on specially designed case Report form (CRF), chart and inference was made by appropriate statically analysis. They are discussed in the following details.

Discussion on Subjective Parameters

The main aim of the present study was understanding the clinical efficacy of compound Unani formulation among the patients of gout. Seven different symptoms were observed in the patients. They are Tenderness, Swelling, Redness, Deformity, increase temperature of affected joints, Painful movement of affected joint. These seven different symptoms were rated with a different grading scale in which the patients can rate some of their symptoms themselves and others symptoms can be rate by physician according to the patient's presentation. These ratings were done before treatment then on subsequent follow up visit during the treatment days i.e. on 30^{th} day and 60^{th} day (after treatment). A statistical analysis was done to understand the efficacy of the medicine by comparing the mean of pre and post symptoms rating with the help of paired sample t test method. Also, a comparison was done between the mean of three visits with the help of linear diagram. A detailed discussion of each table and graph is given below.

Effect on pain: Pain was scored by visual Analogue Scale (VAS). Patient is asked to put a mark on the scale 0-10 at every visit, indicating their pain intensity. The distance between that mark and the origin in measured to obtain the patient's pain score. Table 8 shows the sample size 60, standard deviation of pre and post test score is 1.283 and 1.197 respectively. Their t value is 14.2 and p value is 0.001 given. From the analysis, it is inferred that there is a significant difference between the pre and post test score is 1.283 and 1.197 respectively. Their t value is 14.2 and p value is 0.001 given. From the analysis, it is inferred that is a significant difference between the pre and post test score of pain rating. Table 1, shows the mean score of pain rating for three visits. The mean score of 0^{th} day, 30^{th} day and 60^{th} day is 4.75, 3.86 and 2.91 respectively. Graph 10 it is inferred that there is a remarkable reduction in the rating of pain of three visits. This indicated that the treatment with the *Safoof* was highly effective to reduce the pain among the *Niqris* patients with treatment duration of 0 days. It may be due to ingredients used in the formulation of *Safoof* as the entire ingredients possess *Muskkin* (analgesic) property. Due to this property, the pain in joint was controlled.

Effect on Tenderness: Tenderness was assessed and graded as absent, mild, moderate, severe and was coded as 0,1,2,3 respectively. Table 2 shows the standard deviation of pre and post test score is 0.704 and 0.679 respectively, their t value is 13.126 and p value is 0.001. From the analysis it is inferred that there is a significant difference between the pre and post test scores of tenderness rating. The bar diagram indicates remarkable reduction in the tenderness after treatment. From table 2, shows the mean score of tenderness rating for the three visits. The mean score of 0^{th} day, 30^{th} day and 60^{th} day is 1.75, 1.08 and 0.75 respectively. This indicates that the treatment with *Safoof* was highly effective to reduce the tenderness among the patients of *Niqris*. It may be due to the ingredients used in the formulation of *Safoof* which possess *Muhallil* (Anti-inflammatory) and *Musakkin* properties.

Effect on Swelling: Table No. 3 shows the standard deviation of pre and post test score is 0.548 and 0.662 respectively, rating swelling with their t value is 8.397 and p value is 0.001. From the analysis it is inferred that there is a significant difference between the pre and post test scores swelling rating. The bar diagram indicates remarkable reduction in the swelling after treatment. Table 3 shows mean score of swelling rating for the three visits. The mean score of 0^{th} day, 30^{th} day and 60^{th} day is 1.73,1.43, 1.03 respectively. This indicates that the treatment with the *Safoof* was highly effective to reduce the Swelling among the *Niqris* patients. It may be due to the ingredients used in the formulation of *Safoof* possess *Muhallil* and *Mudir-e-boul* and *mushil* properties as according to Unani concept the causative *khilt* got accumulated into joint will be excreted out through will be excreted out through urine and stool.

Effect on Redness: Redness was assessed and graded as absent and present and was coded as 0, 1 respectively. Table 4 shows the standard deviation of pre and post test score is 0.64 and 0.567 respectively, rating redness with their t value is 13.139 and p value is 0.001. From the analysis it is inferred that there is a significant difference

in between the pre and post test score of redness rating. Graph 6 shows the graphical representation of mean rating of redness before and after treatment. The bar diagram indicates remarkable reduction in the redness after treatment. Table 4 shows the mean score of redness rating for the three visits. The mean score of 0^{th} day, 30^{th} day and 60 day is 1.61, 1.16, 0.68 respectively. This indicates that the treatment with the trialed *Safoof* was highly effective to reduce the redness among the *Niqris* patients. It may be due to the ingredients used in the formulation of *Safoof* possess *Muhallil* (anti-inflammatory) and *Mudir-e-Boul* (Diuretics) properties because anti-inflammatory drugs ultimately reduce the redness also.

Effect on Temperature of joint affected: Table 5 shows the standard deviation of pre and post test score in 0.342 and 0.462 respectively rating temperature with their t value is 8.40 and p value is 0.001. from the analysis it is inferred that there is a significant difference between the pre and post test scores of temperature rating. The mean score of 0^{th} day, 30^{th} day and 60^{th} day is 0.86, 0.61, 0.3 respectively. This indicates that the treatment with the test drug was highly effective to reduce the temperature of affected joint among the *Niqris* patients. It may be due to the ingredients used in the formulation of *Safoof* possess *muhallil* property.

Effect on Movement of affected joint: Movement was assessed and graded as normal, partial restricted, fully restricted coded as 0, 1, 2 respectively. Table 6 shows the standard deviation of pre and post test score is 0.654 and 0.577 respectively, rating movement with their t value is 7.542 and p value is 0.001. From the analysis it is inferred that there is a significant difference in between the pre and post test scores of movement rating. The mean score of 0^{th} day, 30^{th} day and 60^{th} day is 1.25, 0.81 and 0.65 respectively. This indicates that the treatment with the *Safoof* was highly effective to reduce the movement restriction among the *Niqris* patients. It may be due to the ingredients used the formulation of *Safoof* possess muhallil and *Musakkin* properties. Due to these properties, the inflammation and pain got controlled in the joint therefore movement restriction reduce ultimately.

Effect on joint deformity: Deformity was assessed and graded as normal, sever narrowing or obliteration of the joint, moderate loss of sphericity of the joint, slightly narrowing of joint space, none and coded as 3, 2, 1, 0 respectively. Table 7 shows the standard deviation of pre and post test score is 0.696 and 0.555 respectively rating deformity of joint with their t value is 8.16 and p value is 0.001. From the analysis it is inferred that there is a significant difference in between the pre and post test scores of deformity rating. The mean score of 0^{th} day, 30^{th} day and 60^{th} day is 1.61, 0.68, 0.41 respectively. This indicates that the treatment with the *Safoof* was highly effective in above mentioned condition of the patients of *Niqris* also. *Safoof* possess variety of properties like *Muhallil*, *musakkin*, *Mulatiff* (demulscent) and *Mudir-e-boul* (diuretics) that is why it prove to be very effective to restore deformities.

CONCLUTION

Niqris is one of the most painful forms of arthritis. This study is focused on to relieve the signs and symptoms along with identification and correction of factors that contribute to the *Niqris*. In the light of the above-mentioned results, it can be concluded that the trial drug is very effective to relive symptoms of *Niqris* for at least 60days after the treatment significantly. The study also concludes that the test drug *safoof* has statistically significant effect for the improvement of movement and reduction in serum uric acid level, WBC, and overall involvement of joints. But this study was carried out for short duration and long-term safety and efficacy of the trial drug can be not highlighted. Hence, the long-term study of the trial drug is further needed to prove its efficacy and safety to *Niqris*.

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