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Original Research Article

Role of Jawarish Amla as an adjunct to anti-tuberculosis drugs in the symptomatic relief of pulmonary tuberculosis

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ABSTRACT

Background: Tuberculosis is a global emergency, with approximately nine million people developing the disease every year. India has the highest TB burden worldwide, accounting for nearly one-fifth of the global burden. DOTS provides an 85% cure rate and symptomatic relief during therapy. However, it has been observed that some troubleshooting symptoms persist during the regimen; therefore, testing and providing a pharmacologically multipotent herbal adjuvant drug can improve compliance with DOTS chemotherapy.
Methods: This study was conducted to explore whether any benefits could be achieved by adding Jawarish Amla to conventional anti-tubercular chemotherapy. Forty patients with pulmonary tuberculosis were enrolled to evaluate the efficacy of Jawarish Amla as adjuvant therapy. Patients were randomly assigned to the control and test groups, with 20 patients in each group. Jawarish Amla was administered to the test group for 60 days along with DOTS and the control group received a placebo with DOTS; for the same duration.
Results: The test drug exhibited statistically significant improvement in almost all parameters, especially appreciated in weight gain ($p<0.046$), hemoptysis ($p<0.0069$), breathlessness ($p<0.0015$), nausea ($p<0.001$) vomiting ($p<0.001$), abdominal pain ($p<0.001$), itching ($p<0.001$), burning sensation in feet ($p<0.001$), jaundice ($p<0.001$), Hb% ($p<0.001$), ESR ($p<0.010$), SGOT ($p<0.034$), SGPT ($p<0.020$), alkaline phosphatase ($p<0.007$) and total bilirubin ($p=0.069+$).
Conclusions: These results indicate that the test drug is safe and effective and especially checks the adverse effects of anti-tubercular drugs used in DOTS therapy. Thus, it can be used as an excellent adjuvant along with DOTS in community management of diqqe revi (pulmonary tuberculosis).

Keywords: Adjuvant, Diqqe revi, DOTS, Jawarish Amla, Pulmonary tuberculosis

INTRODUCTION

In the early 21st century, combating tuberculosis (TB) has remained one of the biggest obstacles facing healthcare systems. Tuberculosis has plagued humanity for centuries. The World Health Organization (WHO) estimates that 1.86 billion people worldwide had tuberculosis in 2001. 8.74 million people have tuberculosis annually, and approximately 2 million people die. This indicates that one person gets tuberculosis (TB) every four seconds, and that person passes away every ten seconds. The current global TB situation is in danger of worsening due to HIV infections, MDR, and XDR TB

(multi-drug resistant and extensively drug-resistant tuberculosis). Twenty-two countries are considered high-burden countries (HBCs), which are thought to be responsible for almost 80% of newly diagnosed TB cases each year. HBCs are most common in Asia and Africa. Globally, India, China, South Africa, Nigeria, and Indonesia have the highest number of new TB cases. With an estimated 1.9 million cases per year, India has the greatest TB burden worldwide, contributing one-fifth of the global TB incidence. The phrase diqqe revi, which means "pulmonary tuberculosis", has been translated by classical Unani physicians in an effort to clarify the disease entity that pertains to the tuberculosis prevalent today. When reviewing the literature, the clinical characteristics listed under diqqe revi (P. Koch's) are not characterized in the same way as those given under sil and diq by Jalinoos,[1] Abdul Hasan Ahmad bin Muhamad Tabri, and Ibn Sina a popular Unani single drug, amla has many uses in classical Unani literature.[2-6] It is an excellent blood purifier, hepatoprotective, and appetizer that fortifies the stomach and essential organs and is an antitussive, anti-haemorrhagic, nervine tonic, anti-inflammatory, and anti-pyretic that improves vision and prevents the synthesis of morbid balgham and sauda. Amla is the best natural source of vitamin C. The DOTS strategy has been included in India's Revised National Tuberculosis Control Programme and has surfaced as a potential response to the growing number of TB cases worldwide. Chemotherapy, or directly observed therapy short-course (DOTS), is the international standard for managing the illness. To eradicate tuberculosis and prevent the emergence of drug-resistant strains of the disease, prescribed prescription orders are followed. The patient was monitored while taking their prescription under DOTS. This observation helps to ensure that the medication is taken at the appropriate time and dosage. Additionally, it guarantees that the patient does not discontinue treatment. More than 80% of patients respond well to a course of DOTS when administered appropriately, dealing with a serious blow to tuberculosis (TB) worldwide. The need for supplementary therapy is urgent because of the increasing number of dropouts and MDR and XDR cases. Such therapy should be safe, affordable, comprehensive, and helpful in expediting DOTS therapy. It increases immunity and acts as a potent antioxidant. All essential organs are revitalized and given a new life.

The present study was conducted to evaluate the effect of Jawarish Amla administered concomitantly with anti-tuberculosis chemotherapy.

METHODS

This study was approved by the Internal Ethics Committee of the National Institute of Unani Medicine, Bangalore. This single-blinded, randomized controlled, concurrent parallel, comparative study designed, adjunctive trial of jawarish amla with conventional DOTS regimen was carried out at the National Institute of Unani Medicine Hospital by enrolling eligible pulmonary tuberculosis patients in the study and were further randomized into the test group (group B) and control group (group A) using a table of random numbers. The study was conducted between March 2010 and March 2011. Informed consent was obtained from all patients participating in the study. Upon enrollment of the patients into the study, complete history, including general physical and systemic examination, was recorded on a specifically designed Proforma. Patients were assessed at zero days (before starting) and on 60th day (after completion) of treatment. The sputum for AFB and chest X-ray were examined for diagnosis in their respective health centers where they were receiving DOTS therapy as well as in NIUM at regular standard intervals. Pulmonary tuberculosis patients of either sex who were on DOTS between the age group of 15-60 years were included in the study and patients below 15 years of age, known diabetic, HIV/AIDS patients, patients on corticosteroid therapy, extra pulmonary tuberculosis patients, patients with hormonal disorders, patients with severe disability and patients who were not willing to give consent were excluded from the study. Mizaj (temperament) was determined based on the assessment of ajnase ashra (10 parameters) mentioned in classical Unani literature viz. complexion, built, touch, hair, movement, diet, weather, sleep, pulse, and emotions.[7,8] The treatment period in both the control and test groups was 60 days with a fortnight follow up Jawarish Amla 6 gm BD, was administered to all the patients in the test group orally along with DOTS, and all patients in the control group were administered a placebo, made up of starch, edible color, and sugar 6 gm BD along with DOTS. The placebo was physically and dosage-wise, similar to the test drug, but pharmacologically inactive. Efficacy in the test and control groups was assessed using two parameters: subjective and objective. Subjective parameters included cough, expectoration, hemoptysis, chest pain, breathlessness, weight, and appetite, and objective parameters included Hb%, TLC, DLC (polymorphs, lymphocytes, eosinophils, and monocytes), and ESR. Because these parameters differ in severity from patient to patient, an arbitrary grading of subjective parameters was improvised for the appropriate assessment and statistical evaluation of various signs and symptoms to evaluate the efficacy of the test groups. Before starting treatment, signs and symptoms were recorded in the case report form for their grades at the main visit, and any worsening or improvement in parameters was noted at every follow-up visit until the end of treatment. After 60 days of treatment, the pre- and post-treatment values of different parameters (subjective and objective) were analyzed grade-wise and subjected to comparisons and statistical analysis to evaluate the efficacy of the treatment. Patient compliance with treatment and clinical improvement were closely monitored throughout the study. Fisher's exact test was used to analyze the intergroup comparison of post-treatment values, and the paired t-test was used for

intragroup efficacy evaluation between before and after treatment variables.

RESULTS

The total sample size was set to 40. Table 1 presents the details of the different types of variables used in this study.

Table 1: Socio demographic variables.

Variables	Number of patients (n=40)	%
Gender		
Male	27	67.5
Female	13	32.5
Age group (years)		
18-20	5	12.5
21-30	11	27.5
31-50	14	35
51-60	10	25
Marital status		
Married	33	82.5
Unmarried	7	17.5
Religion		
Muslims	29	72.5
Hindus	11	27.5
Socio-economic-status		
Upper lower class	5	12.5
Lower middle class	23	57.5
Upper lower class	12	30
Diet		
Vegetarians	4	10
Mixed	36	90
Treatment of DOTS		
Cat I	34	85
Cat II	4	10
Cat III	2	5
Mizaj (temperament)		
Safravi (biliaric)	17	42.5
Damvi (sanguine)	10	25
Balghami (phlegmatic)	7	17.5
Saudavi (melancholic)	6	15

DISCUSSION

The test drug exhibited statistically significant improvement in almost all parameters, especially appreciated in weight gain ($p<0.046$), hemoptysis ($p<0.0069$), breathlessness ($p<0.0015$), nausea ($p<0.001$) vomiting ($p<0.001$), abdominal pain ($p<0.001$), itching ($p<0.001$), burning sensation in feet ($p<0.001$), jaundice ($p<0.001$), Hb% ($p<0.001$), ESR ($p<0.010$), SGOT ($p<0.034$), SGPT ($p<0.020$), alkaline phosphatase ($p<0.007$) and total bilirubin ($p=0.069+$).

The outcome inferences of clinical features

Weight

The percentage of change in weight gain before treatment (BT) and after treatment (AT) was 2.44% in the control group and 3.86% in the test group taking mean and standard deviation into account, and the inter group difference was 0.046%, showing a significant weight gain in the test group (group B) with $p=0.046$.

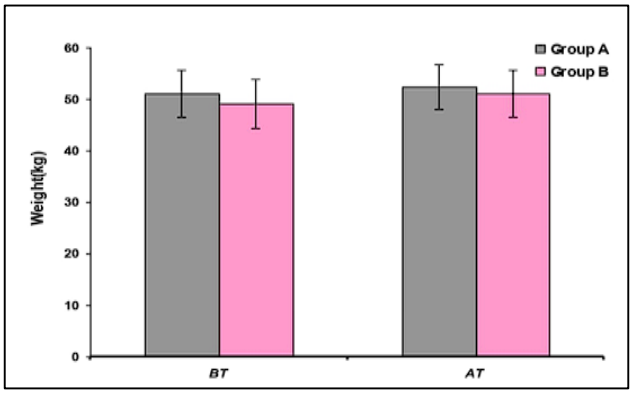

Figure 1: Efficacy evaluation of Jawarish Amla on weight gain (n=40).

Cough

Positive outcome on grade 0 was noticed in test group (group B) with 85% compared to 55% in control group (group A), suggestively significant in group B, with $p=0.0845+$.

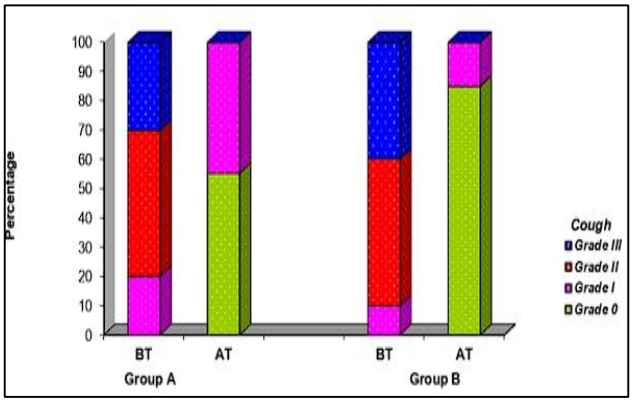

Figure 2: Efficacy evaluation of Jawarish Amla on cough (n=40).

Quantity of sputum

Positive outcome on grade 0 was noticed, statistically similar in group B with 75% compared to 75% in group A with $p=1.000$ but on grade I, there was 25% improvement in group B when compared to -10% in group A with $p=0.029*$.

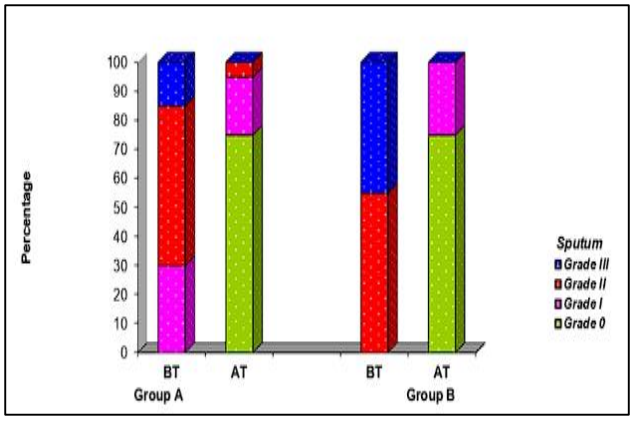

Figure 3: Efficacy evaluation of Jawarish Amla on quantity of sputum (N=40).

Hemoptysis

Positive outcome on grade 0 was noticed, strongly significant in group B with 55.0% compared to 10.0% in group A with p=0.0069**.

Breathlessness

Positive outcome on grade 0 was noticed, strongly significant in group B with 75.0% compared to 20.0% in group A with p=0.0015**.

Chest pain

Positive outcome on grade 0 was noticed statistically comparable in group B with 35.0% compared to 15.0% in group A with p=0.278.

Appetite

Positive outcome on grade 0 was noticed, moderately significant in group B with 80.0% compared to 40.0% in group A with p=0.024*.

The outcome inferences of hematological parameters (complete blood count)

Hemoglobin

The intra-group mean and SD of Hb% observed within the test group (B) at 60th day (AT) was 13.45±1.70 and 0 day (BT) was 11.84±2.25. The increased difference (+1.61) was strongly significant with p=0.001** and the inter-group difference was also highly significant with p=0.002**. But it is non-significant in control group with p=0.191. It was evident enough that Jawarish Amla is effective in increasing the Hb% in patients of pulmonary Koch's who were on DOTS therapy. This study was contrary to adjunctive trial of gallium arsenide laser irradiation at 890 nm on PTB patients on DOTS conducted by Puri and Arora.[9] They observed a non-significant increase in Hb% (p=0.4858).

TLC

Mean and SD of TLC after treatment showed strongly significant decrease with a difference of -2852.5 (p value 0.004**) in group B, whereas group A showed an increase in difference of +257.50 (p value 0.716). Moreover, intergroup is strongly significant (p value 0.009**). The intra-group mean and SD of TLC found within the test group (B) at 60th day (AT) was 6992.50±1833.84 and 0 day (BT) was 9845±4359.23. This decreased difference in TLC was strongly significant with p=0.004** and the inter-group difference was also highly significant with p=0.009** but this decrease was within normal range (i.e., 4000-11000). It was non-significant in control group with p=0.716. This study was in accordance with Koju et al, where WBC count was normal before and after ATT though there was decrease in WBC count after treatment when compared to pretreatment.[10] However, in a study conducted by Nagayama et al, in Japan where there was significant leukopenia after treatment by ATT.[11]

Polymorphs

The intra-group mean and SD of polymorphs percentage found within the test group (B) at 60th day (AT) was 60.65±9.22 and 0 day (BT) was 65.70±11.43. The polymorphs % difference (-5.05) showed suggestive significant reduction (p=0.092+) but within normal range. The inter-group difference was non- significant with p=0.545. This study was in accordance with Koju et al in Nepal and Umeki et al, in Japan where neutrophils percentage was normal before and after ATT though there was decrease in neutrophils after treatment when compared to pre-treatment.[10,12]

Lymphocytes %

The intra-group mean and SD of lymphocyte % found within the test group (B) at 60th day (AT) was 34.00±8.39 and 0 day (BT) was 28.90±11.15. This increased difference (+5.10) was suggestive significant with p=0.063+ and the inter-group difference was non-significant with p=0.430. Here, lymphocytes were increased in both test and control groups after treatment (AT) compared to before treatment (BT) but the increase was within normal range. This study was in accordance with Koju et al in Nepal.[10]

Eosinophils %

The intra-group mean and SD of eosinophils found within the test group (B) at 60th day (AT) was 3.40±1.14 and 0 day (BT) was (3.65±0.81). This decreased difference (-0.25) was statistically non-significant with p=0.425 and the inter-group difference was also non-significant with p=0.249. Here there is marginal decrease of eosinophils % after treatment (AT) in test group compared to pretreatment (BT) and there is a marginal increase of eosinophil % after treatment (AT) in control group

compared to pretreatment (BT) but statistically non-significant and within normal range. This study was in concordance with Koju et al in Nepal and Umeki et al in Japan where eosinophils were normal before and after ATT though there was increase in eosinophils after treatment when compared to pre-treatment.[10,12]

Monocytes %

The intra-group mean and SD of monocytes % found within the test group (B) at 60th day (AT) was 1.80±1.01 and 0 day (BT) was 1.65±0.75. This increased difference was (+0.15) was non-significant with p=0.447 and the inter group difference in was also non-significant with p=0.405.

Basophils %

The intra-group mean and SD of basophils % found at 60th day (AT) was 0.05±0.22 and 0 day (BT) was 0. This increased difference (+0.05) was non-significant with p=0.330 in test group (B) and the inter-group difference was suggestive significant with p=0.073+ and it was moderately significant in control group with p=0.046.

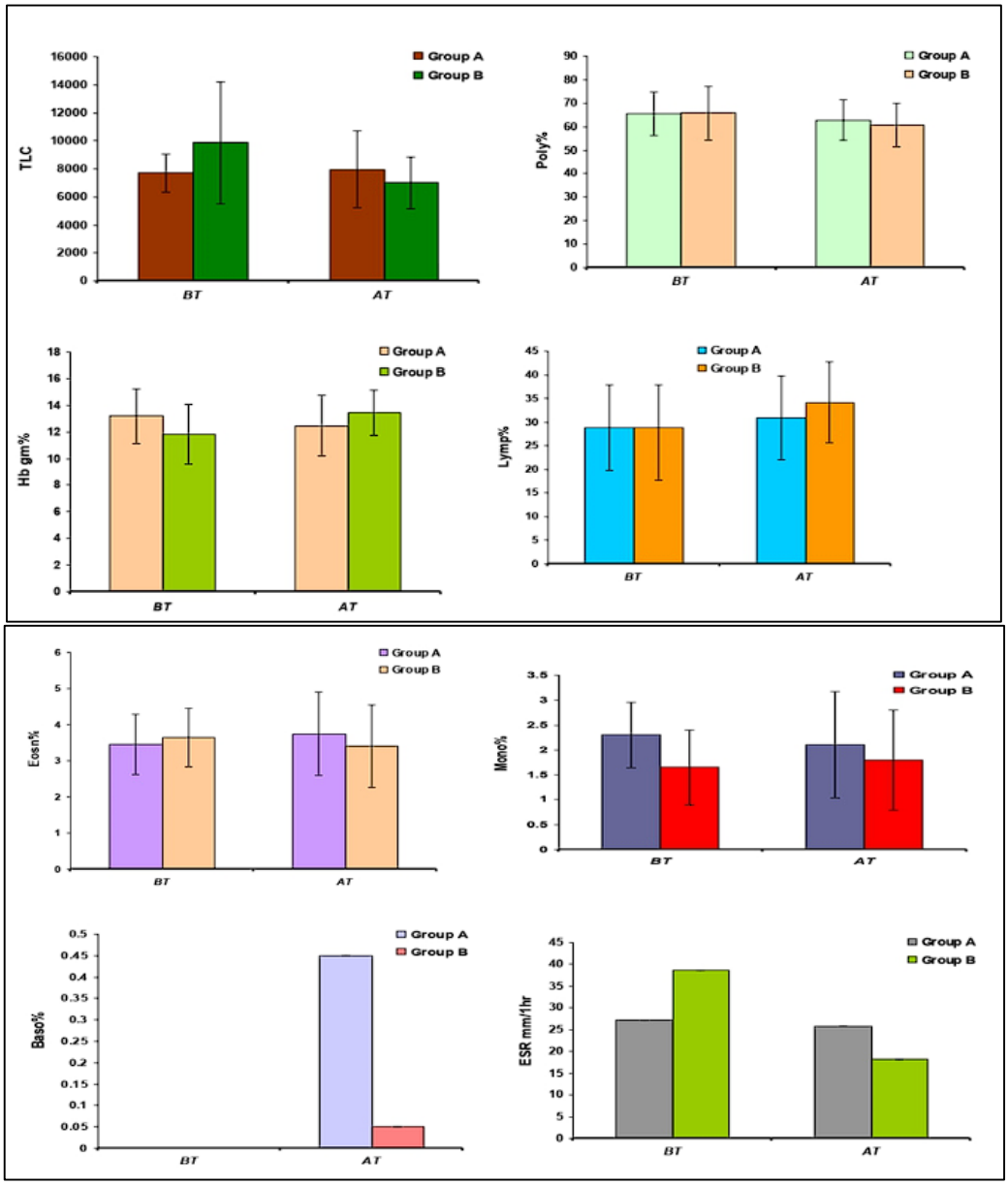

Figure 4: Efficacy evaluation of Jawarish Amla on complete blood count (n=40).

ESR mm/hour

The intra-group mean and SD of ESR found within the test group (B) at 60th day (AT) was 18.30±20.38 and 0 day (BT) was 38.60±27.33. This reduction in difference (-20.30) was strongly significant with p<0.001** and the inter-group difference was moderately significant with p=0.010*. But it was non-significant in control group with p=0.787. Here ESR was decreased in test group (B) at 60th day (AT) compared to 0 day (BT). This is evident

enough that Jawarish Amla enhances the efficacy of DOTS. This study was in concordance with Koju et al in Nepal.[10]

Limitations of the study are: there was no segregation of obese patients, all patient got same dosage of Unani adjunct drugs and all TB patients showed weight gain. There was no dietary restriction for the patients included in the study. All patients were non diabetics because the high content and concentration of sugar in the adjuncts, so the observations and results or effects drug on TB diabetic deadly co-morbidity couldn't be seen. Patients of all categories (I, II, & III) of DOTS were included in the study, so, the observations couldn't be seen according to the severity of disease (pulmonary Koch's). MDR cases and HIV-coinfection were not included in the study, so, the effect of adjunct couldn't be seen in the drug-resistant cases and coinfections, respectively

CONCLUSION

There is no promising treatment for certain diseases in Unani Tib and the remedy for such diseases mainly aims at treating their symptoms and strengthening the "tabiat" or medicatrix naturae or moderating mizaj. Diqqe revi is one such disease, and the curative line of treatment adopted in this disease mainly aims at strengthening the self-resistance power of the body. Once immunity is boosted, it clinches the disease and the patient will be cured of the disease. It is mentioned in the classical Unani literature that in hummae diq, rutubate gharizia of azae aslia dries up, which results in the decline of the assimilative capacity of almost all the organs to extremely low levels, thus hampering the nutritive supply to various organs and the body as a whole, resulting in gradual emaciation, which continues until death. A Unani compound drug called Jawarish Amla was selected, which boosts body immune power, strengthens vital organs, checks and enhances digestive power, and reverts abnormal temperament to normalcy. In addition, there is no doubt that DOTS offers scientifically proven efficacy in treating tubercular patients, and Jawarish Amla, despite having antimicrobial action, has not been tested clinically in tuberculosis ever before. However, their multipotent and digestive properties have been tested for centuries. In the present study, the role of Jawarish Amla as an adjunctive treatment was evaluated in patients with both new and old pulmonary tuberculosis. The overall effect of the test drug was found to be encouraging for diqqe revi. Significant improvements were observed in weight gain, cough, sputum production, hemoptysis, breathlessness, chest pain, appetite, Hb%, TLC, DLC, and ESR. No clinically significant side effects were observed in test group and overall compliance to the treatment was found excellent. These results conclude that the test drug is safe and effective in symptomatic improvement and thus can be an excellent adjuvant along with DOTS in the community management of diqqe revi (pulmonary tuberculosis). This adjuvant therapy may be selected for the pilot study on large sample size for its implementation in RNTCP for checking the adverse reaction of DOTS and efficacy improvement.

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