EFFICACY OF *JOSHANDA ZEEQUNNAFAS* AND *HABBE HINDI ZEEQI* IN *ZEEQUNNAFAS* (BRONCHIAL ASTHMA) - AN OBSERVATIONAL OPEN CLINICAL TRIAL

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ABSTRACT

Background:

Bronchial asthma is a major public health concern, affecting 100-150 million people worldwide and accounts for an estimated 1,80,000 deaths per year. Its incidence is swiftly escalating in India. Unani medicine is augment with many single and compound drugs, which own potential effects to cure the disease, but these formulations are not proof scientifically. **Objective**: To evaluate the efficacy of *Joshanda Zeequnnafas* and *Habbe Hindi Zeeqi* in the treatment of *Zeequnnafas* to provide safe and effective treatment for asthma. **Methods:** The clinical trial to assess the efficacy of *Joshanda Zeequnnafas* and *Habbe Hindi Zeeqi* in the management of asthma. 50 patients were screened and out of them 30 patients were selected for study. *Joshanda Zeequnnafas* and *Habbe Hindi Zeeqi* were administered orally 50 ml (as decoction) twice a day and 125 mg (as tablet form) twice a day for 45 days. Subjective and objective parameters follow up before and after treatment on 0, 15th, 30th, and 45th day of the treatment. In subjective parameter, paroxysmal dyspnoea and wheeze was analysed using paired proportion test. Objective parameter was assessed by the help of Spirometry in terms of ESR, Eosinophilia, FEV_1, FEV_1/FVC% and PEF and student paired t test was applied to get the results. Safety parameters included complete blood count, SGOT, SGPT, Blood urea, S. Creatinine, RBS, and Urine routine and microscopic; and were assessed on student paired t test. **Results:** The overall result was highly significant in terms of subjective and objective parameters specially $FEV_1$and PEF ($P<0.001$) on completion of 45 day treatment course. FEV_1/FVC%, ESR, and Eosinophilia were found to be insignificant as the results were $P>0.178$, 0.785, and 0.220 respectively. **Conclusion:** The study results suggest that the trials formulations are quite effective in the management of *Zeequnnafas*. No adverse effects were noted during the complete course of the study trial. Hence it infers that trial drugs are safe, and effective in the treatment of *Zeequnnafas* (bronchial asthma).

Key Words: Asthma, *Balghami Mizaj, Habbe Hindi Zeeqi, Joshanda Zeequnnafas,* Unani Medicine, *Zeequnnafas,*

INTRODUCTION:

In contemporary perspective *Zeequnnafs* is synonym to Bronchial Asthma **[1]**. In Unani system of medicine, *Zeequnnafs* also known as *Dama*, *Intesabe Tanaffus*, *Zeequnnafas*, *Zeequnnafas Shoabi*, *Rabu*, *Buhar*, etc **[2,3,4,5].** *Zeequnnafs* is a well recognized disease since ancient times **[6]**. The first sighting of *Zeequnnafs* in the nomenclature of western medicine is dated to the corpus hippocraticum initiated by *Buqrat* (**460-375B.C**) **[7]**. *RabbanTabri* **(838-870A.D)** described the *Zeequnnafas Shoabi* in *Firdausul hikmat* later on, *Razi* **(865-932 A.D)** also explained the disease elaborately in 4th volume of *Al-hawi Fit Tib* and in *Kitabul Fakhir* **[8,9].** *Ibn Sina* (**979-1037A.D)** propounded the 'Theories Humorale' he believed that the appearance of Asthma is due to the presence of thick viscid mucus in the chest that filled the bronchioles and impeded respiration causing dyspnea [**10**]. *Ismail Jurjani*, **(980-1037A.D)** described the *Zeequnnafas* in the *Zakhira Khawarizm Shahi*, he wrote, "The incidence of *Zeequnnafas* is more in *Mausam-e-Kharif* (spring season) and *Mausam-e-Sarma* (winter season) and less in *Mausam-e-Garma* (summer)" **[11].**

According to WHO asthma is a chronic disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person **[12].** Bronchial Asthma is an inflammatory airway disease with episodic occurrences of dyspnoea and wheezing. The Global Initiative for Asthma (GINA) has proposed a descriptive definition of Asthma. "Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role.'' Asthma is one of the most common chronic diseases globally **[13, 14].** The prevalence of asthma has progressively increased both developed and developing countries **[15].** Current estimates suggest that it affects approximately 300 million people worldwide **[16]**. An additional 100 million persons will be suffered by 2025. **[15]**. It has increased in affluent countries over the last 30 years but now appears to have stabilized, with approximately 10–12% of adults and 15% of children affected by asthma. [**17**].The line of management for Bronchial Asthma in conventional medicine is mainly with Bronchodilator therapies, Anti cholinergic, Corticosteroids, etc **[18].** Though these drugs give swift relief of symptoms but they have systemic side effects including immunosuppression, obesity, osteoporosis, gastric ulceration, etc **[19]**. Hence to provide an everlasting effects with less or no side effect, Unani formulations may play a vital task in controlling this disease. Unani system of medicine recommended a number of drugs that can be successfully used in the treatment of Bronchial Asthma **[20]**. Unani physicians have been treating this disease for thousands of years and they have mentioned various single as well as compound drugs *viz*; Kakra seenghi (*Pistacia integerrima*) Arusa (*Adhatoda vasica*), Ajmod (*Apium graveolens*), Aslussoos (*Glycyrrhiza glabra*), Bazrul banj (*Hyoscyamus niger*), Biskhapra (*Trianthema portulaca*), Doodhi (*Euphorbia hirta*), Nil(*Indigofera: tinctoria*), Qinnab (*Cannabis sativam*), Sankhahuli (*Evolvulus alsinoides*), Thohar(*Euphorbia tirucalli*), *Kushta Marjan, Kushta Post Bezae Murgh, Kushta Seemab, Kushta Tila, Laooq Khayarshamber, Kushta Abrak Safed*, for its treatment **[21,22]**. However, these drugs have not been scientifically explored so far, for their described effects. So in order to provide safe and more effective drugs for Bronchial Asthma, the present study entitled "Efficacy of *Joshanda Zeequnnafas* and *Habbe Hindi Zeeqi* in *Zeequnnafas* (Bronchial Asthma)" is designed.

METHODOLOGY:

The present study entitled "Efficacy of *Joshanda Zeequnnafas* and *Habbe Hindi Zeeqi* in *Zeequnnafas* (Bronchial Asthma) patients - An Observational Open Clinical Trial " was conducted at National Institute of Unani Medicine hospital under department of Moalajat. Before starting upon the project, a comprehensive protocol was chalked out and submitted for ethical clearance from the institutional ethical committee of National Institute of Unani Medicine, Bangalore. After ethical clearance (**IEC No:NIUM/IEC/2011-12/002/Moal/02**), enrolling patients are. Total 50 patients were screened and out of them 30 patients of asthma were selected for the trial for the duration of 45 days. Informed consent was taken in English and also it was rendered in Kannada, Urdu, and Hindi as per need by the translators before start of the study. The GCP (Good Clinical Practice) guide line followed. This study was conducted between May 2012 to December, 2013 and after complete of clinical trial all documents are submitted to Dept. of Moalajat, NIUM, for documentation.

Criteria for Selection of Cases

Inclusion Criteria:

Stable patients of bronchial asthma; Patients belonging to 15-70 years of age of either sex or patients willing to participate in the study.

Exclusion Criteria

Patients with terminal medical conditions such as cancer; Unstable cardiac diseases; Pulmonary tuberculosis; Renal insufficiency; Pregnant and lactating women; Cognitive impairment; Patients who failed to give written consent and patients below the age of 15 and above 70 years of age.

Procedure for study

After detailed history and examination, those patients fulfilling the inclusion and exclusion criteria were subjected to haematological, radiological investigations, and Spirometry. A written voluntary informed consent was obtained for the clinical trial, and the drug was allotted to the patients. In acute exacerbations of asthma, patients were advised to take inhaler therapy of conventional medicine. In selection of patients, following parameters were taken into consideration.

Subjective Parameters (before and after the treatment**):** Grading for-

- Paroxysmal dyspnoea: (0=absent;1=mild; 2=moderate; and 3=severe).
- Wheeze: (0=absent; 1=mild; 2=moderate and 3=severe).

Objective Parameters (before and after the treatment**):** Grading for-

- Presence of Rhonchi: (0=absent; 1=present).
- Over-inflation (assessed by X-ray): (0=absent; 1=present).
- Pulmonary Function Test: FEV_1, FEV_1/FVC ratio, PEF by Spirometry
- Oesinophilia and ESR

Clinical Evaluation of the Patients

History taking**;** Examination: general physical examination and chest examination**;** Investigations before and after the treatment: **Blood-**(Hb%, TLC, DLC, ESR, SGOT, SGPT, Blood Urea, Serum Creatinine, RBS, AEC);**Urine-(**routine and microscopic) and **Others-**(ECG, and X-ray Chest PA view).

PFT was carried out as a diagnostic criterion before and after the treatment. Spirometry can be helpful in identifying the airflow obstruction, but can't assess the degree of severity. Normal readings of PFT are FEV_1 > 80%, PEF > 80%. Airflow obstruction is established by reduced FEV_1/FVC ratio < 70%. The spirometer that was used in the trial is available with the NIUM hospital. It is a *SpiroWin* (*c*) *GENESIS* brand **[23]**.

Methods of Preparation:

A good quality of drugs was provided by the pharmacy of National Institute of Unani Medicine (NIUM). Before preparing the formula all drugs were properly identified by Chief Pharmacist of NIUM for their originality. *Joshanda Zeequnnafas* is selected for trail is taken from *Qarabadin-e-Azam* **[24].**

The contents of ***Joshanda Zeequnnafas*** comprise of following ingredients.

S.No	Unani names	Botanical name	Wt. of ingredients
1	Badiyaan Neemkofta	*Feoniculum vulgare*	9 gram
2	Pudinaa Khushk	*Mentha viridis*	9 gram
3	Aslussoos Muqashshar Neemkofta	*Glycyrrhiza glabra*	7 gram
4	Taj	*Cinnamomum cassia*	7 gram
5	Sapistan	*Chordia dichotoma*	11 Nos.
6	Neelofar	*Nymphaea nauchali*	12 gram

The above mentioned ingredients were pulverized to make a powder. 50 ml decoction of 10 gm powder of *Joshanda Zeequnnafas* prepared in water was given twice i. e. morning and evening for oral administration before meal.

Habb-e-Hindi Zeeqi is taken as reference from *Qarabadin-e-Azam*, **NFUM Part I**, *Qarabadin Najmul Ghani, and Al-Qarabadin* in the dosage of 125 mg twice daily**[24,25,26,27].**

S.No	Unani Names	Botanical Name	Wt. of ingredients
1	Beesh Mudabbar	*Aconitum chasmanthum*	3 gram
2	Post Beekh-e-Madar	*Calotropis procera*	6 gram
3	Aab-e-Adrak	*Zingiber officinale*	250 ml

Statistical 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. The following assumptions on data is made, **Assumptions: 1.**Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group.

Significant figures

+ Suggestive significance (P value: $0.05<P<0.10$)

* Moderately significant (P value: $0.01<P \leq 0.05$)

** Strongly significant (P value: $P \leq 0.01$)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, Med Calc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Results

The overall result was highly significant in terms of subjective and objective parameters specially $FEV_1$and PEF ($P<0.001$) on completion of 45 day treatment course. FEV_1/FVC%, ESR, and Eosinophilia were found to be insignificant as the results were $P>0.178$, 0.785, and 0.220 respectively. All results are shown in table number **1, 2, 3** and **4**.

Table No.1: An Evaluation of Clinical variables before and after treatment (safety parameters)

	Before treatment	After treatment	difference	t value	P value
Hemoglobin (gm%)	13.94±1.85	13.92±1.99	0.017	0.058	0.954
TLC (cu/mm)	7125.00±1956.10	6996.67±22.09	128.333	0.246	0.807
Neutrophils (%)	60.50±7.51	62.73±8.29	-2.233	-1.135	0.266
Lymphocytes (%)	32.37±6.67	32.03±8.04	0.333	0.178	0.860
Monocytes (%)	1.13±1.07	1.07±1.48	0.067	0.220	0.827
Eosinophils (%)	5.93±5.93	4.13±3.33	1.800	1.655	0.109
Basophils (%)	0.03±0.18	0.00±0.00	0.033	1.000	0.326
ESR (mm/hr)	23.23±17.82	23.87±20.44	-0.633	-0.275	0.785
SGOT (I.U/L)	21.17±6.72	21.00±5.07	0.167	0.162	0.873
SGPT (I.U/L)	20.00±8.64	21.00±5.92	-1.000	-0.791	0.435
Blood Urea (mg/dl)	26.33±5.36	26.60±6.92	-0.267	-0.169	0.867
Serum Creatinine (mg/dl)	0.90±0.13	0.89±0.13	0.003	0.141	0.889
Random blood sugar (mg/dl)	95.80±16.85	102.43±27.77	-6.633	-1.225	0.231

Table No.2: Over inflection

Over inflation	No. of patients (n=30)	%
Before treatment		
• No	27	90.0
• Yes	3	10.0
After treatment		
• No	30	100.0
• Yes	0	0.0

Table No.3: A Comparative evaluation of Subjective parameters before and after treatment

Subjective parameters	Before treatment (n=30)	After treatment (n=30)	% change
Paroxysmal dyspnoea			
• Absent	0	12(40.0%)	+40.0
• Mild	8(26.7%)	16(53.3%)	+26.6
• Moderate	18(60.0%)	2(6.7%)	-53.3
• Severe	4(13.3%)	0	-13.3
Wheeze			
• Absent	0	21(70.0%)	+70.0
• Mild	8(26.7%)	8(26.7%)	0.0
• Moderate	20(66.7%)	1(3.3%)	-63.4
• Severe	2(6.7%)	0	-6.7

P<0.001** paired proportion test

Table No.4: A Comparative evaluation of Objective parameters test before and after treatment

Objective parameters	Before treatment	After treatment	difference	t value	P value
PFT					
FEV1					
• Predicted	2.47±0.58	2.47±0.58	-	-	-
• Actual	1.06±0.49	1.39±0.66	0.320	4.360	<0.001**
• %Predicted	42.46±15.92	54.39±18.73	11.925	4.248	<0.001**
FEV1/FVC %					
• Predicted	81.01±2.97	81.02±2.95	-0.012	1.000	0.326
• Actual	75.53±10.72	78.46±10.11	2.931	1.381	0.178
• %Predicted	93.27±13.31	96.76±11.35	3.489	1.356	0.186
PEF					
• Predicted	6.07±1.13	6.07±1.13	-	-	-
• Actual	1.83±0.96	2.53±1.35	0.696	4.336	<0.001**
• %Predicted	30.02±14.74	40.88±18.44	10.857	4.603	<0.001**
Eosinophilia	510.47±487.81	391.50±254.50	118.96	1.253	0.220
ESR	23.23±17.82	23.87±20.44	-0.633	-0.275	0.785

DICUSSION

Asthma has far reaching connotation both on the children and adult people and if diagnose and treated at an earlier age could have positive outcome on prognosis of the disease **[17]**. Incidence of *Zeequnnafas* is more common in *Mausam-e-Kharif* (spring season) and *Mausam-e-Sarma* (winter season) and less in *Mausam-e-Garma* (summer) **[11].** Balghami mizaj are more prone to this disease **[9].** During the clinical trial, all patients were assessed for their *Mizaj* on the basis of *Ajnas-e-Ashra*. Maximum number of the patients 19 (63.3%) were having *Balghami Mizaj*, followed by 7 (23.3%) *Damvi*, and only 4 (13.3%) were having *Safravi* temperaments. The familial association of asthma is due to genetic predisposition **[29].**The relief in the paroxysmal dyspnoea was achieved due to effects of trial drugs having actions such as *Mukhrij-e-Balgham* (expectorant),, *Muhallil-e-Auwram* (anti-inflammatory), and *Munzij-e-Balgham* properties rendered by *Poodina, Aslus-soos, Sapistan,Aakh,* Badyaan,and *Neelofar* **[30-33].** Wheeze develops due to spasmodic action in the bronchioles. This effect was achieved by *Adrak, Beesh Badyan* and *Taj*, as these possess anti-inflammatory, antitussive and anti-spasmodic action **[34].** During the entire period of study duration, no apparent side effect was reported. Keeping the above evidence based results into consideration; it infers that the test drugs can be safely used in the management of bronchial asthma. However, long term clinical trials are needed to further explore the other pharmacological actions of the test drugs.

CONCLUSION

On the grounds of above cited results and discussions, it infers that test drugs "*Joshanda Zeequnnafas* and *Habbe Hindi Zeeqi*" are quite effective and safer for the management of asthma. However, other aspects of test drugs need to be explored to provide complete and safe remedy for bronchial asthma in large sample size, maximum dose, standard controlled and multicentre study with blinding.

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References:

[1] Anonymous. Standard Unani Medical Terminology. New Delhi: C.C.R.U.M; 2012:201-202.
[2] Khan Azam. Romooz Azam (Farsi). 2nd ed. Vol-1, 2. New Delhi: CCRUM, Ministry of Health and Family Welfare; 2006:247,248,249,252.
[3] Khan Azam. Al-Ikseer. Vol.1. New Delhi:Aijaz Publication House;2003:436-452.
[4] Khan Hakim Ajmal. Haziq. Ed.1. Karachi: Madina Publishing Company; 1983:302-306.
[5] Anonymous. Al-Munjid (Arabic-Urdu dictionary). Delhi: Farid book depot; YNM: 103-4,367,599.
[6] Saunders, M, J.B. Dec. Huang Ti Nei Ching Su Wen, the Yellow Emperor's Classic of Internal Mediciner Calif Med. 1967; 107(1): 125–126.
[7] Jackson, Mark. Asthma: The Biography. UK: Oxford University Press; 2009:10-11.
[8] Tabari Ali Ibn Raban. Firdaus ul Hikmat New Delhi: Idara Kitabush Shifa; 2010:195-197.
[9] Razi Abu Bakr Mohammad bin Zakariya. Kitab Al-Hawi (Urdu translation). Vol.4. New Delhi: CCRUM; 1998:9-39.
[10] Ibn Sina, Al-Qanoon Fit Tib. Vol.3. Part I. New Delhi: Idara Kitabush Shifa; 707-714.
[11] Jurjani SI. Tarjuma Zakheera Khowarizm Shahi. ed.1. Vol.6. Lucknow: Munshi Nawal Kishore; 1878:257-260.
[12] WHO. Chronic respiratory diseases. http:// www.Who.int / respiratory / asthma/en / . Cite on 17 august 2014.
[13] Siddhartha N. Shah. API Text book of Medicine. 8thed. Vol-1. Mumbai: The Association of India; 2008: 355.
[14] Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma. Available from: URL: http://www.ginaasthma.org, 1 - 128 (2012).
[15] Christopher Haslett. Davidson's Principles and Practice of Medicine. Ed.20. London: Churchill Livingston; 2006:670-677.
[16] Anthony SF, Dennis LK, Dan LL, Eugene B, Stephen LH, Larry JJ, et al. Harrison's Principles of Internal Medicine. Ed.18e. Vol.2. USA: The McGraw-Hill Companies; 2012.
[17] Ganaraja B, Bhattacharyya S, Panchami, R, Ramesh B. A Study of Propensity for Development of Bronchial Asthma in Preadolescents with Family History of Asthma by Spirometry and Body Mass Index. Research Journal of Pharmaceutical, Biological and Chemical Sciences.2012; 3(1):291-297.
[18] Calverley P MA. Modern treatment of chronic obstructive pulmonary disease. European Respiratory Journal. 2001; 18 (34):60–66.
[19] Dahl R. Systemic side effects of inhaled corticosteroids in patients with asthma. Respiratory Medicine.2006; 100(8): 1307–1317.
[20] Anonymous.Unani System of Medicine.Dabur Research Organisation. Cited on 21 august 2014.http://www.dsir.gov.in/reports/ittp_tedo/ism/ISM_USM_Intro.pdf.
[21] Kabir H.Introduction to Ilmul advia. Shamsher Publisher and Distributors..U.P Aligarh India.2002.Cited on 21 August 2014. http://www. jamiahamdard. ac. In /PDF /ilmul-advia/Introduction%20to%20Ilmul%20Advia.pdf.
[22] Kabir H. Morakkabat (Unani Formulation). Shamsher Publisher and Distributors..U.P Aligarh India. 2003. Cited on 21 August 2014. http://www.e-bookspdf.org / download /unani-formulations.html.
[23] Arja et al. Genetic Determinants of Chronic Obstructive Pulmonary Disease in South Indian Male Smokers. PLOS ONE. 2014; 9(2): e89957. .doi:10.1371 /journal. Pone. 0089957.
[24] Khan Azam. Qarabadeen Azam. New Delhi: Ejaz Publishing House; 1996: 53,538.
[25] Anonymous. National Formulary of Unani medicine. Part.1. New Delhi: Ministry of Health and Family Welfare, Department of AYUSH; 2006: 18.
[26] Ghani N. Qarabadeen Najmul Ghani. New Delhi: CCRUM,Ministry of Health and Family Welfare; 2010: 804.
[27] Kabiruddin HM. Alqarabadin ed. 2. New Delhi: CCRUM; 2006:129.
[28] Ganesh Kumar S, Gautam Roy, L. Subitha, Swaroop Kumar Sahu. Prevalence of bronchial asthma and its associated factors among school children in urban Puducherry, India. Journal of Natural Science, Biology and Medicine.2014;5(1):59-62.
[29] Fiocchi A, Terracciano L, Martelli A, Guerriero F, Bernardo L. Allergy Asthma Proc 2006; 27(3): 178-85.
[30] Khan MA, Clinical Study of Zeequnnafas Shoabi and evaluation of efficacy of Unani Formulation NIUM:2010.
[31] Ghani HN. Khazaenul Advia. ed.3. New Delhi: Idara kitabush shifa;2011:351.
[32] Kabiruddin A. Makhzanul Mufridat. New delhi: Ejaz Publishing House;YNM.
[33] Ali SS. Unani Advia Mufrida. ed.9. New Delhi:Qaumi kaonsil barae Furoogh Urdu zaban;2002.
[34] Khare CP. Indian Medicinal Plants. New Delhi:Springer;2007.