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Broncho-relaxant activity of *nigella sativa* versus *anthemis nobilis* in chronic bronchial asthma; a comparative study of efficacy

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***Abstract*—Background: Bronchial asthma (BA) is a clinical syndrome with variable causes. It characterizes by episodes of broncho-constriction which leads to shortness of breath. In traditional medicine, some medicinal plants have been used to cure the asthmatic symptoms.**
Objective: To evaluate the broncho-relaxant activity of Anthemis nobilis (Chamomile) and Nigella sativa (Black seeds) then to choose the better.
Methods: An open study was conducted on 54 patients with chronic bronchial asthma. After clinical assessment, estimation of pulmonary function tests and serum electrolytes: calcium, magnesium, potassium and selenium were done before and after the study. Anthemis nobilis was given to 18 patients and nigella sativa to another 18 patients for 21 days.
Results: The comparative study showed that the tested plants have significant elevation in the values of forced expiratory volume in first second (FEV_1%) and forced volume capacity (FVC) with marked reduction in asthmatic attacks, but showed better symptomatic improvement with black seeds as compared to chamomile. Conclusion: The results of all parameters of efficacy prove the superiority of nigella sativa over anthemis nobilis for CBA.

***Keywords*—Black seeds, chamomile, magnesium, pulmonary function tests**

I. INTRODUCTION

Bronchial asthma is an inflammatory syndrome characterized by paroxysmal or recurrent episodes of bronchial obstruction causing shortness of breath, cough, chest tightness, wheezing and rapid respiratory rate.[1] Many factors are involved like air pollutants, mold species[2], emotional factors [2], obesity [3] and some medications as β- blockers and non-steroidal anti-inflammatory drugs.[4] Although the pathogenesis of chronic bronchial asthma (CBA) is complex, reactive oxygen species (ROS) have been shown to be directly associated with asthma pathogenesis and an oxidant-antioxidant imbalance.[5]ROS evoke bronchial hyperactivity through releasing both histamine from the mast cells and mucus from airway epithelial cells.[6]

N. sativa (black cumin) is an annual plant, contains numerous black seeds which were used in folk medicine for the treatment of asthma, diarrhea, and dyslipidaemia.[7]Black seed contains[8]: β-sitosterol, nigelline, nigellone (has anti-histamine activity), and thymoquinone (the major component that blocks cancer cell growth). *A. nobilis* (chamomile) is a fragrant, perennial herb, with daisy-like white flowers, found around gardens and cultured grounds.[9] In traditional medicine, it was extensively used as perfumes and for treatment of indigestion. *A. nobilis* contains[10]: fragranced essential oil (the source of its activity), Anthemene, Antheminic acid (has anti-inflammatory property), flavonoids, tannin, and resin.

The relative absence of data in this domain is an incentive to evaluate the potential smooth muscle relaxation effect of these medicinal plants in CBA.

II. SUBJECTS AND METHODS

Plant material:-The test medicinal plants were purchased from a well-known bureau for herbs (Al-Medina) in Baghdad and were identified and authenticated by Iraqi National center for Herbs. The chamomile and black seeds were cleaned to remove the debris, dried then were stored in airtight container at room temperature. On use, chamomile and black seed were boiled and immediately used by inhalation for 5-10 minutes using vapor machine.

Subjects:-Fifty four patients of CBA, 33 males and 21 females, aged from 22-56 years (mean 38.16 ± 1.9 SD), participated in this randomized, open, and comparative clinical study. The participants were recruited from the outpatient clinic of Department of Medicine of Al-Kadhemiya Teaching Hospital from August 2009 to June 2010 excluding pregnant women, cigarette smokers, alcohol consumers and any disease other than chronic asthma. The trial was explained to all subjects and their consent was obtained.

Experimental protocol:-Approval to conduct this study was granted by the ethical committee in College of Medicine/Al-Nahrain University (Registration No.HEC/42/09/CMANU). The patients were advised to stop medication and prevent any exercise or exposure to any allergen at least 24hrs prior to test. They were randomly allocated to three groups of 18 patients each and received daily one dose of the following for three weeks

Group I -served as positive control – received 0.15 mg/kg/day of prednisolone as a single dose.

Group II - received 100 mg/kg of chamomile by inhalation

Group III - received 100 mg/kg of black seeds by inhalation

Biochemical estimations:-Blood samples were taken before and at the end of experiment from all the participants. Serum magnesium (Mg^{+2}) and serum selenium (Se^{+2}) were estimated by using GFA-4B graphite tube with auto sample absorption photometer. Serum calcium (Ca^{+2}) and serum potassium (K^{+}) were measured by using flame emission spectrophotometer.

Functional tests:-Pulmonary function tests (forced volume capacity FVC and forced expiratory volume in first second FEV_1%) were performed using a computerized spirometer (Autospiron chest corporation Tokyo-Japan).

Statistical analysis:-All the results were expressed as mean ± standard error mean (SEM). The difference among means has been analyzed by student's t test. A probability value of $P<0.05$ was considered to be statistically significant.

III. RESULTS

The results revealed significant elevation in FEV_1% of chamomile and black seeds as (79.33 ± 4.40 vs 77.41 ± 3.30, and 74.91 ± 5.28 vs 53.80 ± 7.49) respectively. Also, significant elevation was showed in FVC/L of chamomile and black seeds in addition to prednisolone as (2.75 ± 0.32 vs 2.38 ± 0.27, 3.54 ± 0.05 vs 1.36 ± 0.12, and 2.25 ± 0.16 vs 1.05± 0.15) respectively, but with superiority to black seeds (Table 1). Elevations in serum electrolyte levels were also significantly confirmed the above obtained results (Table 2).

IV. DISCUSSION

Bronchial asthma is an inflammatory condition with episodes of bronchial muscle contraction resulted from releasing of leukotrienes (LTs). Prednisolone which is used in group I, produces bronchial muscle relaxation indirectly through inhibiting the release of LTs and reversing mucosal edema.[11]In group II with chamomile, significant is poor when given by inhalation. No real improvement occurs in asthmatic symptoms in spite of its relaxant effect on rabbit tracheal muscle contraction when given by inhalation.[12]In group III with black seeds, significant relaxing effect occurred when given by inhalation. This action is related to its active constituent"nigellone" that prevents histamine release from mast cells,[13] besides its well known antioxidant activity.[14]Changes of serum electrolytes levels in asthmatic patients showed positive correlation between serum Se^{+2} and Mg^{+2} levels and each FEV_1% and FVC. Our results agreed with a study showed that if serum Se^{+2} and Mg^{+2} levels decreased the possible risk of asthma would be increase due to reduction in glutathione peroxide and antioxidant activity and vice versa.[15] Most of the asthmatic patients recorded low levels of serum Ca^{+2} before treatment and this is due to increased intracellular Ca^{+2} in leukocytes that directly correlated with severity of asthma.[16]

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Table 1: The effect of Nigella sativa, Anthemis nobilis and Prednisolone on pulmonary function parameters in chronic asthmatic patients

Groups	**FEV_1%**		**FVC / L**	
	Before usage	**After usage**	**Before usage**	**After usage**
I (prednisolone/ positive control)	72.75± 0.09	78.63±3.34*	1.05 ± 0.15	2.25 ± 0.16*
II (Anthemis nobilis- received)	77.41 ± 3.30	79.33 ± 4.40	2.38 ± 0.27	2.75 ± 0.32
III (Nigella sativa-received)	53.80 ± 7.49	74.91 ± 5.28*	1.36 ± 0.12	3.54 ± 0.05*

Values are mean ± SEM, *n*=18 patients for each group, **P*<0.05 compared with before treatment

Table 2: The effect of Nigella sativa, Anthemis nobilis and Prednisolone on serum electrolytes levels in chronic asthmatic patients

S. Mg^{+2} (mmol/L)		**S. Se^{+2} (µg/L)**		**S. Ca^{+2} (mmol/L)**		**S. K^{+} (mmol/L)**	
Material use	**before**	**after**	**before**	**after**	**before**	**after**	**before**	**After**
I (prednisolone)	0.73±0.05	0.81± 0.15*	44.62±6.35	49.17±4.96*	1.97± 0.07	2.10±0.10	3.5± 0.24	3.50 ±0.08
II (Anthemis nobilis)	0.78±0.02	0.80±0.02	54.66±1.32	60.05±3.16*	2.06±0.06	2.17±0.07	3.94±0.05	3.61±0.09
III (Nigella sativa)	0.90±0.07	1.08±0.02*	28.03±7.01	42.10±9.18*	1.97±0.03	2.10±0.04*	3.00±0.18	3.70±0.06*

Values are mean ± SEM, *n*=18 patients for each group, **P*<0.05 compared with before treatment. S. Mg^{+2} =serum magnesium, S. Se^{+2} = serum selenium, S. Ca^{+2} = serum calcium, S. K^{+} = serum potassium