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Full Length Research Paper

Study of *Nigella sativa* oil in the management of wheeze associated lower respiratory tract illness in children

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***Nigella sativa* seeds and its oil had been widely used in traditional medicine (particularly in Unani Medicine) for a wide variety of illnesses including bronchial asthma in adults. The adjuvant effect of *N. sativa* oil in patients of bronchial asthma has already been reported but, no work had yet been done in very common disease of children called wheeze associated lower respiratory tract illness (wheeze associated LRTI). So In the present study 84 patients of wheeze associated LRTI were investigated for any beneficial role of *N. sativa* oil in this condition. Control group (41) and test group (43), were administered with Standard treatment and *N. sativa* oil along with Standard treatment in dose of 0.1 ml/kg/day, respectively. Patients were assessed on 0 (Zero) day and reassessed on 3rd, 7th, 10th and 14th day of treatment by using Pulmonary Index (PI) and Peak Expiratory Flow Rate (PEFR). The PI was reduced more in test group as compared to control group in all days of treatment and difference was statistically significant on 3rd day (P < 0.05) . The inter-group comparison on 3rd, 7th, 10th and 14th day also showed significant reduction in PI of test group compared to control group (P<0.001). PEFR showed higher improvement in test group compared to control group in all days of treatment, although, here the difference was statistically insignificant (P > 0.05). In inter-group comparison, the improvement in PEFR was observed only till 7th day of treatment in the control group but it was unto 14th day of treatment in the test group (P<0.0001).**

Key words: *Nigella sativa* oil, wheeze, pulmonary index, PEFR.

INTRODUCTION

Wheeze is high pitched whistling sound audible with or without the help of stethoscope and is produced due to partial obstruction of bronchi or bronchioles (Kabra and Ghai, 2004). Wheeze associated LRTI occurs in 20% of all children and the prevalence of asthma and wheeze reported in north India were 2.3 and 6.2% respect-tively, in age group 6-7 years and 3.3 and 7.8%, res-pectively, in age group 13-14 years (Awasthi et al., 2004). Wheeze associated LRTI takes into account of bronchiolitis and reactive airway diseases including air-way reactivity, atopic asthma, asthmatic bronchitis and tropical eosinophilia etc. (Boat and Orenstein, 2003).The drugs commonly prescribed for Wheeze associated LRTI are bronchodilators such as short acting β_2 agonists, anti-cholinergic, theophylline and corticosteroids but these drugs have their own limitations and side effects.

Nigella sativa is a small herbaceous plant, one of the Ranunculaceae, commonly grows in different parts of the world including India. Akhtar and Riffat, (1991) used *N. sativa* seeds for deworming the children. The adjuvant effect of *N. sativa* oil in patients of allergic rhinitis, bron-chial asthma and atopic eczema has already been repor-ted by Kalus et al., (2003). The major compounds of the volatile oil identified *are* trans-anethole, p-cymene, limo-nene, thymoquinone and carvone (Nickavar et al., 2003). Randhawa and Al-Ghamdi, (2002) reported that thymo-quinone and dithymoquinone are active pharmacologi-cally constituents of volatile oil. The present work was de-signed to study the role of *N. sativa* oil in wheeze asso-ciated LRTI in children.

MATERIALS AND METHODS

This prospective, randomized open study was done in patients of 5 to 15 years of age, attending Pediatrics Out-Patient and In-Patient of J. N. Medical College and Hospital, AMU, Aligarh (India), after taking prior permission from the Institutional Ethic Committee (IEC).

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Table 1. Pulmonary index.

Score	Respiratory rate (Age)		Wheezing*	Inspiratory-Expiratory Ratio	Accessory Muscle Use	Oxygen Saturation (%)
	<6 yrs	≥ 6 yrs				
0	≤ 30	< 20	None	2:1	None	99-100
1	31-45	21-35	End expiration	1:1	+	96-98
2	46-60	36-50	Entire expiration	1:2	++	93-95
3	>60	>50	Inspiration and expiration without stethoscope	1:3	+++	<93

*If no wheezing due to minimal air entry, score 3Accessory muscle use was scored by assessment of sternocleidomastoid activity: 0, no apparent activity; plus or minus sign, questionable increase; double plus signs, increase apparent; and triple plus signs, maximal activity.

Table 2. Effect of N. Sativa oil on pulmonary index of wheeze associated LRTI patients.

Days	Control Group		Test Group		
	Mean ± SD	%	Mean ± SD	%	P-values
0	5.87±2.44	100	5.97±2.48	100	>0.05
3rd	3.75±1.61	63.9	3.03±1.54	50.7	<0.05
7th	1.85±1.35	31.5	1.69±1.59	28.3	>0.05
10th	1.00±1.00	17.0	1.0±0.76	16.8	>0.05
14th	0.80±0.87	13.6	0.86±0.63	14.4	>0.05

The duration of study was from January 2004 to February 2006. Patients having wheeze audible on auscultation were included after taking the consent from their parents or guardians. Patients having impending respiratory failure or other serious systemic diseases were excluded from the study.

The patients were then randomized into two group viz. Control and Test Groups. Control group was administered with standard treatment prescribed by treating pediatrician in the form of bronchodilator (salbutamol in dose of 0.1- 0.0.4 mg/kg every 8 h or terbutaline,0.1-0.15 mg/kg every 8 h) orally / or through nebulizers (salbutamol/combination of salbutamol and ipratropium bromide) and antimicrobial agents, if needed, while test group was administered essential oil of *N. sativa* in dose of 0.1 ml/kg of the body weight /day in two divided doses (every12 h) for 14 days, orally along with the standard treatment. *N. sativa* oil (vernacular name: Kalonji oil) was arranged from Mohammedia Products, which is a certified GMP (Good manufacturing practice) pharmaceutics of Hyderabad (India). According to the 'Leaflet Information', it is prepared by steam distillation.

All the enrolled patients were assessed on 0 day (that is before starting treatment) and reassessed on 3rd, 7th, 10th and 14th day of treatment by measuring following parameters. Pulmonary Index (PI): PI represented the sum of the score of all five parameters (Respiratory rate, Wheezing, Inspiratory-Expiratory Ratio, Accessory Muscle Use and Oxygen Saturation) on every visit of the patient. The score was assigned as follows: respiratory rate (0 to 3 = high, dependent on age), wheezing (0=none to 3=severe), inspiration/expiration ratio (0=2:1 to 3=1:3), accessory muscle use (0=none to 3 = maximal use) and oxygen saturation (0=99-100% to 3=<93%). It is based on method designed (Table 1) by Allan et al., (1984). Peak expiratory flow rate (PEFR): PEFR was calculated as % of normal predicted values of children and measured by a mini-Wright peak flow meter and the best value of three attempts was recorded. The reference values have been established by Paramesh (2003) in relation to height for normal children.

Statistical analysis

The observations Pulmonary index and PEFR in the study were evaluated by using Repeated measures ANOVA to reduces the unsystematic variability and provides greater power to study the effects and followed by Post hoc test (Bonferroni Statistics) for individual group variation. Post hoc test helped to study the pair wise comparison (group comparison). The P values less than < 0.001 were considered significant. The control and test group were also compared by using Student 't' test (P < 0.05 were considered significant).

RESULTS AND DISCUSSION

In our study the maximum numbers of cases were in the age group of 5 to 7 years, predominantly male. The average weights and heights in control group were 23.09±7.20 kg and 126.09±14.19 cm, respectively, while in test groups the readings were 23.9±7.1 kg and 127.5 ± 14.1 cm, respectively. The mean duration of bronchodilator therapy in control and test groups was 7.78±2.36 and 7.67 ±2.43 days, respectively. One patient developed diarrhea during treatment and was excluded from the study. Effect of *N. Sativa* oil on pulmonary index of wheeze associated LRTI patients: In control group, a gradual reduction in the mean values of PI was observed. It was reduced to 63.9, 31.5, 17.0 and 13.6% on day 3, 7, 10 and 14 day, respectively in comparison to day zero values (Table 3) . While, in test group, it was reduced to 50.7, 28.3, 16.8 and 14.4% on 3rd, 7th, 10th and 14th day respectively. The beneficial effect along with PI reduction

Table 3. Effect of N. Sativa oil on Peak Expiratory Flow Rate of Wheeze associated LRTI patients

Days	Control		Test Group		
	Mean ± SD	% Increase	Mean ± SD	% Increase	P-values
0	62.34±14.11		60.2±10.5		>0.05
3rd	78.21±12.93	25.5	77.2±11.3	28.2	>0.05
7th	85.39±11.0	37.0	84.3±10.7	40.0	>0.05
10th	87.07±9.63	39.7	88.3±8.8	46.7	>0.05
14th	89.58±8.01	43.7	90.4±6.8	50.0	>0.05

was statistically significant on day 3rd of the treatment in test group as compared to control group ($P < 0.05$).

Effect of *N. Sativa* oil on PEFR of wheeze associated LRTI patients: The percentage increase in the mean values of PEFR from 0 day values was more in test group than control group in all days of treatment (Table 4) When inter-group (0-3, 3-7, 7-10 and 10-14th day) comparison was made the significant improvement in PEFR was observed till 14th day of treatment in test group but in control group it was seen till 7th day only. ($P < 0.001$ was considered significant). In our study, the beneficial effect of *N. sativa* oil is seen in the form of de-creased PI and increased PEFR. The reason of these findings may be correlated with earlier studies related to *N. sativa* . Boskabady and Shahabi, (1997) and Boskabady et al. (2004) have shown the anticholi-nergic property by demonstrating the relaxant effect in methacholine induced contracted tracheal chains of guinea pig. *Thymoquinone,* an active constituent *N. sativa* oil was found to decrease tension of the tracheal smooth muscle pre-contracted by carbachol. The spasmolytic and bronchodilatory activities were found in the crude extract of *N. sativa* while studying guinea pig tracheal preparation. The inhibiting effect of *thymoquinone* on *5-lipo-oxygenase* activity in human blood cells and inhibition of leukotrienes syn-thesis is already known. *Thymoquinone* causes con-centration dependent inhibition of both LTC4 and LTB4 (Al-Majed et al., 2001). We know now that the leukotrienes are important mediator of asthma and inflammatory processes. In the same study, authors also observed significant inhibition of LT4 synthase activity. The essential oil was found more effective against gram- positive thangram-negative bacteria (Agarwal et al., 1979; Salman et al., 2008). These pro-perties may be useful since wheeze associated LRTI patients may have some infective component at one or another stage of the disease. Nigellone, isolated from *N. sativa*, also inhibits histamine release. These findings may have role in the beneficial effects of *N. sativa* oil in wheeze associated LRTI patients. Our findings are in consistent with those of Kallus et al. (2003) who had found an adjuvant role of *N. sativa* oil in patients of bron-chial asthma using dose of 40-80 mg/kg/day without any side effects. Boskabady et al. (2007) examined the prophylactic effect of boiled extract of *N. sativa* on asthmatic patients for 3 months and All asthma symptoms, frequency of asthma symptoms/week, chest wheezing, and PFT values in the study group significantly improved in the second (45th day of treatment) and third visits (at the end of the study) compared with the first visit. In our study, by using essential oil of *N. sativa* we have also noted improvement in all days of treatment.

Conclusion

In our study we have found that addition of *N. sativa* oil has beneficial role. So more studies may be needed to make final conclusion regarding the use of this in patients of Wheeze associated LRTI, particularly in children.

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