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Short Note

Effect of *Hingu-Pippali Yoga*, a Herbal Formulation in Respiratory Disorders Caused by Air Pollution in Traffic Police—A Pilot Study

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Abstract: Traffic police in metropolitan cities are exposed to higher level of air pollution and are suffering from respiratory symptoms. Conventional symptomatic treatment is effective to give temporary relief but the lung capacity of the subjects reduces progressively. Present study was aimed to evaluate effect of *Hingu-Pippali* yoga, a herbal formulation in respiratory disorders caused due to air pollution in traffic police. With a prior institutional ethical permission an open, randomised clinical study was carried out. Informed consent was taken from every subject enrolled in trial. An authenticated and standardised test drug was administered twice a day in dose of 250 mg for 28 days with honey and sugar to trial group. Lung function test with spirometer and Haemogram before starting the treatment and at the end of study was done to evaluate the results.

The subjective parameters viz. cough, rhinitis and dyspnoea showed significant reduction ($p < 0.001$) in trial group. Pulmonary Function Tests—FVC, FEV1, MVV and FEF ($p < 0.001$)—showed significant results indicating the increase in lung capacity in trial group. There was significant reduction seen in eosinophil count and ESR. *Hingu-pippali yoga* is effective to reduce the respiratory disorders caused due to air pollution and enhances the lung capacity of subjects.

Key words: Air pollution, *Ferula narthex, Piper longum*, spirometer.

Background

Soil, water, air and climate are the conjoint factors for all the members of the ecosystem (Yadavji Trikamji, 2004a). Any alteration in these factors affects the entire ecosystem. Of these factors, air is perceived to get polluted mainly with the stationary fossil fuel burning sources, such as industries and mobile sources like motor vehicles. Currently it has been reported that approximately 50% of the people in the world live in cities and urban areas and are exposed to progressively higher levels of air pollutants (Salvi and Barnes, 2009). Air pollution is a mixture of particles-particulate matter (PM) and gases released into the atmosphere. The major components of PM are sulphate, nitrates, ammonia, sodium chloride, carbon, mineral dust and water. The particles are measured according to their aerodynamic diameter and are divided into three classes as 30 μm, PM_{10} (inhalable particle), $PM_{2.5}$ (fine PM) and $PM_{0.1}$ (ultrafine PM). The latter three are more dangerous as they may reach the peripheral regions of the bronchioles and interfere with gas exchange inside the lungs (World Health Organization, 2011).

As there is a large contact area between the surfaces of the respiratory system, the environment air quality directly affects respiratory health. The substantial

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quantity of inhaled pollutants reaches the systemic circulation through the lungs and causes deleterious effects on various organs and systems (Brook et al., 2010). Thus air pollutants affect human being in the form of oxidative stress in the upper and lower airways (Brashier and Kodgule, 2012).

In metropolitan cities traffic police, posted at busy intersections for 8-10 hours daily, are exposed to very high levels of air pollution and are at higher risk of lung diseases, cardiovascular diseases, alteration in the body defence system against foreign material, damage to lung tissue, carcinogenesis and premature death (Cotes et al., 1978). The prevalence of lung disorders has direct relationship with concentration of pollution and duration of exposure (Chatterjee and Gangopadhyaya, 1989; Chattopadhyaya et al., 1994). These symptoms force the individual to make repeated visits of physician. Available symptomatic treatment renders temporary relief in the symptoms but the lung capacity of the subjects decreases progressively and may lead to serious health problem.

Air pollution induced respiratory disorder can be equated with the *Vishdushita Vayujanyavikar* described in *Ayurvedic* classics. The test drug of this pilot study *Hingu-Pippali Yoga*(HPY) has been recommended in respiratory disorders initiated due to exposure to polluted air *(Vishdushita Vayu)* (Chikitsasthan, 2004b).

Ferula narthex Regel. (*Hingu*), one of the ingredients of this herbal formulation, has exhibited anti-microbial activity (Gupta and Tandon, 2004). Besides the various species of *Ferula narthex* Regel. have also shown biological activities which include anti-microbial (Asili et al., 2009; Maggi et al., 2009), anti-fungal (Iranshahi et al., 2008), anti-oxidant (Kartal et al., 2009; Dehghan et al., 2007), anti-mycobacterial (Appendino et al., 2004), anti-inflammatory (Mandegary et al., 2004) in various preclinical and clinical studies.

The other component *Piper longum* Linn. (*Pippali*) having principal phytochemical Piperine has shown significant effect on early acute changes in inflammatory processes and chronic granulative changes (Mujumdar et al., 1990). It also has inhibited the TNF-α-induced expression of ICAM-1 in a dose and time-dependent manner (Sarvesh et al., 2005).

In present pilot study the effect of HPY has been evaluated in the respiratory disorders caused by air pollution in traffic police.

Materials and Method

Herbal Formulation

The test drug *Hingu-Pippali Yoga* is a combination of *Ferula narthex* Regel. (*Hingu*) and *Piper Longum* Linn. *(Pippali*) in equal quantity (Sharangadhar Samhita, 1994). The authentication and standardization of the raw drug and the finished product was done as per the *Ayurvedic* classics (Dravyaguna Vigyana, 1995) and Ayurvedic Pharmacopeia of India (Government of India, 2001). The proportion of the ingredients and vehicle (*Anupan)* was finalized as per the guidelines of *Ayurvedic* text. The test drug has been manufactured in the GMP certified pharmacy of Bharati Vidyapeeth Deemed University College of Ayurved, Pune, India as per the guidelines of Ayurvedic classic Sharangadhar Samhita by adopting standard operating procedures.

Study of Population

The subjects (traffic police) exposed to air pollution for 7-8 hrs/day of either sex , in between 25 to 55 yrs of age, showing evidence of at least four symptoms of respiratory system disorder like cough (*Kasa*), dyspnea (*Śhwasa*), sneezing (*Pratiṣhyaya*), congestion of throat (*Shukapurna-Galasyata*), itching sensation of throat (*Kaṇthekaṇdu*), hoarseness of voice (*Svarbheda*), sinusitis (*Pinas*), repeated visit to physician and deviation from normal in pulmonary function test in spirometer were included in the clinical trial.

Traffic police working in indoor office, concomitant condition like hypertension (150/100 mm/Hg), diabetes mellitus, cardiac disease, angioplasty, pulmonary tuberculosis, lung malignancy, pleural effusion and subjects not following the drug administration and regular follow up schedule of the study protocol were excluded from the study.

Study Groups

For this open clinical study, 20 patients (10 in each group) were recruited.

1. Group- A: Control group receiving symptomatic treatment
2. Group- B: Trial group receiving symptomatic treatment along with test drug (HPY).

Study Design

The Institutional Ethics Committee approval was obtained prior to the conduction of the study. Also informed consent was taken from all the recruited subjects.

Enrolled subjects underwent a review of symptoms mainly related to respiratory system and history of period of outdoor duty at their baseline visit. Also height and weight of the individuals were recorded meticulously as these parameters vary the individual predicted values of spirometry.

The test drug was administered twice a day in a dose of 250 mg for 28 days with honey and sugar. Regular follow-up was taken at seven days interval for the subjective parameters. Biochemical assay and Pulmonary function test with spirometer were executed twice i.e. at the base line visit and end of the intervention. For recording of the changes in the subjective criteria, gradation scale on the basis of severity of symptoms as per the guidelines of American Cancer Association was followed.

Statistical Analysis

The parametric data is presented as mean ± SD while the non-parametric data is presented as median (range). For inter-group comparison, unpaired *t* test was used for parametric data and Mann Whitney test was used for non-parametric data.

For intra-group comparison, paired *t* test was used for parametric data and Wilcoxan Rank Sum test was used for non-parametric data.

Results

Study of Population

Primarily 200 subjects were screened of which 90 subjects showed physical symptoms pertaining to respiratory system. Further screening was done with pulmonary function test, of which 50 patients showed deviation from the normal values. Of these 50 subjects 16 were excluded due to the concomitant condition like hypertension (150/100 mm/Hg), diabetes mellitus, cardiac disease, angioplasty, pulmonary tuberculosis, lung malignancy, pleural effusion and 10 patients due to exposure period of less than five years. Thus finally 24 subjects were recruited for the clinical trial. Of these two subjects in each group dropped out due to either transfer in working place or did not follow the treatment schedule. Thus 20 subjects of total 200 screened patients completed the clinical trial (Figure 1).

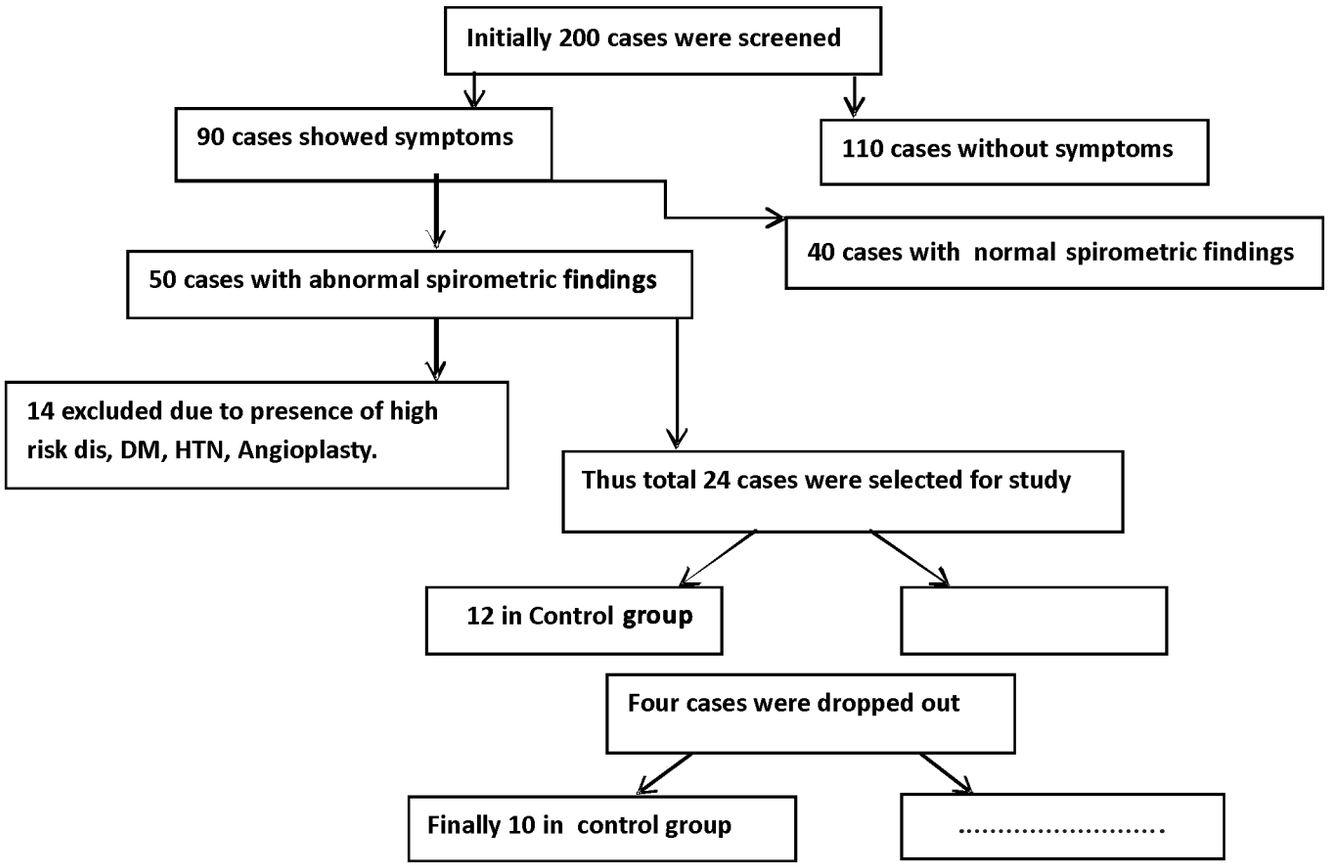

Figure 1: Chart showing recruitment of patients.

Demographic Characteristics

The demographic data viz. age, weight and height were comparable in both groups (Table 1). The duration of duty in years was almost equal, i.e. 5.9 years in control and 5.7 years in trial group. Average height in cms and weight in kgs of subjects from control group was 171.4 ± 4.45 and 76.1 ± 9.81 whereas 172.3 ± 4.24 and 75.6 ± 7.47 in trial group respectively.

Effect on Clinical Symptoms

It was seen that the symptoms cough *(Kasa)*, Dyspnoea *(Shwasa)*, Rhinitis *(Pratishaya)* were most common and found in almost all the subjects suggesting the most frequently affected system by air pollution is the respiratory system. As seen in Figures 2, 3 and 4 the trial group has shown significant reduction in the symptoms ($p < 0.001$) as compared to the control group.

Table 1: Demographic details of the participants enrolled for the clinical study

Parameter	*Control Group*	*Trial Group*
Age (years)	37.5 (28-55)	29 (27-54)
Weight (kg)	76.1 ± 9.81	75.6 ± 7.47
Height (mms)	171.4 ± 4.45	172.3 ± 4.24
Duration of duty (years)	5.9 ± 0.88	5.7 ± 1.06

Data presented as Mean ± SD in case of normally distributed data and median (range) in case of data not distributed normally.

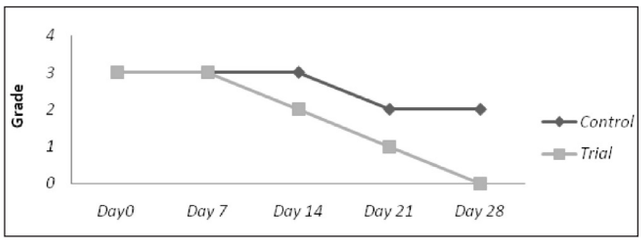

Figure 2: Effect of herbal formulation (*Hingu-Pippali Yoga*) on the symptom cough (*Kasa*).

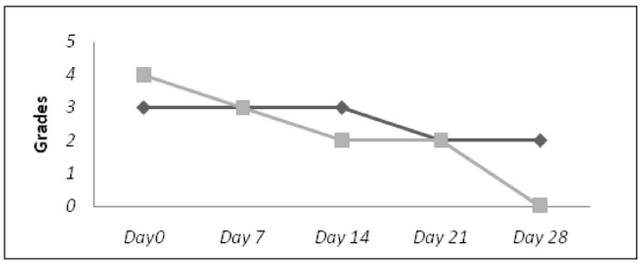

Figure 3: Effect of Herbal formulation (*Hingu-Pippali Yoga*) on the symptom dyspnoea (*Shwasa*).

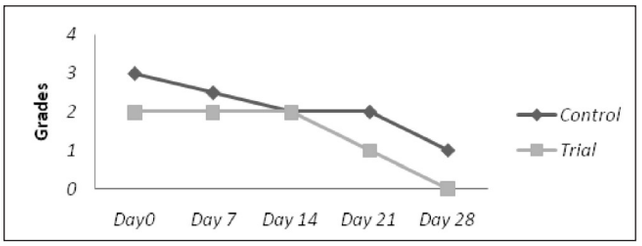

Figure 4: Effect of herbal formulation (*Hingu-Pippali Yoga*) on the symptom Rhinitis (*Pratishaya*).

Effect on Haematological Parameters

The eosinophil count in control group showed elevated values at the end of the study as compared to baseline [9 ± 5.52 *Vs* 10.4 ± 5.06, $p < 0.05$] indicating increased allergic response of body whereas in trial group these values were significantly reduced [8.6 ± 3.60 *Vs* 3.9 ± 1.20, $p < 0.01$] (Figure 5).

Erythrocyte Sedimentation Rate (ESR) was raised in control group [12.3 ± 2.95 *Vs* 13.3 ± 3.27, $p < 0.01$]. However the patients receiving test drug showed significant reduction in the ESR values [11 ± 3.97 *Vs* 8.8 ± 3.05, $p < 0.01$] (Figure 5).

Rest of the haematological parameters did not show any significant change in the baseline and post-treatment values.

It has been also observed that the individuals consuming test drug made less visits to the clinic for respiratory disorders.

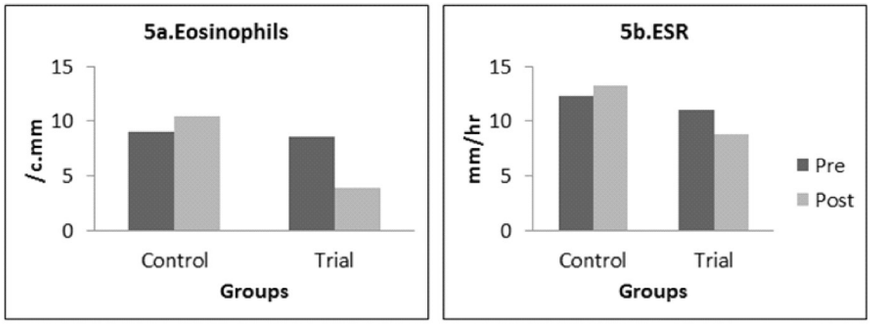

Figure 5: Effect of herbal formulation (*Hingu-Pippali Yoga*) on haematological parameters.

Pulmonary Function Test Analysis Outcome

In the Pulmonary Function Test performed with spirometer, the values FVC, FEV_1, MVV, and PEFR, have shown increase in trial group whereas in control group significant decrease have been observed (Table 3). The ratio values of the FVC%, FEV_1%, MVV % and PEFR% showed significant improvement ($p < 0.001$) in lung capacity in trial group whereas significant reduction in control group ($p < 0.01$).

The value of FEV_1/FVC and FEV_1/FVC% did not show any change in the base line and post-treatment values.

Discussion

In *Ayurved* the concept of air pollution is discussed under the purview of *Vishadushitavayujanya Vikar* where symptoms of respiratory tract have been described as prime manifestations. The same has been reported by recent studies conducted at different geographical areas (Ingale et al., 2005).

Hingu-pippali Yoga (HPY) is among the numerous formulations cited for the treatment of health hazards caused due to air pollution. *Ferula narthex* Regel. (*Hingu*), one of the components of HPY, has a wide range of chemical compounds including sugars, sesquiter penecoumarins and polysulphides. It is a culinary spice and traditionally used to treat various diseases like asthma, gastrointestinal disorders and intestinal parasites. It is also known to possess antifungal, anti-diabetic, anti-inflammatory, anti-mutagenic and anti-viral activities (Milad and Mehrdad, 2011). It has been also proved as potent antioxidant and can offer protection against free radical mediated diseases like carcinogenesis (Saleem et al., 2001).

Piper Longum Linn. *(Pippali*), another ingredient of the HPY, is quoted as best rejuvenating agent for respiratory system in Ayurvedic pharmacopeia *Bhavprakasha*. *Piper longum* is a drug of choice in the Ayurvedic system of medicine for the respiratory disorders. The main phytochemicals present in piper longumarepiperine, piperlongumine, piperlonguminine and methyl-3,4,5-trimethoxycinnamate (Chauhan et al., 2011). *Piper Longum* has been proven for its immune-modulatory and hypo-cholesterolaemic (Mananvalan and Singh, 1979), anti-inflammatory (Sharma and Singh, 1980), anti-depressant (Pal et al., 2011), anti-oxidant and anti-hepatotoxic (Samudram et. al., 2009) activities.

Considering the above mentioned property of the ingredients, HPY was selected along with the vehicle sugar and honey for this clinical trial. As per the guidelines of the Ayurvedic text, *Sharangadhar*

Table 2: Effect of herbal formulation (*Hingu-Pippali Yoga*) on the pulmonary function test

Parameter	*Control group*			*Trial group*		
	Predicted	*Observed*		*Predicted*	*Observed*	
		Pre	*Post*		*Pre*	*Post*
FVC	3.88 ± 0.46	2.72 ± 0.31	2.28 ± 0.27	3.96 ± 0.30	2.77 ± 0.38	3.63 ± 0.28
FEV_1	3.22 ± 0.43	2.37 ± 0.32	1.97 ± 0.25	3.31 ± 0.31	2.46 ± 0.35	3.16 ± 0.26
FEV_1/FVC	80.17 ± 2.08	87.43 ± 4.45	85.68 ± 5.75	80.95 ± 1.83	88.75 ± 4.00	87.61 ± 3.15
MVV	133.38 ± 13.88	81.46 ± 11.99	68.94 ± 8.70	136.39 ± 9.77	86.06 ± 12.14	110.43 ± 8.94
PEFR	8.93 ± 0.73	5.79 ± 1.23	4.66 ± 1.33	9.09 ± 0.51	6.36 ± 0.62	8.39 ± 0.96

Table 3: Effect of herbal formulation (*Hingu-Pippali Yoga*) on the % deviation from predicted values in PFT parameters

Parameter	*Control group*			*Trial group*		
	Pre	*Post*	*Difference*	*Pre*	*Post*	*Difference*
FVC %	70.20 ± 5.90	59.60 ± 5.36	-10.60 ± 4.99***	69.00 ± 5.12	91.70 ± 5.79	22.70 ± 7.47***
FEV_1%	73.50 ± 6.67	61.50 ± 7.72	-12.00 ± 6.55***	74.00 ± 6.43	95.60 ± 5.73	21.60 ± 7.34***
FEV_1/FVC%	109.20 ± 5.22	107.10 ± 8.21	-2.10 ± 11.58	109.7 ± 5.58	107.58 ± 4.48	2.20 ± 4.44
MVV%	61.10 ± 7.09	51.9 ± 5.97	-9.20 ± 6.49***	62.9 ± 5.92	81.00 ± 5.46	18.10 ± 5.95***
PEFR%	64.60 ± 10.08	55.10 ± 8.70	-9.50 ± 12.03***	70 ± 5.42	92.30 ± 11.13	22.30 ± 14.04***

Samhita, the quantity of sugar was accepted as twice the individual ingredient. This quantity is helpful to reduce untoward effect of hot and penetrating (*Ushnatikshna*) *Piper longum*. Honey is a best catalyst and also has anti-tussive activity too and thus helps to remove extra mucous and enhances the overall curative effect of the formulation on respiratory tract.

It has been observed that the police working at traffic junction for the period more than five years are more prone to health hazard related to upper respiratory tract and showed evidence of decreased lung capacity in pulmonary function test. The same findings were revealed in the previously conducted studies (Chatterjee and Gangopadhyaya, 1989; Chattopadhyaya et al., 1994). The air containing vehicular exhaust of more than 10 micron size (PM_{10}) accumulates in the lung and produces respiratory abnormality (Ingaleet al., 2005). The particulate matter provokes alveolar inflammation (Seaton et al., 1995). Thus the incidence of respiratory disorders seen in study population might be due to the fine particulate matters present in air pollution.

All the subjects of both the groups showed physical symptoms related to respiratory system. All these symptoms reflect the inflammatory response of the body caused due to particulate matter of air pollution (Revathi et al., 2012).

It is known that the inflammatory response is closely entangled with the process of repair and as inflammation destroys, dilutes and walls off the injurious agent, it sets a series of events that try to heal the damaged tissue. Repair begins during inflammation but reaches completion usually after the neutralization of injurious influence (Vinay et al., 2004).

The test drug showed significant reduction ($p < 0.001$) in the subjective parameters viz. cough *(Kasa)*, dyspnoea *(Shwasa)* and rhinitis *(Pratishaya)*. This results might be the anti-inflammatory, anti-viral (Milad and Mehardad, 2011) and anti-oxidant (Saleem et al., 2001) activity of the *Hingu* i.e. *Ferula narthex* of the HPY formulation and anti-inflammatory (Sharma and Singh, 1980) and anti-oxidant activity (Samudram et al., 2009) of *Piper longum.*

In blood biochemical assay ESR and eosinophil count showed significant reduction ($p < 0.01$) in trial group and significant increase ($p < 0.05$) in control group at the end of intervention. Rest of the biochemical assay didn't show any significant result. ESR is the biochemical marker to assess the inflammatory response of the body. The infiltration of eosinophil into the airways has been linked to the production of IL-5, which is important for eosinophil proliferation, activation and migration (Foster et al., 1996). It has been suggested that eosinophil contributes to tissue damage and airway inflammation. TNF-α is also an important chemo-attractant for the recruitment of eosinophil into the lungs. It is also a potent modulator of immune and inflammatory response. Hence HPY might be acting by inhibiting IL5 cytokine of Th2 lymphocyte activation and its downstream signaling. This results in enhancement of the immune system of individuals receiving test drug. Thereby reduction in the recurrent visits of subjects to the physician for respiratory disorders may be observed.

In pulmonary function test conducted with spirometer, FVC is a forced volume capacity of exhalation in 1 min which determines obstructive pattern and severity whereas FVC% gives idea about severity of obstruction/ restriction. FEV_1 is the forced expiratory volume in 1 sec. FEV_1 between 50% and 80% of predicted value is considered as normal. MVV is a parameter to measure maximum breathing capacity and PEFR i.e. peak expiratory flow rate which indirectly assess the airway hyper responsiveness/degree of airway inflammation. It measures large and medium airway obstruction whereas FEV_1/FVC measures smaller airway obstruction. FEV_1/ FVC<70% indicates the obstructive lung disease.

The decrease in lung function capacity in traffic policemen of both the groups in base line investigation has been speculated. FVC reduction could be due to the changes in the lungs by the chronic irritation of particulate substance of the air pollution. PEFR and FEV_1 reduction in the pulmonary function may be due to the obstruction of airways during expiration. The FEV_1/FVC% ratio in both the groups was found to be normal which indicated restrictive type of lung disorder. All the changes found in both the groups at base line examination could be due to chronic inhalation of particulate matter and toxic gases emitted from the vehicular combustion leading to inflammatory changes (Revathi et al., 2012).

The spirometeric values FVC%, FEV_1%, MVV% and PEFR% showed significant reduction in control group ($p < 0.001$) signifying deterioration in the lung capacity whereas in trial group these values are significantly enhanced ($p < 0.001$) presenting improvement in lung capacity.

As *Piper longum* extracts and piperine possesses inhibitory activities on prostaglandin and leukotrienes COX-l inhibitory effect as well as NF-κB activation and thus exhibit anti-inflammatory activity (Bharat et al., 2011; Jun et al., 2009) also had shown immunomodulator effect, anti-asthamatic activity

(Chauhan et al., 2011). Hence the inflammation caused due to particulate matter gets resolved by test drug resulting in the enhancement in the lung capacity of subjects of trial group.

The present study is conducted on a very small sample size and to generalize the findings extensive trial with greater sample size is essential. Also assessment parameters used were very basic and requires to be carried out with higher and specific biomarkers.

Conclusion

Thus the noteworthy improvement in subjective and objective parameters in the subjects receiving test drug proves that the *Hingu-pippali yoga* (HPY), an Ayurvedic formulation, is effective to reduce the respiratory disorders and enhances the lung capacity in subjects, produced due to the exposure of air pollution.

Acknowlegement

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