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Evaluating the effect of ashwagandharishta on human respiratory system by utilizing spirometry

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Abstract

The key objective of this present study is to analyze the effect(s) of Ashwagandharishta on the lung function of human males. After completing the 45 days of study, the parameter FVC decreased by 3.315 % than the initial period of the study of the control group. On the other hand, the parameters FEV_1, FVFC, PEF, $FEF_{25–75\%}$, MEF 75%, MEF 50% and MEF 25% level was increased by 0.2951 %, 5.600 %, 0.971 %, 4.137 %, 1.909 %, 4.590 %, 5.777 %, 7.182 % and 10.635 % respectively after the 45 days of study than the initial period of the control group. Here no result was statistically significant. After the Chronic administration of Ashwagandharishta (ASG) to human male subjects for 45 days, the values of the parameters FVC, FEV_1, FVFC, PEF, $FEF_{25–75\%}$, MEF 75% and MEF 50% was decreased by 4.109 %, 5.351 %, 1.077 %, 16.042 %, 7.199 % and 21.074 % respectively than the values of the initial period of the study of the ASG treated group. On the other hand, the parameter MEF 25% level was increased by 2.202 % after the 45 days chronic administration of the ASG. No result was statistically significant.

Keyword: Ashwagandharishta, healthy volunteers, male, lung function, spirometry.

INTRODUCTION

Spirometry is designed to identify and quantify functional abnormalities of the respiratory system. Other indications for spirometry are to determine the strength and function of the chest follow disease progression, assess response to treatment, and obtain baseline measurements before prescribing drugs that are potentially toxic to the lungs, such as amiodarone (Cordarone) and bleomycin (Blenoxane). Spirometryalso is helpful in preoperative risk assessment for many surgeries and often is used in workers' compensation and disability claims to assess occupational exposure to inhalation hazards (Timothy *et al.*, 2004).

Spirometry measures the rate at which the lung changes volume during forced breathing maneuvers. Spirometry begins with a full inhalation, followed by a forced expiration that rapidly empties the lungs. Expiration is continued for as long as possible or until a plateau in exhaled volume is reached. The most important spirometric maneuver is the FVC. To measure FVC, the patient inhales maximally, then exhales as rapidly and as completely as possible. Normal lungs generally can empty more than 80 percent of their volume in six seconds or less. The forced expiratory volume in one second (FEV_1) is the volume of air exhaled in the first second of the FVC maneuver. The FEV_1/FVC ratio is expressed as a percentage (e.g., FEV_1 of 0.5 L divided by FVC of 2.0 L gives an FEV_1/FVC ratio of 25 percent). The absolute ratio is the value used in interpretation, not the percent predicted.

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In this present study, spirometry was used to detect any functional abnormalities of the respiratory system after taking Ashwagandharishta for 45 days. Ashwagandharishta is used for the treatment of syncope, in poor digestion, etc.

According to the World Health Organization (WHO), about 80 percent population of the world presently uses herbal medicines for some aspect of primary health care. There is a new interest in traditional medicines because of lower incidence of side effects (Sandhu *et al*., 2010). Ashwagandharishta is a classical ayurvedic formulation which is used in the treatment of *Murchha* (syncope) and *Mandagni* (poor digestive power). It is reported that *Ashwagandha* (*Withaniasomnifera*D.), the key component of *Ashwagandharishta* (Table 1), (Anonymous, 1992), has got anti-stress and anxiolytic activities because it has brain-derived neurotrophic factor (BDNF) that boosts synaptic plasticity, delivers neuro-protection, augments neurotransmission, and produces antidepressant effects (Tanna *et al*., 2012). Moreover it gives anti-ageing, immune-modulatory, cardiovascular protection and hypothyroidism actions as well (Kushwaha & Karanjekar, 2011). Thus *Withania somnifera*, has been recognized as an important herb in the Ayurvedic and indigenous medical systems. The roots of this plant is categorised as *Rasayanas*which promote health and longevity by arresting the ageing process and revitalizing the body in debilitated conditions. Thus it is used as a general tonic as well. Some studies suggest that, it may promote growth in children and improve hemoglobin level by increasing red blood cell count in adults (Sandhu, *et al*., 2010) and increases heart weight and glycogen in myocardium and liver representing intensification of the anabolic process (Kushwaha *et al*., 2012). This study was therefore undertaken to evaluate the effects of Ashwagandharishta on lung function in human males.

MATERIALS AND METHODS

Research design: The present study was designed to investigate the effect of Ashwagandharishta on Lung Function, i.e, the respiratory health condition during the use of this Auyrvedic liquid preparation.

Test drug: For this study, *Ashwagandharishta* was collected from Sri KundeswariAushadhalaya Limited, Chittagong.

Ingredients: Ashwagandharishta was used in a liquid dosage form and the form was prepared using the formula as shown in Table 1.

Sample: Twenty six healthy human males, with a mean age of 22.94 ± 2.66 (aged between 20 and 24 years) years and BMI 21.9 ± 2.2 kg/m^2 (ranged between 18 to 25) from the population of Jahangirnagar University campus volunteered for the study. Here two groups, Control and Ashwagandharishta treated group were utilized for the experiment. Each group contained 13 healthy human male volunteers. The ASG treated group took the ASG for 45 days twice daily at a 15 ml dose [daily total dose 30 ml] with equal amount of water after meal and the control group took only normal water.The subjects were randomly assigned into two groups. Group I (n=13): Ashwagandharishta (ASG) treated group and Group II (n=13): Control group.

Table 1. Botanical name of ingredients along with the amount used to prepare Ashwagandharishta (ASG)

Sanskrit Name	Botanical Name	Amount of ingredient
Ashwagandha	*Withania somnifera*	2.400 kg
Sweta Musli	*Asparagus adscendens*	960 g
Manjishtha	*Rubia cordifolia*	480g
Hareetaki	*Terminalia chebula*	480g
Haridra	*Curcuma longa*	480g
Daruharidra	*Berberis aristata*	480g
Yashtimadhu	*Glycyrrhiza glabra*	480g
Rasna	*Pluchea lanceolata*	480g
Vidarikanda	*Pueraria tuberose*	480g
Arjun Tvak	*Terminalia arjuna*	480g
Mustaka	*Cyperus rotundus*	480g
Trivrit	*Ipomoea turpethum*	480g
Anantamool	*Hemidesmus indicus*	384 g
Krishna Sariva	*Cryptolepis buchanan*	384 g
Rakta Chandan	*Pterocarpus santalinus*	384 g
Chandan	*Santalum album*	384 g
Vacha	*Acorus calamu*	384 g
Chitrak Mool	*Plumbago zeylanica*	384 g
Water for decoction	98.304 L reduced to	12.288L
Dhatakipuspa	*Woodfordia fruticosa*	768 g
Madhu	*Honey*	14.400 kg
Shunthi	*Zingiber officinale*	96 g
Maricha	*Piper nigrum*	96 g
Pippali	*Piper longum*	96 g
Tvak	*Cinnamomum zeylanicum*	192 g.
Tejpata	*Cinnamomum tamala*	192 g.
Elach	*Elettaria cardamomum*	192 g.
Priyangu	*Callicarpa macrophylla*	192 g.
Nagakeshar	*Mesua ferrae*	96g.

Selection of subject: University enrolled young male adults with age between 20 and 24 (mean age 22.94 ± 2.66 years) years were screened. To avoid confounding effects, we included only those whose BMI was between 18 and 25, those individuals who had not participated in regular exercises in gym from past 6 months or more and who were free from any lower limb injury within past six months. Individuals who were engaged in regular strenuous physical activity, suffering from chronic illness or had undergone major surgery recently, were suffering from any cardiovascular, musculoskeletal or neurological condition or were under medication of other drugs were excluded. There was no history of drug allergy, smoking, chewing tobacco in any form, alcoholism or other drug addiction.

Variables for effect: The following variables were assessed before and after drug administration under supervision and while ensuring safety of the subjects:

1. Weighing machine (Auto-Inc) and kinanthropometric rod were used to measure body mass (kg) and vertical height (meter) to calculate Body Mass Index (BMI).
2. Spirometer (Cosmed, 37, Via dei Piani di Monte Savello, I-00041-Rome, Italy.) was used to measure the different parameters of lung function.

Procedure: The study was approved by the Board of Advanced Studies of the Department of Pharmacy, Jahangirnagar University, Savar, Dhaka, Bangladesh. Prior to the start of data collection, participants were explained about the drugs and previous research supporting the effectiveness on physical performance and possible side effects due to overdose. After that discussion, the University students agreed for the study.

Monitoring of subjects: All subjects were healthy University enrolled young adults with moderately active life style. The subjects were instructed to follow the usual routine without any excess physical exertion or exercises throughout the duration of experiment. All the subjects consumed the same meals given in the dormitory throughout the experimental period and were requested to have meals within specified time. The researcher(s) always monitored the volunteers while taking the experimental drugs. Volunteers were asked to consume the drug (ASG) after the breakfast and dinner to maintain uniformity of the drug administration. Though the subjects were informed about possible side effects of the drugs in high dosage, subjects were also asked to report immediately if they feel any side-effect of the drugs but none of them felt any kind of the side-effect.

Statistical analysis: The group data were expressed as Mean ± SEM (Standard Error of the Mean). The data was analyzed for statistical significance by using the Statistical Package for Social Sciences (SPSS 17.0) software. The Independent -'t' test were done for statistical significance tests for the clinical study. 95% confidence limit was taken as level of significance.

For the analysis, the 'p' value used for statistical significance was 0.05, 0.01 and 0.00 (Steel and Torrie, 1986; Snedecor and Cochran, 1980; Hannan, 2007; Mahajan, 1997).

RESULTS AND DISCUSSION

Spirometry is a method of assessing lung function by measuring the volume of air that the patient is able to expel from the lungs after a maximal inspiration. It is a reliable method of differentiating between obstructive airways disorders (e.g. COPD, asthma) and restrictive diseases (where the size of the lungs is reduced, e.g. fibrotic lung disease). Spirometry is the most effective way of determining the severity of COPD. However, other measures such as the MRC dyspnoea scale1 and quality of life assessment forms a more complete picture. Severity cannot be predicted from clinical signs and symptoms alone (David *et al.*, 2005*).*

Spirometric values: The most common parameters measured in spirometry are Vital capacity (VC), Forced vital capacity (FVC), Forced expiratory volume (FEV) at timed

intervals of 0.5, 1.0 (FEV_1), 2.0, and 3.0 seconds, forced expiratory flow 25–75% (FEF 25–75) and maximal voluntary ventilation (MVV) also known as maximum breathing capacity (MBC). Other tests may be performed in certain situations.

Results are usually given in both raw data (litres, litres per second) and percent predicted—the test result as a percent of the "predicted values" for the patients of similar characteristics (height, age, sex, and sometimes race and weight). The interpretation of the results can vary depending on the physician and the source of the predicted values. Generally speaking, results nearest to 100% predicted are the most normal, and results over 80% are often considered normal.

Forced Vital Capacity (FVC): It is the volume of air that can forcibly be blown out after full inspiration (Perez, 2013), measured in liters. FVC is the most basic maneuver in spirometry tests.

Forced Expiratory Volume in 1 second (FEV_1): FEV_1 is the volume of air that can forcibly be blown out in one second, after full inspiration (Perez, 2013). FEV_1 (forced expired volume in one second) is the volume expired in the first second of maximal expiration after a maximal inspiration and is a useful measure of how quickly full lungs can be emptied (David & Pierce, 2008).

Average values for FEV1 in healthy people depend mainly on sex and age (LUNGFUNKTION, 2010).

FEV_1/FVC ratio (FEV_1%): It is the ratio of FEV_1 to FVC. In healthy adults this should be approximately 75–80%. In obstructive diseases (asthma, COPD, chronic bronchitis, emphysema) FEV_1 is diminished because of increased airway resistance to expiratory flow; the FVC may be decreased as well, due to the premature closure of airway in expiration, just not in the same proportion as FEV_1 (for instance, both FEV_1 and FVC are reduced, but the former is more affected because of the increased airway resistance). This generates a reduced value (<80%, often ~45%). In restrictive diseases (such as pulmonary fibrosis) the FEV_1 and FVC are both reduced proportionally and the value may be normal or even increased as a result of decreased lung compliance.

Forced Expiratory Flow (FEF): It is the flow (or speed) of air coming out of the lung during the middle portion of a forced expiration. It can be given at discrete times, generally defined by what fraction remains of the forced vital capacity (FVC). The usual intervals are 25%, 50% and 75% (FEF25, FEF50 and FEF75), or 25% and 50% of FVC. It can also be given as a mean of the flow during an interval, also generally delimited by when specific fractions remain of FVC, usually 25–75% (FEF25–75%). Average ranges in the healthy population depend mainly on sex and age. Values ranging from 50-60% and up to 130% of the average are considered normal (LUNGFUNKTION, 2010).

Maximum Expiratory Force (MEF): It is the peak of expiratory flow as taken from the flow-volume curve and measured in liters per second. It should theoretically be identical to peak expiratory flow (PEF), which is, however, generally measured by a peak flow meter and given in liters per minute (Hedenström, 2009).

Recent research suggests that FEF25-75% or FEF25-50% may be a more sensitive parameter than FEV1 in the detection of obstructive small airway disease (Simon, Michael *et al.,* 2010; Ciprandi *et al.,* 2011). However, in the absence of concomitant changes in the standard markers, discrepancies in mid-range expiratory flow may not be specific enough to be useful, and current practice guidelines recommend continuing to use FEV1, VC, and FEV_1/VC as indicators of obstructive disease (Pellegrino *et al.,* 2005; Kreider, 2011).

Peak Expiratory Flow (PEF): It is the maximal flow (or speed) achieved during the maximally forced expiration initiated at full inspiration, measured in liters per minute or in liters per second.

Spirometry Test Results: The result of the Control group and ASG treated group is summarized in Table 2 and 3.

Table 2. The paired-samples t -test for lung function test parameters level analysis utilizing adult human male volunteers of control group before (c_1) and after (C_2) 45 days

Parameters	Group				Percentage of change	p = probability value
	CON (C_1) (N=13)		CON (C_2) (N=13)			
	Mean	± SEM	Mean	± SEM		
FVC	3.721	0.168	3.598	0.087	↓3.315 %	0.558
FEV_1	3.117	0.127	3.126	0.083	↑0.295 %	0.952
FVFC	81.833	3.577	86.416	1.611	↑5.600 %	0.169
PEF	7.383	0.354	7.455	0.329	↑0.971 %	0.893
$FEF_{25–75\%}$	3.405	0.333	3.546	0.216	↑4.137 %	0.664
MEF 75%	6.243	0.388	6.362	0.315	↑1.909 %	0.822
MEF 50%	3.975	0.355	4.158	0.238	↑4.590 %	0.540
MEF 25%	1.774	0.191	1.876	0.163	↑5.777 %	0.647

Values are presented as mean ± SEM (n=13). Independent paired students "t" tests were performed to analyze the data set. *p <0.05, *p<0.01 and *p<0.001 was considered statistically significant. *(asterisk) marks represents statistically significant. Values are self explanatory. ↑: increase, ↓: decrease.

After completing the 45 days of study, the value of the parameter FVC decreased by 3.315 % than the value of the starting moment of the study of the control group. On the other hand, the parameters FEV_1, FVFC, PEF, $FEF_{25–75\%}$, MEF 75%, MEF 50% and MEF 25% level was increased by 0.2951 %, 5.600 %, 0.971 %, 4.137 %, 1.909 %, 4.590 %, 5.777 %, 7.182 % and 10.635 % respectively after the 45 days of study than the starting moment of the control group. Here no result was statistically significant. This data is summarized in Table 2.

Table 3. The paired-samples t -test for lung function test parameters level analysis utilizing adult human male volunteers of asg group before (d_1) and after (D_2) 45 days

Parameters	Group				Percentage of change	p = probability value
	ASG (D_1) (N=13)		ASG (D_2) (N=13)			
	Mean	± SEM	Mean	± SEM		
FVC	3.760	0.185	3.605	0.208	↓4.109 %	0.592
FEV_1	3.195	0.168	3.024	0.175	↓5.351 %	0.540
FVFC	84.363	0.754	83.454	1.460	↓ 1.077 %	0.558
PEF	8.035	0.469	6.746	0.557	↓16.042 %	0.155
$FEF_{25–75\%}$	3.497	0.249	3.245	0.254	↓7.199 %	0.564
MEF 75%	7.070	0.463	5.580	0.464	↓21.074 %	0.111
MEF 50%	4.167	0.293	3.760	0.297	↓9.773 %	0.430
MEF 25%	1.607	0.117	1.642	0.176	↑2.202 %	0.879

Values are presented as mean ± SEM (n=13). Independent paired students "t" tests were performed to analyze the data set. *p <0.05, *p<0.01 and *p<0.001 was considered statistically significant. *(asterisk) marks represents statistically significant. Values are self explanatory. ↑: increase, ↓: decrease.

After completing the 45 days of study, the values ofthe parameters FVC, FEV_1, FVFC, PEF, $FEF_{25–75\%}$, MEF 75% and MEF 50% was decreased by 4.109 %, 5.351 %, 1.077 %, 16.042 %, 7.199 % and 21.074 % respectively than the values of the starting moment of the study of the ASG treated group. On the other hand, the parameter MEF 25% level was increased by 2.202 % after the 45 days chronic administration of the ASG. No result was statistically significant. This data is summarized in Table 3.

So, from the above results, this can be summarized that in all cases that is in comparing between the control and drug treated group, the changes of results were not statistically significant.

Conclusion: In this study, no statistically significant change was observed for the lung function test of the human male volunteers by utilizing Ashwagandharishtha. The present study was limited to a 45 days period on healthy young male adults. The future research should focus on longer treatment duration as well as gender specific effects of the drug. From the summary of this study, it can be noted that ASG has no injurious or beneficial effect on the lung function parameters. So this drug can't improve or deteriorate the lung function parameters. So this preparation can be used for the *Murchha* (syncope), *Mandagni* (poor digestive power) etc without any harmful effect on the lungs. Further studies are also required to assess whether the drug can improve other physical parameters or not and to see the effectiveness in elite sportsmen or sportswomen or even defense personal in special duty assignment so that in future these drugs can be taken as ergogenic preparation. At this stage, it is important to find out the effect of Ashwagandharishtha to the cellular level. Thus, it is strongly recommended to look at this ground for future study. However, further studies are necessitated to identify the exact mechanism of action of this formulation.

Ethical approval: The present study was approved by the Biosafety, Biosecurity and Ethical Committee of Faculty of Biological Sciences, Jahangirnagar University, Savar, Dhaka-1342, Bangladesh, Reference no BBECJU /M2017 (3)2.

Conflicts of interest: No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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