Assessment Of Reversibility Of Airway Obstruction In Bronchial Asthma With Pulmonary Function Tests

N T CHAUDRY S J KHAN* T A KHAN**

Department of Physiology, Allama Iqbal Medical College, Lahore. Department of Physiology, King Edward Medical College, Lahore.* *, Department of Physiology, Fatima Jinnah Medical College, Lahore.*

Correspondance to: Dr. Nayla Tariq Chaudry.

Pulmonary function tests (PFTs) are a useful tool in diagnosis of respiratory disorders, assesment of their severity and response to therapy. The evaluation of PFT was conducted in mild asthmatics. The differential evaluation was based on the use of salbutamol as a bronchodilator for 20 cotrol and 20 mild asthmatic subjects in the study group both age and sex matched. The baseline value of FEV_1 below 80% of predicted standard was used as an index for subclinical hyperresponsive behaviour of asthmatic group. Reversibility was defined as a response in FEV_1 of 15% or more from baseline or a minimum increase of 200ml after bronchodilator inhalation. Spirometric as well as volume related parameters were measured. Blood gas analysis was also performed. The response of asthmatic group was compared with control group before and after salbutamol inhalation. In mild asthmatic group, statistically highly significant difference ($p<0.01$) in pre and post bronchodilator values of vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), forced expiratory flow 25-75% (FEF 25-75), thoracic gas volume (TGV), airway resistance (Raw) and peak expiratory flow rate (PEFR) shows a decreased hyper responsive behaviour. There was highly significant difference ($p<0.01$) in base line values of VC, FVC, FEV_1, FEV_1/FVC %, FEF 25-75%, TGV, Raw and PEFR amongst asthmatic and control groups. This study reveals that flow rates and static lung volumes are helpful in assessing reversibility in airway obstruction.

Key Words Pulmonary function tests, reversibility, $ß_2$ Agonists, Bronchial asthma.

Bronchial hypersensitivity to specific and nonspecific stimuli is one of the characteristic properties of bronchial asthma[1]. There is a relation between airflow limitation and bronchial hyper-responsiveness, defined as narrowing of the airways in response to a wide variety of provoking agents that have little or no effect in normal subjects[2,3].

Airflow obstruction in asthma is partially or completely reversible either spontaneously or with appropriate treatment[4]. Assessment of a bronchodilator response is used as a tool to distinguish "reversible" from "irreversible" airway obstruction, a key difference between asthma and chronic obstructive pulmonary disease (COPD)[5]. Reversibility is defined as a change in Forced Expiratory Volume in first second (FEV_1) of 15% or greater from baseline or a minimum increase of at least 200ml[6].

It is essential to assess lung function at baseline and after the administration of inhaled bronchodilator, to determine what improvements in airflow are possible[7]. Bronchodilators with $ß_2$ selectivity are suitable for use in pulmonary function laboratory as having lesser cardiovascular side effects and produce greatest bronchodilation in subjects with airway hyper responsiveness[8]. Salbutamol is among the most potent of these drugs and acts primarily to dilate small diameter airways[9,10].

The characteristic response to bronchodilator administration in reversible obstructive airway disease is an increase in flow rates at a given lung volume. The degree of responsiveness can be assessed by comparing measurements, before and after administration of bronchodilator, of timed expiratory volumes, flow parameters as forced expiratory flow (FEF 25-75%) or airway resistance (Raw)[11]. Static lung volumes such as Thoracic gas volume (TGV), Total lung capacity (TLC) and specific conductance (sGaw) may improve significantly[12]. Peak expiratory flow rate (PEFR) is useful in assessing severity of obstruction and reversibility in patients with asthma[13].

Blood gas measurement is used as an index of state of lung function. Arterial pO_2, pCO_2 and pH reflect not only the state of lung but also the condition under which lung is operating[14].

Present study was aimed to assess and compare the respiratory functions in middle aged non-smoker, non-asthmatic males with non-smoker mild asthmatics. Response to inhaled salbutamol 200µgm in all these subjects was also assessed.

Materials And Methods

In this study, 40 male subjects aged 40-60 years, belonging to middle socio economic group were included[15]. They were divided into:

a) Control Group (20 cases)-- Selected by simple random technique from students and staff of PGMI, Lahore. Inclusion criteria: no structural deformity of thoracic cage, no respiratory infection for at least three months prior to testing, no history of wheeze, non-smokers, baseline FEV_1 above 80% of predicted value[16].

b) Mild Asthmatic Group (20 cases)- Selected from out-patient departments of Services Hospital and Asthma Clinic, Mayo Hospital, Lahore.

Subjects having infrequent episodes of cough and wheeze with long symptom free periods or subjects having mild disease with some daily symptoms controlled by simple inhaled bronchodilator therapy were included[17]. Subjects having baseline FEV_1 less than 60% of the predicted value were excluded[6].

None of the subjects had any other cardio-pulmonary disease, as assessed by detailed history, physical examination, chest radiography, and electro-cardiography. Smokers were not included. A consent proforma was obtained.

Pulmonary function tests (PFTs) were carried out with Body Plethysmograph (Model 2.2 P.K Morgan, U.K) having fleish type pneumo-techograph. Readings were obtained from attached computer. The equipment was calibrated fully every day before starting the tests.
Standing height to the nearest centimetre without shoes, weight in kilograms, age and occupation were recorded for each subject. Tests were carried out with subject seated and nose clip applied.

Baseline Vital capacity (VC), Forced vital capacity (FVC), FEV_1, FEV_1/FVC %, FEF 25-75%, TGV, TLC, Raw, PEFR, PaO_2, $PaCo_2$ & pH were performed prior to drug administration. Tests were repeated 30 minutes after drug administration (salbutamol 200 µgm by metered dose inhaler). In mild asthmatic group, use of bronchodilator was with-held 12 hours before basal testing[10].

At least three FVC maneuvers according to standard methods recommended by American Thoracic Society were obtained for each subject[18]. The largest of the three FVCs and FEV_1 was accepted. The ratio of FEV_1 to FVC was expressed as a percentage. FEF 25-75% and PEFR were also measured.

TGV and TLC were measured while subjects were seated in the body box. Doors of the body box were sealed while subject performed the maneuver. Mouth pressure and plethysmographic pressure were sampled and used to calculate TGV at a point against a closed mouth shutter. During next stage the mouth shutter opened and subject inspired to total lung capacity and expired forcefully to residual volume (RV).

Airway resistance (Raw) was measured by panting at an approximate rate of 120 per minute. Blood gas analysis was performed on a radial artery blood sample obtained antiseptically. Testing was done within three minutes of taking out the sample on gas analyzer (Corning Model 1.20).

Data is reported as mean ± standard deviation (S.D.). Groups were compared by student t-test. A p-value less than 0.05 was considered statistically significant.

Results

Table 1: Effect of salbutamol inhalation on pulmonary function testsIn control group

PFTs	*Before Inhalation (n = 20) Mean±S.D.*	*After Inhalation (n = 20) Mean±S.D.*	*P-Value*	*Sig.*
VC, lit.	4.30±0.62	4.46±0.70	p>0.05	NS
FVC, lit.	3.90±0.42	3.98±0.44	p>0.05	NS
FEV_1, lit.	3.32±0.37	3.37±0.39	p>0.05	NS
FEV_1/FVC, %	86.34±6.58	84.74±4.07	p>0.05	NS
FEF 25-75%	3.83±0.61	3.85±0.67	p>0.05	NS
TGV, lit.	3.55±0.41	3.44±0.29	p>0.05	NS
TLC, lit.	6.47±0.53	6.52±0.65	p>0.05	NS
Raw	0.12±0.04	0.11±0.03	p>0.05	NS
PaO_2, mmHg	96.51±4.49	96.56±4.95	p>0.05	NS
$PaCo_2$ mmHg	38.95±2.91	39.28±2.95	p>0.05	NS
pH	7.41±0.02	7.41±0.02	p>0.05	NS
PEFR, lit/sec	6.98±0.84	7.34±1.03	p>0.05	NS

NS = Non-significant,n = Number of subjects

Table: 3 Pulmonary function testsin control and mild asthmatic groups before salbutamol inhalation

Pfts	Control Group (N = 20) Mean±S.D.	Mild Asthmatics (N = 20) Mean±S.D.	P-Value	Sig.
VC, lit.	4.30±0.62	3.75±0.54	p<0.01	HS
FVC, lit.	3.90±0.42	3.04±0.43	p<0.01	HS
FEV_1, lit.	3.32±0.37	2.46±0.27	p<0.01	HS
FEV_1/FVC, %	86.34±6.58	80.48±9.52	p<0.01	HS
FEF 25-75%	3.83±0.61	2.32±0.71	p<0.01	HS
TGV, lit.	3.55±0.41	4.27±0.64	p<0.01	HS
TLC, lit.	6.47±0.53	6.75±0.97	p>0.05	NS
Raw	0.12±0.04	0.51±0.26	p<0.01	HS
PaO_2, mmHg	96.51±4.49	97.39±3.98	p>0.05	NS
$PaCo_2$ mmHg	38.95±2.91	39.61±2.63	p>0.05	NS
pH	7.41±0.02	7.41±0.02	p>0.05	NS
PEFR, lit/sec	6.98±0.84	4.39±1.17	p<0.01	HS

HS = Highly Significant.NS = Non-significant.n = Number of subjects

Table: 4 Effect Of Inhaled Salbutamol On Pulmonary Function Tests In Control And Mild Asthmatic Groups

PFTs	Control Group (n = 20) Mean±SD	Mild Asthmatic group (n = 20) Mean±SD.	p-Value	Sig.
VC, lit.	4.46±0.70	4.56±0.56	p>0.05	NS
FVC, lit.	3.98±0.44	3.84±0.50	p>0.05	NS
FEV_1, lit.	3.37±0.39	3.13±0.48	p>0.05	NS
FEV_1/FVC, %	84.74±4.07	82.76±8.12	p>0.05	NS
FEF 25-75%	3.85±0.67	3.38±0.57	p<0.05	S
TGV, lit.	3.44±0.29	3.29±0.45	p>0.05	NS
TLC, lit.	6.52±0.65	6.12±0.64	p>0.05	NS
Raw	0.11±0.03	0.13±0.05	p>0.05	NS
PaO_2, mmHg	96.56±4.95	98.27±3.82	p>0.05	NS
$PaCo_2$ mmHg	39.28±2.95	39.99±2.58	p>0.05	NS
pH	7.41±0.02	7.41±0.01	p>0.05	NS
PEFR, lit/sec	7.34±1.03	6.31±1.04	p<0.01	HS

S = Significant, HS = Highly Significant ,NS = Non-Significant ,N = Number Of Subjects

Table: 5 Comparison Of Mean Age,Weight & Height In Control And Mild Asthmatic Groups

Parameters	Control group (n = 20) Mean±S.D.	Mild Asthmatic Group (n = 20) Mean±S.D.
Age (Yrs)	42.90±7.48	38.50±7.47
Weight (Kg)	71.10±9.44	65.35±9.38
Height (M)	1.68±0.07	1.68±0.06

n = Number of subjects

The spirometric and lung volume data collected from

40 subjects before and after bronchodilator inhalation is presented/compared in Tables 1-4. The mean physical characteristics of all the subjects in control and mild asthmatic groups are given in Table:5 and shown in
Effect Of Bronchodilator Inhalation On PFTs In:

Mild Asthmatic Group

Effect of salbutamol inhalation on PFTs in mild asthmatic group is given in Table:1. It shows statistically highly significant ($p<0.01$) difference in pre and post bronchodilator values of VC, FVC, FEV_1, FEV_1/FVC %, FEF 25-75%, TGV, TLC, Raw & PEFR while statistically non-significant ($p>0.05$) difference in case of PaO_2, $PaCo_2$ and pH.

Control Group

Effect of salbutamol inhalation on PFTs in control subjects is summarized in Table:3. It shows statistically non-significant difference ($p>0.05$) in pre and post bronchodilator values of all the PFTs.
Comparison of PFTs in control & mild asthmatic groups:

Pre-Inhalation

A comparison of PFTs in control and mild asthmatic groups before salbutamol inhalation is given in Table:2. It shows statistically highly significant difference in the values of VC, FVC, FEV_1, FEV_1/FVC %, FEF 25-75%, TGV, Raw and PEFR while incase of TLC, PaO2, PaCo2 and pH, the difference is statistically non-significant.

Post-Bronchodilator Inhalation

Effect of inhaled salbutamol in control and mild asthmatic groups is compared in Table:4. The difference is statistically significant ($p<0.05$) in the values of FEF 25-75% and highly significant ($p<0.01$) in case of PEFR whereas in all other PFTs it is statistically non-significant ($p>0.05$).

Discussion

It is recognized that the degree of airflow limitation rather than symptoms of disease is the important factor in determining outcome in patients with obstructive lung disease. Airflow limitation is improved in many patients by bronchodilator drugs.

It is common clinical practice to include an assessment of reversibility as a part of diagnostic evaluation of patients with asthma. The percentage of post-bronchodilator change from base line in various parameters is used to interpret this type of study.

In our study the data indicate that patients with reversible obstructive airway disease can be identified in the pulmonary function laboratory by improvement in post-bronchodilator dynamic lung function parameters as FVC, FEV_1 and FEF 25-75%. Also there is improvement in static lung volumes as is in case of VC, TGV and Raw. These results are comparable to the results reported by Ramsdell and Tisi[19] and Brand etal[5], showing statistically significant improvement in FVC, FEV_1, FEF 25-75% and also in static lung volumes after inhaled bronchodilator in mild asthmatic group[20]. So spirometric parameters as FEV_1, FVC and FEF 25-75% give a satisfactory method of evaluating reversibility of airways obstruction in majority of patients. In borderline hyperresponsive cases assessment of volume related parameters are helpful in identifying reversibility following inhalation of β_2 agonists.

There was statistically significant improvement in post-bronchodilator PEFR in mild asthmatic group. Dekker et-al have shown that increase in PEFR is an equally good parameter as percentage increase in FEV_1, to assess reversibility in asthma or chronic obstructive airway disease[13]. Mild asthmatic subjects showed that baseline FEV_1/FVC % was reduced which is a primary indicator of airflow obstruction. Once obstruction is diagnosed, its severity is classified by using FEV_1% of predicted value[21]. Analysis of the baseline parameters revealed a statistically significant difference in values among control and mild asthmatic groups. These results are in agreement with those reported by Hussain and Ansari[22].

The effect of a single bronchodilator dose reflects only acute reversibility, which is probably largely determined by relaxation of airways smooth muscles. In common usage reversibility implies a complete abolition of physiological impairment seen in asthmatic patients. It is used to signify an improvement in pulmonary function greater than could be predicted by random variation of measurement. Improvement in volume related parameters may be due to several factors; volume related plethysmographic parameters are not as effort dependent as forced maneuvers of spirometry and are thus more reliable in subjects who are unable to produce consistently maximal effort. In addition during a forced maneuver, airway collapse or compression due to loss of elastic recoil may mask a beneficial effect to bronchodilator.

Control group showed a statistically nonsignificant difference in values of pre and post bronchodilator PFTs. Our results are comparable with the normal range of values in Pakistani adult males[16,23].

The data demonstrates values of PaO_2 , $PaCO_2$ and pH to be within normal range for both pre and post-bronchodilator PFTs in all the subjects and are in accordance with the previous reports showing that until there is some restrictive disorder these values remain within normal limits[24].

Conclusion

1. Pre bronchodilator PFTs show a highly significants difference between values of control and mild asthmatic groups in flow rates and static lung volumes.
2. After salbutamol inhalation there was more improvement in the flow rates and volumes in mild asthmatic group as compared to control group.
3. FEV_1% change is a useful and valid measure of bronchodilator response.
4. Assessment of FVC, FEF 25-75%, static lung volumes and Raw yield meaningful additional information regarding reversibility of airways obstruction.

5. Absolute improvement in PEFR is a useful and simple criteria to measure reversibility.

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