

Interpretation of Bronchodilator Response for Assessment of Airway Obstruction.

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ABSTRACT: Improvement in lung function studies following bronchodilator inhalations leads to different pattern of response in ventilatory parameters which are helpful in categorizing these patients into groups for correct interpretation of bronchodilator response and assessment of prognosis of the disease.

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INTRODUCTION

The assessment of lung function before and after Bronchodilator therapy is of value to the physician for diagnosis.^{1,2} Determination of simple spirometric volumes in initial and after bronchodilator therapy helped in finding out the change in pattern of obstruction of airways which led to the categorization of various functional groups in the present study.

Salbutamol chosen as BD(Broncho dilator), has been administered through metered dose aerosol. In the course of evaluation of large number of patients with BD medication in our respiratory laboratory the potential efficacy of BD therapy in airway obstruction has been confirmed by improvement in either “forced volumes” or “flow rates” or” both”.

MATERIALS AND METHODS

Ventilatory parameters of 2170 adult patients were included for the study. The study conducted for a period of 18 months. Among them 60.2% were males (1307 nos) and 39.8 were females (863 nos). All are with chronic airflow limitation (CAL) & regular visitors of our Op & with frequent exacerbation of symptoms.(TABLE-1)

Conventional spirometry used to be performed using Dry rolling seal computerized spirometer in sitting posture three times and results calculated from the best of the three tracings. No patient was studied during acute attack and when the PEFr is less than 100 lit/minute. patients were put on nebulizer till they become free from breathlessness. These Patients were taught as to how to inhale BD from pressurized canister and how to record daily 4-5times (7am. 11am 2pm, 6pm 9 pm) their PEFr reading using the mini peak flow meter and the readings has to be recorded in a pocket note book . When they find a dip in PEFr reading they have to take 2 puffs of BD with an interval of one minute from the pressurized canister by themselves. The patents will be reviewed after 3 days and conventional spirometry will be repeated. Baseline parameters such as FVC, FEV₁, FEV₁% and flow-rates such as FEFR_{25-75%} and FEFR_{25-50%} and 75% were analysed for all patients included for study.

Patients used no BD atleast 12 hours prior to study.. Within 15-20 mints after Salbutamol spray pulmonary function tests were repeated.

The results of pre and post BD effect on ventilatory indices were evaluated and patients were grouped according to the pattern of response on ventilatory parameters. VC, FVC were used for assessing lung volumes and FEV₁, FEFR 25%, 50%, 75% & FEFR_{25-75%} for assessing flow rates. The significant level of change in these parameters for initial grouping were as follows.

Change in post BD value for VC, FVC differ from baseline by greater than 11-13 %. Change in post BD FEV₁ from baseline was greater than 15%. Similarly change in post BD FEV₁% differed from baseline value by 5% and post bronchodilator changes with FEFR_{25-75%} was 12-15%

greater than baseline. These differences in response in volumes and flow rates were taken for consideration for categorizing the patients into the above three groups.

Thus patients were categorized according to the type of response of these indices to BD therapy as follows.

Flow responders— showed significant improvement in flow rates such as FEFR₂₅, 50-75% and FEFR_{25-75%} (Table-2)

Flow-Volume responders (or Dual responders)- showed significant improvement in volumes FVC, VC as well as flow rates (FEFR at 25%, 50%, 75% and FEFR_{25-75%}). The statistical significance of intergroup difference in baseline pulmonary function and response to BD were evaluated. (Table-3)

Volume responders— Statistically significant improvement in VC and FVC alone.(Table4)

Non responders-are those whose bronchospasm could not be relieved by single administration of salbutamol spray and required oral/ parenteral administration of combination of BD with steroids. . Therefore their data was not included for this study.

RESULTS & OBSERVATION

The magnitude of change in lung volumes (VC, FVC) for Volume responders was very high. There was no significant difference between volume responders and dual response group when change in VC, FVC was considered. The increase in volume in these two groups were significantly different from the volume response in the isolated flow responders ($p < 0.001$)

Similarly there was no significant difference between the Flow Responders and the dual response group in the level of improvement in forced flow rates. The increase in expiratory flow in these two groups were significantly different from the flow response in the volume Responders ($p < 0.001$).

In the Flow Responders and in the Dual Response group there was significant fall in the difference between slow (SVC) and Forced Vital Capacity (FVC) maneuvers following inhalations of salbutamol. But there was no significant change in the measurement in the Volume Responders. The VC for the volume responders was smaller than the baseline VC of both the flow responders and the dual responders but this is not statistically significant ($p < 0.12$) There was no significant difference in baseline VC between the flow responders and Dual Responders.

The Volume Response and the Dual Response were not significantly different in terms of $FEV_{1\%}$ and both had significantly more impaired $FEV_{1\%}$ than the flow responders ($p < 0.05$). The volume response group had a significantly lower $FEFR_{25-75\%}$ and also $FEFR$ at 25%, 50% and 75% than the flow response group ($p < 0.001$). The flow rates of Dual Response group was intermediate between the other Responder group ($p < 0.05$). Therefore it is apparent from the study that the Volume Responders had significantly severe airways obstruction than the Flow Responders.

Another observation made from the study is that mostly patients in the younger age group are Dual Responders. In Dual Responders the obstruction is mild to moderate, there is less hyper inflation (revealed by VC-FVC difference) of the lung for this group. Flow Responders are

identified to be having milder airways obstruction. There was not much difference between the age among flow and dual responders.

Volume Responders in our study had moderate to severe airways obstruction. They were ill patients with chronic airflow limitation and belonged to older age group. There appeared to be more hyperinflation of the lung (VC-FVC difference is minimum). Some had emphysematous changes in lung (supported by x-ray findings). Flow Responders and Dual Responders were mostly adult men and women between 30-50 years of age and most of them with definite atopy and responding well to BD and prophylactics whereas prognosis was poor in Volume Responders. In about 70 patients (43 male & 27 females) there were no clearcut responses to aerosol therapy and they required steroid administration with more than one BD for relief of their bronchospasm. They responded sometimes with improvement in both volumes and flow-rates and sometimes improvement with either flow-rate alone or volume alone.

DISCUSSION

Several studies have shown that bronchodilator inhalations brings about effective bronchodilation³. salbutamol was chosen as the BD for following reasons. salbutamol differs from other sympathomimetic drugs by acting selectively on beta adrenergic receptors.⁴ Also it differs from other sympathomimetic drugs in being a saligenin derivative instead of catechol.⁵ salbutamol is the most potent, powerful, rapid and long acting BD.^{6,7} with very minimal side effect on cardiovascular system when given as aerosol^{6,8} This indicates that patients with reversible airway obstruction can be identified by selective improvement either in lung volumes or flow rates. There were clear

differences in response of these patients in these three groups and with different patterns of obstruction occurring in episodic attack of airway obstruction⁹.

The differences in response to BD may be attributed to several aspects of airway function such as status of smooth muscle tone, secretion of sub mucous gland, broncovascular tone and permeability and secretion from mast cells which brings about different degree of narrowing of airways at all levels during attack¹⁰.

Thus control of human airways is more complex than previously recognized.⁴ The interpretation of results may be attributed to total closure of some airways or partial closure of majority of airways or complete closure of minor airways with narrowing or partial obstruction of rest of airways¹¹. The varying pattern of response demonstrated in the present study is probably due to differences in the status of airways and their response to BD⁷.

Identification of either Lung Volume Response or Flow-Rate Response shown in the study as an index of bronchodilatation has far reaching implication for the clinical pulmonary function laboratory where direct measurements of airway resistance is not available. If changes in FEV1 & its % alone were utilized to recognize bronchodilatation as done before, then a significant number of patients in the present study would not be recognized as having bronchodilatation in response to BD with reversible airway obstruction. Such incorrect characterisation may be translated at a clinical level to withholding of BD.

We interpret these data to indicate that changes in any "Ventilatory Volumes" or either "Flow-Rates" after BD to be utilized as an index of bronchodilation and categorization of patients into groups mentioned

in our study and another significant information obtained from the present study is categorization of degree of airways obstruction as mild, moderate and severe as well as hyperinflation of lung will be helpful in assessing the prognosis of the disease.

CONCLUSIONS

Bronchodilator response in COPD assessed by Ventilatory function tests is useful not only in categorizing the patients according to their response in "only flow rates" or "volume" or "both" but also helps in determining the prognosis of disease and assessment of patients involved with "only airways" or "volume" with involvement of parenchyma & alveoli or "both". Thus helps in treatment of patients with only BD or BD with antibiotics or BD with antibiotics and steroids. BD response assessment with ventilator function also helps to differentiate cardiac asthma (non-responders) from atopy.

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TABLE-1

CATEGORISATION OF PATIENTS INTO GROUPS FOR STUDY

GROUP	MALE- NO	MALE%	FEMALE-NO	FEMALE%
2170	1307	60.2	863	39.8
FLOW-VOL RESPONDERS	561	42.9	275	31.9
FLOW RESPONDERS	503	38.5	437	50.6
VOLUME RESPONDERS	200	15.3	124	14.4
NON--RESPODERS	43	3.3	27	3.1

TABLE 2

VENTILATORY INDICES FOR FLOW RESPONDERS

INDICES	PRE BD	POST BD	% OF	P
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	VALUE/SD	VALUE/SD	RESPONSE	VALUE
VC-- LIT	3.183/0.220	3.132/0.310	2	NS
FVC-LIT	3.000/0.219	3.240.0.229	5	NS
FEV ₁ -LIT	1.680/0.189	1.984/0.174	18.1	0.05
FEV1%	56/8	64/6	9	0.5
VC-FVC	163/50	--110/41	49	0.05
FEFR _{25%} LIT/SEC	3.8/0.12	5.3/0.13	39.5	0.001
FEFR _{50%} LIT/SEC	2.9/0.9	3.9/0.11	34.5	0.001
FEFR _{75%} LIT/SEC	0.8/0.05	1.2/0.06	50	0.001
FEFR _{25-75%} LIT/SEC	2.2/0.12	3.2/0.14	45	0.001

TABLE.3

VENTILATORY RESPONSES IN DUAL RESPONDERS

INDCES	PRE BD	POST	%	P
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	VALUE/SD	BDVALUE/SD	RESPONSE	VALUE
VC - LIT	2.950/0.26	3.60/0.285	13	0.05
FVC-LIT	3.00/0.199	3.90/0.219	25	0.001
FEV1-LIT	1.74/0.99	2.29/0.107	32	0.001
FEV1--%	59/7	68/6	9	0.05
VC-FVC-LIT	80/36	-50/44	40	0.05
FEFR _{25%} LIT/SEC	3.2/0.12	4.1/0.19	28	0.05
FEFR _{50%} LIT/SEC	2.90/0.09	3.6/0.10	24	0.001
FEFR _{75%} LIT/SEC	0.85/0.02	0.97/0.40	33	0.001
FEFR _{25-75%} LIT/SEC	2.0/0.06	2.9/0.08	31	0.001

TABLE-4
 VENTILATORY INDICES IN VOLUME RESPONDERS

INDICES	PRE BD VALUE/SD	POST BD VALUE/SD	% RESPONSE	P VALUE
VC--LIT	2.65/0.250	3.24/0.223	14	0.001
FVC-LIT	2.66/0.189	3.25/0.214	22	0.001
FEV ₁ --LIT	1.32/0.111	1.49/0.122	12	0.05
FEV1 %	48/5	46/6	-4	NS
VC-FVC-LIT	-10/6	-5/2	8.8	NS
FEFR _{25%} LIT/SEC	2.8/0.12	2.28/0.10	1.3	NS
FEFR _{50%} LIT/SEC	2.25/0.14	2.28/0.10	1.3	NS
FEFR _{75%} LIT/SEC	0.65/0.08	0.71/0.09	5.9	NS
FEFR _{25-75%} LIT/SEC	2.0/0.12	2.1/0/18	5.1	NS