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STUDY OF PATTERNS OF BRONCHIAL HYPERRESPONSIVENESS IN RELATIVES OF PATIENTS OF BRONCHIAL ASTHMA

KEY WORDS:

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ABSTRACT

OBJECTIVES: To determine the patterns of bronchial hyperresponsiveness in relatives of patients of bronchial asthma and to observe its relationship with atopic state and exercise.

METHODS: Group A (control) had 25 subjects who were normal with no family history of Bronchial Asthma. Group B had 50 subjects with first degree relative having Bronchial Asthma. They were further subjected to intradermal skin testing with six common commercially prepared antigens, histamine challenge test and exercise testing.

RESULTS: On histamine challenge 15 out of 50 subjects reacted with a fall of 20% or more in PEFR in group B as compared to just 1 subject in group A . 5 subjects showed atopy in group B while only 1 was atopic in group A. . In both the groups there was a rise in PEFR on exercise initially followed by a fall in PEFR . A good correlation was seen between histamine and exercise broncho-provocation tests. However no relation was seen between Bronchial hyperresponsiveness with atopic status.

CONCLUSION: A significantly greater incidence of bronchial hyperresponsiveness was seen in healthy first degree relative of patients of Bronchial Asthma .

INTRODUCTION

Bronchial Asthma is one of the chronic diseases in both children and adults characterized by variable airway obstruction . Bronchial hypereresponsiveness is not a new concept. The first demonstration of BHR to provocation by nonspecific stimulation was by J.J Curry in 1946[1]. In his study he found that there was a significant reduction in vital capacity in asthmatics after intramuscular and intravenous adminstartion of histamine , whereas in healthy individuals fall was insignificant. The reactivity of airways could be increased if there is an elevation in the inherent hyperresponsiveness of the smooth muscle. Apart from genetic factors ,various environmental agents are capable of precipitating or exacerbating respiratory symptoms in asthmatics . Exposure to allergens being one of them . The present study aims at testing the hypothesis of the hypereresponsiveness of airways in first degree relatives of asthmatics and its relationship to atopy, the provoking stimuli being exercise and histamine inhalation.

METHODS

The study was conducted in a tertiary care hospital in NewDelhi . 75 subjects who were apparently healthy , of either sex between ages of 15-30 years were selected by random sampling and divided further into two groups . Group A (control) had 25 subjects who were normal with no family history of Bronchial Asthma. Group B had 50 subjects with first degree relative having Bronchial Asthma.

No drug or cigarette smoking was allowed before the tests . The subjects who were taking antihistaminics during last 48 hours of corticosteroids in last 4 weeks were excluded from the study.

Height (in cms) and weight (in kgs) was recorded for each subject after which an electrocardiogram and chest xray was done. Informed consent was taken and thereafter patients were called in the laboratory after general physical exam . They were subjected to intradermal skin testing with six common commercially prepared antigens . the antigens were 1) house dust 2) dog dander 3) Amaranthus 4) Prosospis 5) Chenopdium 6) Imperata. The concentration of antigen used was 1 in 500. The skin test was performed on the anterolateral aspect of arm and flexor surface of forearm. Minimum distance of 4 cms was kept between every two injections (shivpuri,1985[2]) to avoid overlapping of reactions .Buffered saline and histamine acid phosphate were used as positive and negative controls respectively. The skin tests were read after 20 minutes and graded according to the following criteria.

Grading of skin reactions	Definitions
_	Nearly same as negative control
+	Less than one plus
+	Wheal over twice the size of negative control and more than 6 mm , erythema +15-20mm
2+	Wheal about 3 times the size of negative control , erythema over 20mm
3+	Wheal about 3.5 to 4 times the size of negative controlwith pseudopaedia, erythema > 30mm
4+	Wheal about 4 to 6 times the size of negative control with pseudopaedia , erythema >30 mm

Resting Ventillatory status of each subject was assessed using spirometry and wright peak flow meter. Forced Vital Capacity , Forced expiratory volume in first second and and peak expiratory flow rate was recorded . Subjects having forced vital capacity of less than 80% of predicted were excluded from the study .

Histamine challenge test : histamine acid buffered solution was prepared in doubling concentration from0.03 mg/ml to 8 mg/ml , ph being 7.4. the subjects were asked to inhale through mouth by tidal breathing , buffered saline which was used as dilutent control , for 2 minutes after which PEFR was measured at 30 and 90 seconds. The percentage fall in PEFR was determined by following formula

$$\% \text{ fall in PEFR} = \frac{\text{post saline inhalation PEFR} - \text{post histamine inhalation PEFR}}{\text{post saline inhalation PEFR}} \times 100$$

Exercise testing : subjects were asked to perform exercise in the form of climbing two flight of stairs for 6 minutes after which their pulse rate was recorded . The exercise was repeated till the subjects attained a heart rate of 160 beats / minute . PEFR was recorded just before, during and after exercise and at 5,10,20 minutes after exercise. The following formula was used to calculate the % rise and fall

$$\% \text{ rise in PEFR} = \frac{\text{maximum PEFR} - \text{resting PEFR before exercise}}{\text{resting PEFR before exercise}} \times 100$$

$$\% \text{ fall in PEFR} = \frac{\text{resting PEFR before exercise} - \text{minimum PEFR}}{\text{resting PEFR before exercise}} \times 100$$

for each variable group mean and standard deviation were

calculated according to accepted statistical method . intergroup mean differences were tested for significance by standard t tests.

RESULTS

75 subjects were divided into 2 groups . Group A (control) had 25 (14 males and 11 females) subjects who were normal with no family history of Bronchial Asthma. Group B had 50 (28 males and 22 females)subjects with first degree relative having Bronchial Asthma.

Age distribution : subjects of group A had mean age of 22.52 + 3.765 years while subjects of group B had mean age of 21.76 + 3.623 years . the difference between the mean age between 2 groups is stastically insignificant . similarly , there was no significant difference in height seen in the mean height of two groups .

TABLE 1 :Pulmonary function tests at rest

	MEAN FVC	MEAN FEV1	MEAN PEFR
GROUP A	3398+653.1	2741+499.2	493.0+74.33
GROUP B	3485+706.1	2870+597.2	490 +76.04

The FVC,FEV1,PEFR are slightly higher in group B as compared to group A but the difference is not statistically significant [TABLE 1]

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3 subjects in group A reacted positively to antigens , and only 1 had a 2+ reaction while the other two had 1+ reaction . In group B 13 subjects had positive reaction of which 8 were 1+, 4 had 2+ , and one had 3+ reaction [TABLE 2].

TABLE 2 :Testing with antigens

SKIN REACTION	GROUP A	GROUP B
-ve	22	37
1+	2	8
2+ or more	1	5

On histamine challenge test a 20 % or more fall in PEFR was considered indicative of bronchial hyperreactivity . 15 out of 50 subjects reacted with a fall of 20% or more in PEFR in group B as compared to just 1 subject in group A . In both the groups there was a rise in PEFR on exercise initially followed by a fall in PEFR[TABLE 3].

TABLE 3 : Exercise testing

Parameter	Group A	Group B	P value
% rise	5.988+2.701	8.374+4.643	<0.05
% fall	3.904 + 2.509	6.342+4.773	<0.05
Ex - lability	9.892+3.747	14.67+8.460	<0.05

TABLE 4: comparison of bronchial hyperreactivity (BHR) on exercise

	Group A	Group B
Number	25	50
BHR +ve	1	16
%	4	32
P value < 0.05		

A good correlation was seen between histamine and exercise broncho-provocation tests . All subjects , except 3 who responded positively to exercise responded positively to histamine challenge also[TABLE 4].

RELATIONSHIP BETWEEN BRONCHIAL HYPERREACTIVITY (BHR) AND ATOPY

In group A the mean+ SD % rise and fall in PEFR on exercise in negative reactors to antigens (22 subjects) was 5.823+2.830% and 3.832+2.65 5 , while in subjects having a 1+ reaction (2 subjects) it was 7.35+1.34% and 4.65+1.63 % respectively. The lone subject with 2+ reaction had % rise and % fall of 6.9% and 4% respectively . The mean + SD rise and fall in positive reactors to antigens (3 subjects) was 7.20+0.99 and 4.43+1.21 respectively [TABLE 5,7,9}.

TABLE 5:Mean + SD percentile changes in PEFR on exercise and exercise lability in relation to atopy and positive skin reaction sin group A

	-ve	1+	2+or more (atopic)	Combined positive reactors (1+ + 2+)
Number of cases	22	2	1	3
% rise in PEFR	5.823+2.83	7.35+1.34	6.90	7.20+0.99
% fall in PEFR	3.832+2.65	4.65+1.63	4.00	4.43+1.21
Ex –lability	9.655+3.94	12.00+2.83	10.9	11.63+.666

In group B the mean+ SD rise and fall in PEFR on exercise, in subjects not reacting positively to antigens (37 subjects) was 8.397+4.45% and 6.208+5.01% in comparison to a mean+ SD rise and fall in PEFR of 8.31+5.32% and 6.72+4.19 %in subjects showing positive reaction to antigens (13 subjects) . Subjects showing 1+ reaction to antigens (8 subjects) showed a mean+ SD rise and fall in PEFR of 7.41+4.62% and 6.54+4.69% while atopic individuals had a mean+ SD rise and fall in PEFR of 9.740+ 6.60% and 7.020+3.73% [TABLE 6,8,10].

TABLE 6:Mean + SD percentile changes in PEFR on exercise and exercise lability in relation to atopy and positive skin reaction sin group B

Parameters	-ve	1+	2+or more (atopic)	Combined positive reactors (1+ + 2+)
Number of cases	37	8	5	13
% rise in PEFR	8.397+4.45	7.41+4.62	9.740+ 6.60	8.31+5.32
% fall in PEFR	6.208+5.01	6.54+4.69	7.020+3.73	6.72+4.19
Ex –lability	14.54+8.71	13.95+7.84	16.76+8.92	15.03+8.03

TABLE 7:Relationship of bronchial hyperreactivity (exercise induced) to atopy and positive skin reactions in group A

	-ve	1+	2+ or more	Combined positive reactors (1+ + 2+)
Number of cases	22	2	1	3
BHR +ve	1	0	0	0
% +ve	4.54	0	0	0

P value group -ve vs group 1+ > 0.05
P value group -ve vs group 2+ > 0.05
P value group -ve vs group 1+ + 2+ > 0.05

TABLE 8:Relationship of bronchial hyperreactivity (exercise induced) to atopy and positive skin reactions in group B

	-ve	1+	2+ or more	Combined positive reactors (1+ + 2+)
Number of cases	37	8	5	13
BHR +ve	12	2	2	4
% +ve	32.43	25	40	30.76

P value group -ve vs group 1+ > 0.05
P value group -ve vs group 2+ > 0.05
P value group -ve vs group 1+ + 2+ > 0.05

TABLE 9:Relationship of bronchial hyperreactivity (histamine induced) to atopy and positive skin reactions in group A

	-ve	1+	2+ or more	Combined positive reactors (1+ + 2+)
Number of cases	22	2	1	3
BHR +ve	1	0	0	0
% +ve	4.54	0	0	0

P value group -ve vs group 1+ > 0.05
P value group -ve vs group 2+ > 0.05
P value group -ve vs group 1+ + 2+ > 0.05

TABLE 10: Relationship of bronchial hyperreactivity (histamine induced) to atopy and positive skin reactions in group B

	-ve	1+	2+ or more	Combined positive reactors (1+ + 2+)
Number of cases	37	8	5	13
BHR +ve	11	2	2	4
% +ve	29.72	25	40	30.77

P value group -ve vs group 1+ > 0.05
P value group -ve vs group 2+ > 0.05
P value group -ve vs group 1+ +2+ > 0.05

DISCUSSION

Most of the asthmatic patients show bronchial hyperresponsiveness , a condition causing the airways to narrow excessively in response to a provoking stimulus . Numerous studies have suggested that there is a hereditary component in expression of asthma . It has been further proposed that even apparently healthy relatives of patients of asthma react abnormally to broncho-provoking stimuli . This study was undertaken to observe the pattern of bronchial hyperreactivity to a provoking stimulus in relatives of asthmatics , as there is paucity of data on the sunject . A parallel study was conducted on healthy subjects with no family history of asthma , with histamine and exercise being the provoking stimuli

Family studies examining both nuclear and extended families confirm the commonly held belief that children born into families with history of asthma and other atopic diseases are more likely to be atopic than those born into families with no such history . some workers proposed that the presence of atopy may enhance the frequency and severity of bronchial hyperreeactivity . Similarly relationship between positive skin test to allergens and Bronchial hyperreactivity has been tested by some (Cookson et al 1986[3]).

The value of incidence of bronchial hyperreactivity obtained on histamine challenge in present study thus conforms to that found by Julius Crane et al , 1989[4]. They had reported a 35% incidence of BHR among first degree relatives of asthmatics on histamine challenge. On exercise testing the mean PEFR shows a rise followed by a fall in both the groups . However the mean rise and fall was more pronounced in healthy relatives of asthmatic subjects.

In subjects with family history of asthma , 13 out of 50 reacted positively to antigen and of these, 5 were atopic. This gives the incidence of positive skin reactors as 26% and atopy 10%. The mean % rise in PEFR on exercise in positive reactors to antigen was almost same as in nonreactors (8.308% vs 8.397%) though the mean % fall was slightly higher in positive skin reactors . Similarly the incidence of BHR to histamine bronchoprovoking test in relatives of asthmatics was same in subject reacting positively to skin test with allergen (31%) as compared with the negative reactors (30%). The incidence of BHR in atopic relatives of patients of Bronchial Asthma was 40% (2 out of 5), as xompared to 32% in subjects not reacting positively to allergens when exercise was used as bronchoprovocative stimulus. Similarly , the incidence of BHR was 40% in atopic relatives of asthmatics as compared to 30% in nonreactors when histamine was the provoking stimulus . These differences were found to be statistically nonsignificant.

The above results thus show no relation between skin reactivity to antigen , atopy and BHR in accordance with observation of S.K.Chabra[5] . However some workers such as Burrows et al[6], Dong and Young [7] and Julian crane et al[4] have found a positive correlation .

CONCLUSION

A significantly greater incidence of bronchial hyperresponsiveness was seen in healthy first degree relative of patients of Bronchial Asthma as compared to control subjects with no family history . However no relation was seen between Bronchial hyperresponsiveness with atopic status .

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