Effect of Aerosol Salbutamol, Ipratropium Bromide and Beclomethasone on Chronic Bronchitis

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Summary :

Chronic bronchitis is a common clinical problem in Bangladesh. The prevalence of chronic bronchitis has been difficult to establish, because of their gradual development, variable definition and population differences. Surveys have shown that a good number of the population have some degree of chronic bronchitis depending on age, sex, smoking habits, occupation and urbanization, Chronic bronchitis is one of the largest cause of loss of working days and its overall socio - economic burden is vast. Various therapeutic regimens have been advocated for the management of chronic bronchitis with varying success. Very few studies have been done with salbutamol, ipratropium bromide. Beclomethasone combination. The present study was designed to find out the relationship and effects of salbutamol, ipratropium and beclomethasone in chronic bronchitis. In the present study it was observed that pulmonary function improved effectively with ipratropium bromide. Combination of salbutamol-ipratropium and salbutamol-ipratropium-beclomethasone has no added advantage over ipratropium alone.

Introduction :

Chronic bronchitis is the principal disease of the central airways. It is a functional disorder and is characterised by excess secretion of mucus in to the tracheobronchial tree[1]. Chronic bronchitis has tended to be regarded as The British Disease; prevalence figures vary considerably and vary with definition, with the age group studied and with somoking habits and industrialization. Figures tend to be higher in industrialized countries, although in recent years high prevalence rates have emerged from countries such as India, Malaysia, Papua New Guinea. In Bangladesh 21.6% of all respiratory cases in private consultation were chronic bronchitis, II% of all respiratory cases in S. S. M. C. and 5.58% of all respiratory cases admitted in Dhaka medical college hospital were due to chronic bronchitis[2].

The cause of chronic bronchitis is poorly understood and opinion differs among authorities

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cocerning the relative importance of known or presumed factors. Much more is known about factors that aggravate the disorders than is known about the pathogenesis[3]. Smoking habitis, environmental pollution, socio-economic status, occupation, recurrent bronchopulmonary infection are associated with abnormally high incidence of chronic bronchitis[4]. Aerosal bronchodilators are important therapy for patients with chronic bronchitis. Aerosol therapy is well accepted by patients and physicians because it is effective, has a rapid onset of action and is usually free of side effects[5]. The use of aerosol to treat chronic bronchitis allows an almost ideal therapeutic ratio to be achieved, since minute doses of inhaled medication provide optimal maintenance therapy with minimal side effects[6].

The bronchodilator agents are the mainstay for managing bronchospasm associated with chronic bronchitis and for control of any reversible component of chronic bronchitis. They are also useful in conjunction with bronchial hygine therapy. The inhaled route of administrating beta-adrenergic drug is usually more effective & rapid in relieving bronchospasm than the oral route[7]. Inhaled ipratropium bromide exhibit a combined beneficial effects of reducing copious amount of sputum and partially relieving bronchospasm in pattents with chronic bronchitis. In patients with chronic bronchitis however the bronchodilator effects of anticholinergic drug is comparable to that of sympathomimetics[8]. Inhalation of a new anticholinergic drugs ipratropium bromide was followed by a bronchodilatation response which was submaximal in a group of asthma patients but maximal in one of bronchitic patient that is subsequent inhalation of isoprenaline produced no further fall in airways resistance [8]. The use of steroids in chronic bronchitis is highly controversial and no generally accepted guidelines are available to help in selecting patients . The response to steroids in patients with apparently stable chronic bronchitis can not be predicted reliable but occasionally this form of treatment is unexpectedly beneficial[9].

The present study was designed to see the effects of inhaled salbutamol and ipratropium bromide individually and in combination in chronic bronchitis and to see what further improvement could be obtained with inhaled steroids in addition to both drugs. In this study an attempt was made so that an uniformly effective therapy may be established for chronic bronchitis and the sufferings of the patients may be alleviated.

In setting of limited resources and in the face of increasing number of patients with chronic bronchitis presenting to the hospital, studies are needed to assess the real weight of burden of chronic bronchitis in order to plan the optimal utilization of prevailing resources. Keeping all these attributes in mind, this study was planned in I. D. C. H. Mohakhali Dhaka which is playing a pivotal role in handling such common clinical problem prevailing in Bangladesh.

Materials and Methods :

The study was a prospective single blind cases contrtolled study done in I. D. C. H. Mohakhali Dhaka. A total number of 26 patients were included in the study. The diagnosis of chronic bronchitis followed the medical research council criteria for chronic bronchitis[10]. Only clinically clean cases were included. Significantly disabled patients due to chronic bronchitis, patients with diabetes mellitus, heart failure, chronic renal failure, ischaemic heart disease, pregnancy and corpulmonlae were excluded from the study. Treatment regimen comprised of four consecutive 3 days period after a pretrial two days assessment.

Regimen I : First salbutamol or ipratropium bromide, anyone was given by random selection than alternate drug was given

Regimen II : Salbutamol and ipratropium bromide was given together.

Regimen III : Salbutamol, ipratropium bromide and beclomethasone was given.

Allocation to the order of salbutamol or ipratropiumin the first two treatment period was by random selection, with each drug given singly. Thereafter salbutamol and ipratropium bromide were given together and whichever drug was administered in the first 3 day period was the first to be given when both drugs were used in combination. The last 3 days period was with salbutamol. ipratropium and beclo-methasone. Sallbutamol given was 200 micgm, ipratropium 40micgm and beclomethasone 100micgm. All the drugs given at 8.00 , 12. 00, 18. 00 & 22.00 hours daily.

Each day patients were asked if they noticed any change in their condition compared with pre-treatment state. Any side effects were recorded. Peak expiratory flow. (PEF) was measured two times daily with wrights peak flow meter. The best of three measurements was recorded. Forecd expiratory vlume in one second (FEV1) and Forced vital capacity (FVC) was recorded on the third day with Spirometer. The best of three measurements was recorded.

Fishers exact probability test were used for statistical analysis. P value <0.05 were taken as significant in all analysis.

Observation and Result:

Table I shows clinical and demographic profile of patients A total number of 26 patients were included in the study. The age of the patients ranged 38-70 (mean 48.8) years. Male and female ratio 4.2:I. Number of acute exaggerbation of symptoms ranged 2-8 (mean 3.5) times. Duration of smoking ranged 9-22 (mean II) years in 22 Patients and 4 patients had no history of smoking. The respiratory rate ranged 15-25 (mean 16.5) times per minute, pulse rate ranged 85-105 (mean 90.5) per minute. Weight of the patients ranged 49. 55 (mean 58) kg.

Table - I

Shows the clinical and demographic profile of patients.

No. of patients	26
Age (years)	
Mean	48.8
Range	38-70
Sex	
Male	21
Female	5
M:F	4.2:1
Weight (kg)	58.5 (49-65)
Height (m)	1.59(1.51-1.60)
Duration of symoptoms (years)	
Mean	8.5
Range	3-12
Blood pressure (mm Hg)	
Systolic	140.5(120-165)
Diastolic	85(75-90)
Respiratory rate	16.5(15-25)
Exaggerbation of symptoms (no. of times)	3.5(2-8)
Smoking History	22
Duration (years)	11(9-20)
No smoking history	4

Table II shows the pulmonary function before starting trial. PEF ranged 180-290 (mean214.8) litre, FEV1 ranged 1.10-1.85 (mean1.41) and FVC ranged 1.3-2.2 (mean 1.17) litre respectively.

Table - II

The pulmonary functions before starting trial.

Pulmonary functions	mean±SE	range
Peak expiratory flow (PEF)	214.8±8.9	180-290
Forced expiratory volume in one second (FEV_1)	1.41±0.15	1.10-1.85
Forced vital capacity (FVC)	1.17±0.13	1.3-2.2

Table III shows the subjective changes of symptoms with different drugs. With salbutamol 11 (42,.3%) has relief / improvement of their symptoms, with ipratropium 21(80.8%) showed relief / improvement with salbutamol- ipratropium 23(88.5%) has relief / improvement of symptoms. Addition of beclomethasone with salubutamol-ipratropium showed 24 (92.3%) patients to be improved. Improvement of symptoms were significant with ipratropium (P<0.01) , when salbutamol and ipratropium used independently. Combination of salbutamol-ipratropium showed significant improvement of symptoms than to salbutamol alone (P<0.001) but when compared to ipratropium alone it is insignificant (P>0.05). There was no further significant improvement of symptoms when beclomethasone was added to salbutamol-ipratropium combinations than to combination or ipratropium alone (P>0.05) but to salbutamol alone it was highly significant (P0.001).

Table - III

Subjective chages of symptoms with different aerosols.

Drugs		Improved/Relieved		Unchanged	
		No	%	No	%
Salbutamol	a	11	42.3	15	57.7
Ipratropium	b	21	80.8	5	19.2
Salbutamol+ Ipratropium	c	23	88.5	3	11.5
Salbutamol + Ipratropium Beelomethasone	d	24	92.3	2	7.7

b vs a p=s<0.01 d vs a p=S<0.001

c vs b =NS>0.05 d vs b P=NS>0.5

d vs c P=NS 0.05 c vs a p=S <0.001

Table IV shows the changes in pulmonary function after different therapy. There is significant change in PEF when comparison is made between salbutamol to ipratropium (P<0.05), salbutamol to salbutamol ipratropium beclomethasone (P<0.01) and salbutamol to salbutamol -ipratropium (P<0.01) respectively. No significant change in PEF is observed when comparison is made between ipratropium to salbutamol-ipratropium (P>0.05) salbutamol ipratropium beclomethasone to salbutamol-ipratropium (P>0.05) respectivly. FEV_1 is insignificant (P>0.5) when compared in all regimens. There is no significant changes in FVC when different regimens are compared.

Tabel - IV

The changes in pulmonary function after different aerosol therapy

Drugs	PEF	FEV	FVC
Salbutamol	238±8.6	1.58±0.19	1.88±0.14
Ipratropium	262±7.2	1.65±0.21	2.10±0.16
Salbutamol+ Ipratropium	267±6.6	1.70±0.28	2.25±0.15
Salbutamol+ Ipratropium + Beclomethasone	270±6,6	1.72±0.30	2.30±0.18

Table - V shows the correlation between changes in pulmonary functions before and after treatment . With salbutamol changes in PEF. FEV_1 and FVC is insignificant, with ipratropium changes in PEF is significant ($P<0.001$). Changes in FVC is also significant ($P<0.05$) but changes of FEV1 is not significant ($P>0.05$) . When salbutamol-ipratropium is given together there is significant changes in PEF($P<0.001$) and FVC ($P<0.01$) but change in FEV1 is insignificant ($P>0.05$). Addition of beclomethasone showed no further significant improvement than salbuta mol-ipratropium combinations.

Table-V

Correlation between changes in pulmonary functions before and after aerosol therapy

Drugs	PEf		PEV		FVC	
	B	A	B	A	B	A
Salbutamol	2I4.8±8.9	238±8.6	1.41±0.15	1.58±0.19	1.17±0.13	1.88±0.14
	P>0.05		P>0.05		P>0.05	
Ipratropium	214.8±8.9	262±7.2	1.41±0.15	1.65±0.21	1.17±0.13	2.10±0.16
	P<0.001		P>0.05		P<0.05	
Salbutamol + Ipratropium	214.8±8.9	267±6.6	1.41±0.15	1.70±0.28	1.17±0.13	2.25±0.15
	P<0.001		P>0.05		P<0.01	
Salbutamol + Ipratropium + Beclomethas -one	214.8±8.9	270±6.6	1.41±0.15	1.72±0.30	1.17±0.30	2.30±0.18
	P<0.001		P>0.05		P<0.01	

*B=before trial *A=after trial

Discussion :

Chronic bronchitis is a common respiratory problem in Bangladesh. Cigrette smoking is clearly the most important cause of chronic bronchitis even though only 10-15% of smokers developchronicbronchitis.Patients characteristically present in the 5th or 6th decades of life and symptoms often been present for 10 years or more. In the present study it was observed that patients presented mostly in the late 5th decades of life. Studies from Britain also showed that it is more prevalent in late 5th and early 6th decades of life[11]. It is currently thought that loss of ventilating function which characterizes chronic bronchitis occurs at relatively slow rate. so that the cumulative effects of lung damage become clinically manifest only in older people. However the relationship between aging and chronic bronchitis also can be attributed in part to the deliterious effect of age itself on lung function[12].

This study showed the prevalence of disese in male (M: F 4.2:1) Millicent et al in one study also showed male preponderance[13]. It may be due to increased smoking habits & exposure to external environment as because atmospheric pollution and smoking are two principal predisposing factors for chronic bronchitis. In this study out of 26 patients 22 had smoking habits/history. A causal relationship between cigarette smoking and chronic bronchitis is so firmly established that its existance is no longer doubted by expert and unbiased observers. Millicent et al[12] in a study showed that a higher prevalence of chronic bronchitis among smokers. In this study out of 26 patients 4 was non smokers. In non smokers chronic bronchitis is uncommon. The development of chronic bronchitis among nonsmokers needs further evaluation. Atmospheric pollution, occupational hazards and infection may have contribution in developing chronic bronchitis among nonsmokers[11].

PEF, FEV_1, FVC all found to be decreased in all patients studied. The fall in pulmonary functions results from generalised airway obstruction. Factors contributing to the obstruction are; mucous in the lumen of airways, thickening of the bronchial mucous membrane by hypertrophy of mucous gland and by oedema and inflammation , increased bronchial muscle tone

In this study PEF was significantly improved with ipratropium than to salbutamol ($P<0.05$) . Changed in PEF with salbutamol-ipratropium was significant to salbutamol alone ($P<0.01$) but insignificant to ipra tropium ($p>0.05$). Salbutamol-ipratropium-beclomethasone produce significant change in PEF ($P<0.01$) than to salbutamol alone, but in all other cases increase in PEF was insignificant ($P>0.05$) . This study revealed that ipratropium can cause change in PEF more effectively than salbutamol or beclomethasone. Booij Norred et al in their study also obsreved that ipratropium bromide can cause change in pulmonary functions significantly and concluded that it is due to the fact that bronchitic are more sensitive to the vagal reflexes and ipratropium inhibits vagal reflexes[14].

Other components of pulmonary function such as FEV_1 did not show any significant change with salbutamol, ipratropium, salbutamol-ipratropium, salbutamol,-ipratropium-beclomethasone combinations respectively. The response to bronchodilator in chronic airways obstruction is limited by various factors notably those imposed structural changes in the bronchi such that obly a limited response is possible to any bronchodilartor drug.

Though there was increase in mean FEV_1 with ipratropium than salbutamol the difference was not significant statistically. The combnination of the two drugs produced a slightly greater and larger response than either alone but the effect

was not significant. Addition of beclomethasone showed no significant difference than either alone or in combination. Similar finding also observed by others15. In this study mean value of forced vital capacity (FVC) was increased but there was no statistically significant difference of FVC with salbutamol, Ipratropium. salbutamol-ipratropium, Salbutamol-ipratropium-beclomethasone combinations. Further study will be helpful to draw a definite conclusion.

When pre trial post trial values of pulmonary functions were correlated it was found that with salbutamol PEF, FEV_1, and FVC, were not significantly improved ($P>0.05$) With ipratropium PEF and FVC was significantly improed ($P<0.05$) but improvement of FEV was insignificant ($P>0.05$). With salbutamol-ipratropium improvement of pulmonary functions was like ipratrlpium alone, when beclomethasone was added to salbutamol ipratropium conbinations there was no remarkable improvement of pulmonary functions.

Conclusions:

From the above findings it can be concluded that though salbutamol-ipratropium combinations causes clinical improvement in chronic bronchitic patients, ipratropium is more effective than salbutamol. Pulmonary functions improves more effectively with ipratropium. The combinations of salbutamol and ipratropium has marginal benefit than ipratropium alone. Inhaled steroid is not that much helpful as in bronchial asthma. Thus in chronic bronchitis ipratropium may be used as first line drug to get symptomatic improvement and improvement of pulmonary function.

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