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ORIGINAL ARTICLE

Outcome of Long Term Nebulization of Gentamicin on Lung Function and Respiratory Health Status among Non-Cystic Fibrosis Bronchiectasis

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Abstract:

Background: *Bronchiectasis is a disease state defined by irreducible dilations of the airways. If the changes occur in diseases other than cystic fibrosis they are termed non-CF bronchiectasis. Long-term therapy with nebulized gentamicin can eradicate the infection or reduce the bacterial load, decrease the risk of subsequent infections and improve the quality of life in patients with non-CF bronchiectasis with a minimal risk of side effect.*

Aims: *The aim of this study was to find out the outcome of long term nebulization of gentamicin on lung function and respiratory health status among non-CF bronchiectasis.*

Materials & Methods: *This prospective randomized controlled trial (RCT) was conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from April 2020 to March 2021 in collaboration with the Department of Pathology, Radiology and Respiratory Laboratory. A total of 50 Non-CF Bronchiectasis patients were equally divided into 2 groups, gentamicin group and placebo group. All data were analyzed by using computer based SPSS-23(Statistical Packages for Social Sciences). P value of less than 0.05 was considered as significant*

Results: *Out of 50 patients with non-CFbronchiectasis, mean age was found 50.0±11.0 years in gentamicin group and 46.3±11.4 years in placebo group.Eighteen (72.0%) patients were male in group A and Sixteen(64.0%) in group B. Male to female ratio was 2.6:1 in group A and 1.8:1 in group B. Age, sex, occupational status, co-morbidities and BMI, were not statistically significant (p>0.05) between two groups. Following gentamicin therapy,SGRQ (36.0±10.2 vs 41.8±7.9) and 24 hour sputum volume (5.2±3.9 vs 7.8±2.5) was significantly decreased in gentamicin group than placebo group (p= 0.001). After gentamicin therapy, mean mMRC was not statistically significant between two groups (p=0.267). After therapy FEV_1 was significantly increased in gentamicin group than placebo group (42.5±9.4% vs 37.4±6.0, p=0.001).*

Conclusion*. We observed that gentamicin could significantly improve SGRQ and FACED score and reduce sputum volume compared to placebo. After therapy FEV_1 was significantly increased in gentamicin group than placebo group. Nebulized gentamicin may be used as an effective suppressive antibiotic therapy in these patient group.*

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Introduction:

Bronchiectasis is defined as an abnormal and permanent dilatation of one or more bronchi[1].It is a chronic respiratory disease presenting with chronic cough, sputum production, some have hemoptysis and shortness of breath. Increased production of mucous together with impaired mucociliary clearance leads to accumulation of secretion in dilated bronchi and causes recurrent respiratory infections. A vicious cycle is established involving persistent bacterial colonization, chronic inflammation of the bronchial mucosa, airway damage and remodeling. In most cases, infection is the primary force behind this ongoing cycle[2].

Bronchiectasis has a diverse range of pathological processes, including primary disorder of bronchial structure, impairment of mucociliary clearance, infectious cause (childhood pneumonia, PTB, Ig deficiency), inflammatory diseases such as rheumatoid arthritis, ulcerative colitis etc. In around 50% of adult patients, a specific etiology is not identified[3].Patients with bronchiectasis are prone to frequent exacerbations which have traditionally been viewed as being exclusively bacterial, evidenced by epidemiological data. Cohort studies showed that those patients treated with intravenous antibiotic therapy had a good clinical response[4,5].There were fewer exacerbations during the 12 months' treatment in the nebulized gentamicin group compared to the placebo group (0 [0–1] exacerbations and 1.5 [1–2] exacerbations, respectively; P<0.0001)[4].

Gentamicin is an aminoglycoside antibiotic. It acts primarily by disrupting protein synthesis leading to altered cell membrane permeability, progressive disruption of the cell envelope and eventual cell death.Nebulizedgentamicin, compared with intravenous administration can deliver high concentrations directly to the site of infection, eliminating the need for high systemic concentrations and reducing the risk of systemic toxicity.

The adverse events are dyspnea, chest pain, cough and bronchospasm. Although bronchospasm is well recognized side effect, it can be avoided by screening test and premedication with nebulized beta 2 agonist bronchodilator[4].

Materials and method:

This was prospective, randomized controlled trial (RCT) with no blinding.

This study was conducted in the Respiratory Medicine Department, National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka between the period of April 2020 to March 2021.

Patients withnon-CF bronchiectasis were selected by history, clinical and radiological examination from the inpatient department of Respiratory Medicine of NIDCH. Eligible patients were randomly assigned in blocks of two parallel groups such as gentamicin group and placebo group to receive either gentamicin nebulization plus conventional treatment or only conventional treatment. Patients were not stratified on the basis of any criteria. The test group was given gentamicin nebulization 80 mg2 times daily for 4 weeks by nebulizer. The placebo group was taken only conventional treatment. Data was collected through appropriate questionnaire. Each patient was evaluated clinically and also by laboratory procedures before and after the nebulization. All the data were recorded systematically in a preformed data collection sheet and analyzed by using computer based SPSS-23(Statistical Packages for Social Sciences). P value of less than 0.05 was considered as significant

Observations and Results:

Table-I

Demographic characteristics of the study patients (n=50)

Demographic characteristics	Group A(n=25)		Group B (n=25)		P value
	N	%	N	%	
Age (years)					
≤20	0	0.0	1	4.0	
21-30	1	4.0	1	4.0	
31-40	4	16.0	7	28.0	
41-50	7	28.0	6	24.0	
51-60	9	36.0	6	24.0	
>60	4	16.0	4	16.0	
Mean ±SD	50.0 ±11.0		46.3±11.4		[a]0.246[ns]
Range (min-max)	26.0-66.0		19.0-62.0		
Sex					
Male	18	72.0	16	64.0	[b]0.544[ns]
Female	7	28.0	9	36.0	

(ns= not significant,[a]P value reached from unpaired t-test, [b]P value reached from chi square test, Group A= Gentamicin group, Group B= Placebo group)

Table-II

Occupational status of the study population(n=50)

Occupational status	Group A(n=25)		Group B (n=25)		P value
	n	%	n	%	
Farmer	0	0.0	1	4.0	
Businessman	8	32.0	7	28.0	
Cultivator	8	32.0	5	20.0	0.635^{ns}
House wife	7	28.0	7	28.0	
Service	2	8.0	4	16.0	
Student	0	0.0	1	4.0	

(ns= not significant, P value reached from chi square test,Group A= Gentamicin group, Group B= Placebo group)

Table-III

Smoking status of the study population (n=50)

Smoking history	Group A(n=25)		Group B (n=25)		P value
	N	%	n	%	
Current	10	40.0	7	28.0	
Ex-smoker	8	32.0	7	28.0	0.476^{ns}
Never	7	28.0	11	44.0	

(ns= not significant, P value reached from chi square test, Group A= Gentamicin group, Group B= Placebo group)

Table IV

Yield of sputum culture(n=50)

Microorganism culture	Group A(n=25)		Group B (n=25)		P value
	N	%	n	%	
No	15	60.0	13	52.0	0.569^{ns}
Yes	10	40.0	12	48.0	
Name of the bacteria					
Pseudomonas aeruginosa	5	20.0	6	24.0	
Klebsiella pneumoniae	3	12.0	4	16.0	
Streptococcus pneumoniae	1	4.0	2	8.0	
Staphylococcus aureus	1	4.0	0	0.0	

(ns= not significant, P value reached from chi square test, Group A= Gentamicin group, Group B= Placebo group)

Table-V

Parameters before and after therapy

Spirometric follow upFEV_1 (%)	Group A(n=25) Mean±SD	Group B(n=25) Mean±SD	P value
Before therapy	32.3±7.9	31.5±6.6	[a]0.715[ns]
Range (min-max)	18.0-49.0	20.0-46.0	
After therapy	42.5±9.4	37.4±6.0	[a]0.027[s]
Range (min-max)	22.0-56.0	28.0-50.0	
Mean change	10.2±4.1	5.9±1.7	0.001[s]
St. Georges Respiratory Questionnaire score (SGRQ) in different follow up			
Before therapy	56.3±12.2	50.8±10.4	[a]0.096[ns]
Range (min-max)	40.0-77.0	32.0-65.0	
After therapy	36.0±10.2	41.8±7.9	[a]0.029[s]
Range (min-max)	16.0-52.0	27.0-57.0	
Mean change	-20.3±6.6	-9.0±4.3	0.001[s]
Change in sputum volume (ml)			
Before therapy	17.6±5.0	16.8±4.5	[a]0.557[ns]
Range (min-max)	10.0-25.0	10.0-25.0	
After therapy	5.2±3.9	7.8±2.5	[a]0.008[s]
Range (min-max)	0.0-10.0	5.0-10.0	
Mean change	-12.4±3.6	-9.0±3.5	0.001[s]
mMRC score in different follow up			
Before therapy	2.72±0.45	2.64±0.49	[a]0.554[ns]
Range (min-max)	2.0-3.0	2.0-3.0	
After therapy	1.44±0.50	1.60±0.50	[a]0.267[ns]
Range (min-max)	1.0-2.0	1.0-2.0	
Mean change	-1.28±0.45	-1.04±0.20	0.020[s]
FACED severity score			
Before therapy			
Mild bronchiectasis (0-2)	4(16%)	7(28%)	
Moderate bronchiectasis (3-4)	19(76%)	15(60%)	0.475[ns]
Severe bronchiectasis (5-7)	2(8%)	3(12%)	
After therapy			
Mild bronchiectasis (0-2)	18(72%)	15(60%)	0.370[ns]
Moderate bronchiectasis (3-4)	7(28%)		10(40%)

Discussion:

The mean age was 50.0±11.0 years in gentamicin group (group A) and 46.3±11.4 years in placebo group (group B). The difference was not statistically significant (p>0.05) between two groups. Almost similar study was conducted where they showed median age was 58 years with range from 53 to 67 years in gentamicin group and 64 years with range from 55.7 to 69 years in placebo group[4].

Sputum culture yield growth of organisms in 40% and 48% in group A and group B respectively. *Pseudomonas aeruginosa was the most common organism found in both group. Literature shows that* Pseudomonas aeruginosa and Haemophilus influenza are the most common pathogen[6]. Pathogens in the airways of people with bronchiectasis and the geographical and community differences together with ethnic variation warrant further investigation.

In this study it was observed that in after therapy, mean FEV_1 was found 42.5±9.4 % in gentamicin group and 37.4±6.0% in placebo group. Mean change of FEV_1 was found 10.2±4.1% in gentamicin group and 5.9±1.7 % in placebo group. Which were statistically significant (p<0.05) between two groups. Mean FEV_1after therapy was statistically significant (p<0.05) within the gentamicin group compare with screening day. Previous studies reported mean change of FEV1 from baseline was predicted and they obtained suitable data from all study but one of these trials for pooling of the results[1,4,7,8]. The meta-analysis of eight trials with 558 patients showed a small, but statistically significant, difference in mean change in FEV_1 in favor of the control group. Murray et al. reported that there was no significant difference ofFEV_1 between the groups[4]. This may be due to using other conventional medications or patients condition either stable or exacerbation of non-CF bronchiectasis.

We found that after therapy, mean SGRQ was 36.0±10.2 in gentamicin group and 41.8±7.9 in placebo group. Mean change of SGRQ was -20.3±6.6 in gentamicin group and -9.0±4.3 in placebo group. Which was statistically significant (p<0.05) between two groups. Mean SGRQafter therapy was statistically significant (p<0.05) within the Gentamicin group compare toscreening day. Murray et al. observed that at each 3-monthly interval during treatment, significantly more patients in the gentamicin group achieved a clinically significant improvement in both LCQ score and SGRQ score compared with patients in the placebo group[4].

In this present study it was observed that followingtherapy, mean daily sputum volume was found 5.2±3.9 ml in gentamicin group and 7.8±2.5 ml in placebo group. Mean change of daily sputum volume was found -12.4±3.6 ml in gentamicin group and -9.0±3.5 ml in placebo group, which was statistically significant (p<0.05) between two groups. Mean daily sputum volumeafter therapywas reduced in group A compared to group B which was statistically significant (p<0.05).

Regarding mMRC in different follow up between two groups in this study we found mean change of mMRC was -1.28±0.45 in gentamicin group and -1.04±0.20 in placebo group which was statistically significant (p<0.05). Mean mMRCafter therapy was statistically significant (p<0.05) in the gentamicin group compare toscreening day. Mean mMRCafter therapy was also statistically significant (p<0.05) in the placebo group compare to screening day. Studies observed that the perception of dyspnea in subjects with bronchiectasis determined by using the mMRC score was significantly higher than that of healthy subjects[9] (p<0.05). Dyspnea is seen in 60% of patients with bronchiectasis[10,11]. Study used mMRC score to evaluate dyspnea[9], which was considered one of the major factors defining bronchiectasis[12] and affects the survival along with airway obstruction, pulmonary hyperinflation and frequency of disease[13].

In this study at screening day, nineteen (76.0%) patients were found to have moderate bronchiectasis (3-4 FACED score)in gentamicin group and fifteen (60.0%) in placebo group. After therapy, eighteen(72.0%) patients were found to have mild bronchiectasis (0-2 FACED score) in gentamicin group and fifteen (60.0%) in placebo group. This difference was not statistically significant (p>0.05). It was observed that in gentamicin group, moderate bronchiectasis was found 19 cases in screening day among them 14 cases were converted to mild and 5 remainsmoderate after therapy. In placebo group, moderate bronchiectasis was found 15 cases in screening day among them 8 were converted to mild and 7 remainsmoderate after therapy. All severe bronchiectasis 2(8%) in Gentamicin group and 3(12%) in placebo group converted to Moderate after therapy. So improvement of FACED score in group A was more compare to group B after therapy.

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