

USEFULNESS OF ANTIBIOTICS IN ACUTE EXACERBATIONS OF COPD

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ABSTRACT

BACKGROUND

COPD is characterised by frequent exacerbations, mostly infective. These are usually treated with antibiotics, even when the aetiology is non-infective. The efficacy of antibiotics in this setting is controversial. Hence, the study was planned to look for any added advantage for antibiotics in COPD exacerbations.

Aim- To study the usefulness of antibiotics in acute exacerbations of COPD in a) reducing relapse of exacerbation and b) reducing duration of hospital stay.

MATERIALS AND METHODS

110 COPD patients admitted with an exacerbation, after excluding infection, were randomised into two groups. The treatment group received oral Amoxicillin for five days while the control group did not. They were followed up for two weeks to look for relapses. Duration of hospital stay was also noted.

Settings and Design- Randomised controlled trial done in Pulmonary Medicine Department, GMC, Trivandrum.

Statistical Analysis- SPSS version 11.0 was used. Chi square and student t test were used for analysing variables.

RESULTS

The baseline characteristics of the two groups were comparable. The mean duration of hospital stay was 6.6 ± 2.48 in treatment group and 6.96 ± 2.24 in control group ($p = 0.421$). The number of relapses in two weeks was almost similar in both the groups with no statistically significant difference.

CONCLUSION

Empirical antibiotics were not found to be useful in COPD exacerbations without clinical or radiological evidence of infection.

KEYWORDS

COPD, Exacerbation, Antibiotics, Infection.

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BACKGROUND

COPD is a common disease encountered by pulmonologists and is characterised by frequent exacerbations, mostly due to infective aetiology. According to Anthonisen, the exacerbations can be type 1, 2 or 3 depending on the symptoms of increased dyspnoea, sputum volume or sputum purulence.⁽¹⁾ GOLD guidelines recommend use of antibiotics apart from the usual management, for exacerbations where sputum purulence is present or any combination of other symptoms where one of those is sputum purulence.⁽²⁾ Antibiotic overuse is still prevalent in treating all exacerbations, though their usefulness is controversial. This study tried to find out whether use of antibiotics in acute exacerbation of COPD helps reduce the number of relapses and duration of hospital stay.

MATERIALS AND METHODS

This was a randomised control study done in the Pulmonary

Medicine Department of GMC, Trivandrum. Sample size was calculated using the following formula after doing a pilot study of 20 cases.

$$\text{Sample size (n)} = 2SD^2(Z_{\alpha/2} + Z_{\beta})^2/d^2$$

N = 55 in each arm

110 COPD patients admitted in the department during the period of February to December 2009, with features of acute exacerbation as per Anthonisen criteria were included in the study. Those with definite clinical evidence of infection, new CXR infiltrates and those on mechanical ventilation were excluded. The patients were block randomised into treatment and control groups, 55 in each arm. All patients were given the standard treatment for COPD exacerbations according to GOLD guidelines. The treatment group, in addition, received oral antibiotic Amoxicillin 500 mg thrice daily for five days. Patients were discharged once they satisfied the GOLD discharge criteria. The outcome variables studied were the number of days of hospital stay and the number of relapses in two weeks (Defined as return to the same or any other hospital with persistent or worsening symptoms within two weeks of discharge). The patients were followed up in two weeks to assess the number of relapses. Reduction in duration of hospital stay and reduction in number of relapses were taken as favourable outcomes.

Statistical analysis was done using SPSS version 11.0. Chi square and student t test were used for analysis of variables.

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Ethical clearance was obtained from the Institutional Ethics Committee. Confidentiality of the study subjects were maintained at all stages of the study.

RESULTS

There were 55 patients each in treatment and control groups. The baseline characteristics of the two groups are summarised in Table 1.

Variable		Treatment Group (n = 55)	Control Group (n = 55)	P value
Average Age		59.1 ± 10.2	60.5 ± 11.5	0.305
M:F		51:4	51:4	1.000
Disease Severity	Grade 1	6	5	0.733
	Grade 2	28	30	
	Grade 3	15	17	
	Grade 4	6	3	
Smoking Index	Nil	8	5	
	<400	17	17	
	>400	30	33	
	Average	543.2 ± 449.7	499.6 ± 390.6	0.576
Kitchen Smoke	No	49	48	0.768
	Yes	6	7	
Cor Pulmonale	Yes	9	10	0.801

Table 1. Baseline Characteristics of Treatment and Control Groups

Sputum culture reports of the patients are summarised in Figure 1. Majority of patients in both groups didn't have an organism isolated from their sputum sample. The study showed no significant relationship between sputum culture results and duration of hospital stay or number of relapses in both groups. The mean duration of hospital stay and the mean number of relapses among the treatment and control groups are shown in Figure 2 and Table 4 respectively. There was no significant relationship between the stage of COPD and the number of relapses in two weeks (Table 2). But the disease stage was found significant in the duration of hospital stay (Table 3).

Group	Disease Stage	Relapse in Two Weeks				p
		No		Yes		
		Count	%	Count	%	
Treatment	Grade 1	3	12.0	3	10.0	0.845
	Grade 2	14	56.0	14	46.7	
	Grade 3	6	24.0	9	30.0	
	Grade 4	2	8.0	4	13.3	
Control	Grade 1	1	3.8	4	13.8	0.159
	Grade 2	15	57.7	15	51.7	
	Grade 3	10	38.5	7	24.1	
	Grade 4	0	0.0	3	10.3	
Table 2. Disease Severity and Number of Relapses in Two Weeks						

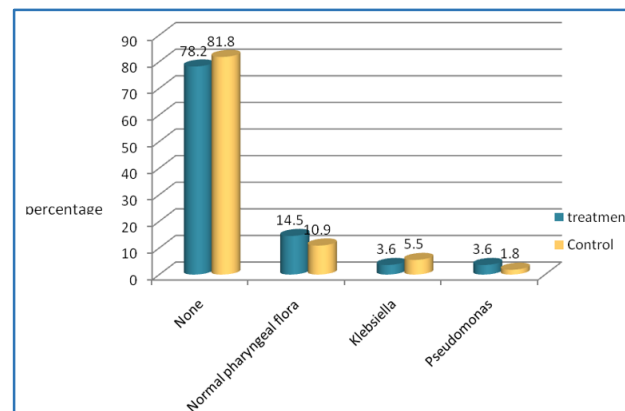


Figure 1. Sputum Culture Reports of Treatment and Control Groups (p value 0.834)

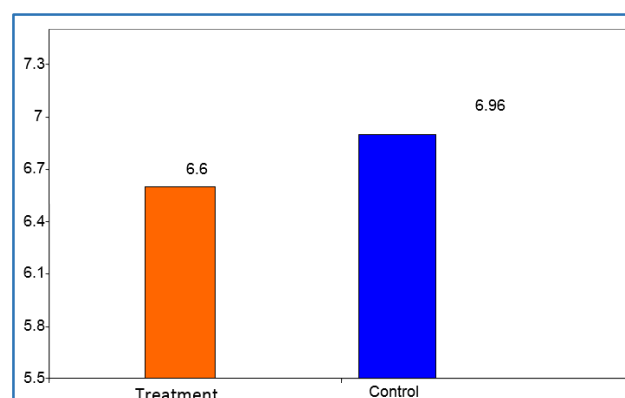


Figure 2. Mean Duration of Hospital Stay in Days (p value 0.421)

Group	Disease Stage	Days as IP				p
		<= 7 Days		>7 Days		
		Count	%	Count	%	
Treatment	Grade 1	6	14.6	0.0	0.0	<0.001
	Grade 2	26	63.4	2.0	14.3	
	Grade 3	9	22.0	6.0	42.9	
	Grade 4	0	0.0	6.0	42.9	
Control	Grade 1	4	12.1	1.0	4.5	0.018
	Grade 2	22	66.7	8.0	36.4	
	Grade 3	7	21.2	10.0	45.5	
	Grade 4	0	0.0	3.0	13.6	

Table 3. Disease Severity and Duration of Hospital Stay

Relapse in 2 Weeks	Treatment		Control	
	Count	Percent	Count	Percent
0	25	45.5	26	47.3
1	21	38.2	21	38.2
2	8	14.5	6	10.9
3	1	1.8	2	3.6

Table 4. Comparison of the Number of Relapses in Two Weeks Between Treatment and Control Groups

The number of relapses in two weeks were almost similar in the two groups as is evident from Table 4.

There was a significant relationship between duration of stay and cor pulmonale both in Treatment group and Control group. The p value was 0.023 and 0.004 respectively. Only

16.7% of Treatment group and 20.7% of Controls with cor pulmonale had relapse in 2 weeks. The relationship was not significant. The p value was 0.947 and 0.611 among Treatment and Control groups respectively.

There was no significant relationship between number of relapses in two weeks and age of the patient, stage of the disease, smoking index, presence of cor pulmonale, etc. Similarly, age and smoking index had no relation with the duration of hospital stay also. However, a significant relation was found between the disease stage and duration of hospital stay in both treatment ($p < 0.001$) and control ($p < 0.018$) groups. Significant association was there between the presence of cor pulmonale and duration of hospital stay in both treatment and control groups with p values of 0.023 and 0.004 respectively.

The study also assessed the need for a routine sputum Gram stain and culture in all COPD exacerbations, even if the exacerbation is secondary to non-infective causes. This was done as a secondary objective. Gram-negative bacilli were seen in 30.9% of treatment group and 36.4% of control group. Gram-positive cocci were isolated in 1 case each in both the groups. This finding was not statistically significant ($p = 0.831$).

Sputum culture and sensitivity yielded no organism growth in 78.2% of the treatment group and 81.8% of the control group. Pathogenic organisms were grown in 4 patients each in both groups. The rest showed normal pharyngeal flora growth in culture of sputum. The distribution is shown in Figure 1. This too was not statistically significant ($p = 0.834$).

DISCUSSION

Our study concluded that there was no significant advantage of using antibiotics routinely in all COPD exacerbations without any clinical evidence of infection, in terms of the number of relapses or the duration of hospital stay. This has been recommended in the GOLD guidelines too.⁽²⁾ Comparable findings were observed in other studies^(3,4,5) by Wim et al and Ram et al. If this practice is followed, we can control the overzealous use of antibiotics in COPD and the emergence of antibiotic resistance.

The study also showed that the stage of COPD and the presence of cor pulmonale were significant in determining the duration of hospital stay. But these did not affect the number of relapses. Other studies have come up with factors affecting the length of hospital stay in COPD exacerbations.^(6,7) Disease stage including presence of cor pulmonale is one among the factors studied and the results are comparable to ours.

Later studies have shown use of biomarkers like CRP, procalcitonin, etc. to identify patients with COPD exacerbations requiring antibiotic therapy.^(8,9,10) This may soon get integrated into the guidelines for using antibiotics in COPD exacerbations.

Literature clearly says that half of all COPD exacerbations are due to infections, bacterial or viral. Studies investigating the bacterial isolates in COPD exacerbations state that most of the infections are by *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pneumoniae*. A recent study by Dalia et al shows a pathogenic organism in culture of sputum

in two third of the samples studied. Majority of the isolates were *Streptococcus pneumoniae* (43.3%) in this study.⁽¹¹⁾ Whether to give antibiotics to all exacerbations of COPD is still a debated question. Most studies favour their use with an infective exacerbation. GOLD guidelines also advocate the same.^(4,12) A systematic review by Milo et al describes how the use of antibiotics in severe exacerbations of COPD effectively reduces treatment failure and mortality rates. The review says antibiotics may not be generally indicated in mild-to-moderate exacerbations.⁽¹³⁾

CONCLUSION

Based on our findings, we conclude that apart from the fact that empirical antibiotics are not useful in COPD exacerbations without any clinical or radiological evidence of infection, a routine Gram staining and culture is also not indicated in these cases. The Gram stain and culture positivity also did not have any significant impact on the number of relapses in these patients.

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