

## Original article

# A comparative study of systemic versus topical ciprofloxacin in the treatment of chronic rhinosinusitis

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## INTRODUCTION

Rhinosinusitis is one of the most common conditions in routine ENT practice. The prevalence of sinusitis (146/1000) has been reported to exceed that of any other chronic condition and is apparently on the rise. It is estimated that between 30 and 50 % of all patients seen by the family practitioner suffer from some form of rhinosinusitis. With a lifetime prevalence of about 5%, Chronic Rhinosinusitis (CRS) is one of the most frequently occurring chronic disorders worldwide [1,2].

Estimates suggest that sinusitis is more widespread than arthritis or hypertension. It has been shown that CRS has a significant impact on the quality of life [3]. Although the symptoms of rhinosinusitis are not life threatening they are associated with a dramatic reduction in Quality of Life [4]. Comparisons with other common chronic diseases revealed significantly lower scores for bodily pain and social functioning in patients with CRS compared to patients with pulmonary diseases or cardiac disease [5].

Chronic Rhinosinusitis has a multifactorial etiology which is attributed not only to bacterial infection but also to allergy, immune dysfunction, sinonasal mucosal inflammation, impaired ciliary function and/or anatomic obstructions within the sinonasal cavity [6,7,8]. Antibiotic therapy comprises a significant component of medical treatment of CRS [9]. A recent survey showed that 94% of US otolaryngologists prescribe prolonged courses (minimum of 2 weeks) of oral antibiotics for the treatment of CRS [10]. However, the efficacy of antibiotic therapy is dependent on a wide variety of factors such as the class of antibiotic, dose and duration of therapy, as well as whether a significant bacterial infection is present. Recently, there has been increased interest in the use of topical antibiotic formulations for CRS. Although oral and intravenous deliveries consistently achieve the therapeutic minimum inhibitory concentration (MIC) for the common pathogens of CRS in the sinonasal mucosa [11,12], topical administrations can localize drug delivery to the sinonasal cavity and minimize the systemic effects of the antibiotics [13,14]. Recent technologic advances, such as nebulized drug delivery systems, are known to show effective drug delivery mechanism in the sinonasal tract [15], with more effective drug deposition than spray formulations [16]. Additionally, common pathogens in CRS, such as *Staphylococcus aureus* and *P. aeruginosa*, are known to form biofilms, which have been found in up to 75% of CRS patients undergoing sinus surgery [17]. Bacteria present in a biofilm formation require higher antibiotic concentrations, up to 1000x the known MIC, in

order to significantly reduce the bacterial count [18,19]. Topical antibiotic therapy may achieve the necessary drug concentrations to eradicate the common pathogens while minimizing systemic toxicity.

Ciprofloxacin is the most potent first generation Fluroquinolone active against a broad range of bacteria including the gram negative spectrum and also gram positive bacteria.

Ciprofloxacin is rapidly absorbed orally but food delays absorption and first pass metabolism occurs [20]. Nebulisation can offer distinct advantage of directly acting over the sinonasal mucosa and increasing the effectiveness of drug and minimizing the adverse effects [14,15]. Ciprofloxacin was used in our study because of its availability, less cost, minimal side effects and proven efficacy in the Hospital Antibiotic Poiley.

#### **MATERIALS AND METHODS:**

All established cases of Chronic Rhinosinusitis diagnosed clinically at the ENT outpatient department at tertiary care centre.

#### **SAMPLE SIZE**

40 subjects

#### **PLACE OF STUDY**

Tertiary care centre

#### **DURATION OF STUDY-2 years**

#### **SUBJECT SELECTION-**

##### **Inclusion criteria**

(a)Prospective cases of Chronic Rhinosinusitis established clinically using the Rhinosinusitis Task Force Criteria

(b) Sex: both

(c) Age: 14 to 60

(d) Symptomatology present for more than 3 months

(e)Nasal swab culture sensitive to Ciprofloxacin

##### **Exclusion Criteria**

(a) Patients who are unwilling to participate

(b) Non Infective Rhinosinusitis

(c) CRS associated with complications

(d) Pregnant women and breast feeding mothers

(e) Patients with cardiac, hepatic or renal diseases

(f) H/O alcohol or drugs abuse

A diagnostic Nasal Endoscopy was done for all the patients. On the basis of Lund Mackay endoscopic scoring system all these patients were given scoring depending upon presence of discharge, edema and polyps.

Also a endoscopy guided nasal swab was taken and sent for culture and sensitivity. The culture reports were reviewed and only patients with a positive bacterial culture which was sensitive to Ciprofloxacin were selected for the study. 40 patients were selected considering all the inclusion and exclusion criterias. These 40 patients were

divided into 2 groups of 20 each by simple random sampling. The patients were explained the treatment procedure. All of them were asked to sign a written informed consent so as to undergo this study. All the patients either filled up the SNOT-20 questionnaire on their own or by the help of the doctor prior to the treatment.

**TREATMENT AND DATA COLLECTION-**

After the selection of cases the patients were divided into two groups by simple random sampling. Both the Groups had 20 patients each. The Treatment received was -

Group 1 which had 20 cases received Treatment with Tablet Ciprofloxacin 500mg two times daily along with Topical Steroid Nasal Spray in the form of Fluticasone nasal spray 2 puff once a day in both nostrils for 15 days.

Group 2 which had 20 cases received Treatment with Ciprofloxacin Nebulisation (solution containing 45mg) two times daily along with Topical Steroid Nasal Spray in the form of Fluticasone nasal spray 2 puff once a day in both nostrils for 15 days.

The patients were again subjected to a Clinical examination and Rigid nasal endoscopy at the end of the treatment. Endoscopic Lund Mckay scoring was done. Also a endoscopy guided nasal swab was taken and sent for culture. SNOT score was again taken from the patients. All the 40 patients were further followed up for next 2 weeks and reassessed for the symptomatology if present or not.

All the pretreatment and Post treatment scores and data were recorded and tabulated. These were then analysed using appropriate statistical tools.

**RESULTS -**

The information was collected using a Master sheet and information entered in computer software. Cross checking and data clearing was done.

Nominal data such as gender, indications were presented as number (N) and percentage (%). Continuous variables (age, etc) were expressed as mean and standard deviation (SD).

Student’s paired T-test was applied for comparison of nominal data. p value of < 0.05 was considered as statistically significant.

The analysis of data was performed using Microsoft excel and SPSS(Statistical Package for Social Sciences) version 19.0.

**A) Comparison of mean SNOT in group 1 and group 2:**

	Number of patients	SNOT				P-value
		Group 1		Group 2		
		Mean	SD	Mean	SD	
At Baseline	20	68.15	7.77	70.05	5.80	0.39
At 2 weeks	20	36.85	5.58	35.05	5.78	0.186

By using 2 independent sample t-test p-value > 0.05 therefore there is no significant difference between mean SNOT in group 1 and group 2 at baseline and at 2 weeks.

**B) Comparison of mean LM endoscopic score in group 1 and group 2.**

	Number of patients	LM Endoscopic Score				P-value
		Group 1		Group 2		
		Mean	SD	Mean	SD	
At Baseline	20	9.60	1.54	9.25	1.59	0.48
At 2 weeks	20	4.15	1.53	3.95	1.23	0.652

**C) Distribution of patients with respect to symptomatic/Asymptomatic at 4<sup>th</sup> follow up:**

4 <sup>th</sup> week follow up	Group		Total	P-value
	Group 1	Group 2		
Asymptomatic	15	17	32	0.695
Symptomatic	5	3	8	
Total	20	20	40	

By using chi-square test p-value > 0.05 therefore there is no significant association between 4<sup>th</sup> week follow up with group 1 and group 2.

**D) COMPARISON OF MEAN SNOT IN POST FESS PATIENTS:**

	SNOT				P-value
	Group 1 (n=3)		Group 2 (n=5)		
	Mean	SD	Mean	SD	
At Baseline	67.67	11.72	70.80	4.60	0.70
At 2 weeks	37.33	5.51	30.60	3.36	0.154

By using 2 independent sample t-test p-value > 0.05 therefore there is no significant difference between mean SNOT at baseline and at 2 week with respect to group 1 and group 2 for patients with previous FESS done.

**E) COMPARISON OF MEAN LM ENDOSCOPIC SCORE IN POST FESS PATIENTS:**

	LM endoscopic score				P-value
	Group 1 (n=3)		Group 2 (n=5)		
	Mean	SD	Mean	SD	
At Baseline	8.67	2.08	8.00	1.22	0.65
At 2 weeks	4.33	2.31	3.20	0.84	0.489

By using 2 independent sample t-test p-value > 0.05 therefore there is no significant difference between mean LM endoscopic score at baseline and at 2 week with respect to group 1 and group 2 for patients with previous FESS done.

**DISCUSSION**

Chronic rhinosinusitis is one of the most prevalent chronic illnesses in the world and is known to affect all the age groups [21]. Apart from the symptom profile as described in the diagnostic criteria, nasal examination is done to visualise the nasal mucosa, purulent discharge or evidence of polyps or any other nasal mass. Deviated nasal septum and turbinate hypertrophy are amongst the contributing factors which also need to be ruled out. A diagnostic nasal endoscopy supplements the routine rhinoscopy examination.

Topical Antibiotic Therapy with culture directed antibiotics is a novel treatment in the treatment of Chronic Rhinosinusitis. Very few studies are conducted in use of this modality of treatment of Chronic Rhinosinusitis.

In our study total 40 patients participated with a range of age from 22 to 66 years. The mean age for Group 1 being 39.70 yrs and group 2 being 41.30 yrs. Group 1 had 12 males and 8 females, Group 2 had 13 males and 7 females. Out of the 40 patients in our study 8 (3 patients in Group 1 and 5 patients in Group 2) had already undergone a FESS for the CRS and were still symptomatic.

In a study done by Winston C. Vaughan et al Nebulised antimicrobial therapy was studied as a treatment option in patients after surgery. In the study results symptomatic and endoscopic data before and after nebulized therapy showed a longer infection free period (average 17 weeks) compared to the standard therapy (average 6 weeks). Improvement in posterior nasal discharge , facial pain and pressure, and emotional consequences were also noted [22].

In a study done by Philip A. Scheinberg et al., effectiveness of aerosol delivery of antibiotics to the sinuses via a nebulizer in 41 patients with chronic sinusitis was assessed. The pre and post treatment symptom scores in five categories : nasal obstruction, facial pain, facial pressure, mucopurulent nasal discharge and malaise was compared. Following 3 to 6 weeks of treatment 34 patients (82.9%) experienced either an excellent or good response to treatment. The study concluded that nebulized antibiotics should be considered for all patients with chronic sinusitis who have undergone FESS and who have failed to respond to oral antibiotics or who do not tolerate them [23].

Woodhouse BM et al in 2011 carried a meta analysis for Nebulized antibiotics for the treatment of refractory bacterial chronic rhinosinusitis. The study concluded that based on the current studies, use of nebulised antibiotics cannot be recommended at this time. Culture-directed nebulized antibiotic therapy may be a treatment option in patients with CRS refractory to conventional treatments supportive evidence though is limited [24].

This study aims to analyse the effectiveness of Topical Antibiotic therapy in the form of Ciprofloxacin nebulisation and its comparison to the Systemic Antibiotic therapy in the form of Oral Ciprofloxacin in diagnosed cases of Chronic Rhinosinusitis with bacterial culture sensitive to Ciprofloxacin.

In our study with the culture directed antibiotic therapy with Ciprofloxacin was well tolerated by the patients in both the groups. The patients in Group 2 were symptomatically better than that of Group 1 but the difference was not statistically significant. In patients who had already undergone a FESS and still had persistent CRS were also included in the study. In the post FESS patients comparing the outcomes with culture directed Ciprofloxacin symptomatic relief and symptom free interval was better in Group 2 but this difference was not statistically significant.

In the previous studies that were carried out with topical antibiotics it has been shown that the symptom free interval increases after topical antibiotic therapy. The studies showed that Topical antibiotics were effective in Post FESS patients.

The sample size in our study was very less to make any conclusion. Therefore extrapolating the results in clinical practice will not be correct. Therefore it is recommended that more studies should be carried out to come to a satisfactory level of evidence before using them in clinical practice.

## CONCLUSION

Antibiotic therapy is an important aspect of medical management of Chronic Rhinosinusitis. Culture directed Topical Antibiotic therapy is a novel treatment option for Chronic Rhinosinusitis. Literature on Topical Antibiotic therapy is limited. Our study attempted to evaluate culture directed topical Ciprofloxacin in chronic rhinosinusitis. However before the results are put into clinical practice, studies with larger, sample size followed by systematic analysis and meta-analysis are required to provide evidence of higher level.

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