RESEARCH ARTICLE

A STUDY ON THE DRUG PRESCRIBING PATTERN IN PARA-NASAL SINUSITIS AT A TERTIARY CARE HOSPITAL

Background: Infections of paranasal sinuses involve the mucus membrane of maxillary, ethmoid, frontal or sphenoidal sinuses, which frequently coexist. They can be acute, sub-acute and chronic, based on the duration of symptoms, and may occur usually due to viral or bacterial infections and very rarely fungal infection. Sinusitis is of particular concern because of the anatomical proximity, which may lead to various sequelae and complications involving the brain and the orbit.
Aims & Objective: To determine the drug prescribing pattern in paranasal sinusitis and to assess the efficacy and tolerability of antimicrobials used in paranasal sinusitis.
Materials and Methods: 50 subjects of either gender were included in the study to assess the pattern of drugs prescribed; details of drug therapy, therapeutic class of antimicrobial agents, dose, route, frequency, duration of administration, and tolerability of antimicrobials used were recorded.
Results: Out of 50 study subjects 42 % were male and 58% were female. All the subjects had multiple symptoms with mean duration of the symptoms for 8.06±3.59 days. Only 14 subjects had used the antimicrobials for the previous episodes and data was not available in 36 subjects. 72% had acute bacterial sinusitis. 96% subjects received the antimicrobials from beta-lactam group, Co-amoxiclav was the commonly prescribed antimicrobial agent. The concomitant medications like non-steroidal anti-inflammatory and decongestants used in the present study. All the subjects showed significant clinical improvement with mild and self-limiting adverse effects.
Conclusion: Acute, recurrent and chronic bacterial paranasal sinusitis can be effectively treated by empirical use of various antimicrobials. Co-amoxiclav can be considered as the mainstay /primary option because of the proven efficacy, good tolerability and low cost.
Key Words: Antimicrobials; Paranasal Sinusitis; Non-Steroidal Anti-Inflammatory Drugs

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INTRODUCTION

Para-nasal sinusitis is the inflammation of mucosal lining of the paranasal sinuses. Although most cases of sinusitis involve more than one sinus, the maxillary sinus is most commonly involved; next in frequency are the ethmoid, frontal, and sphenoid sinuses.[1,2] Inflammation of the sinuses rarely occurs without concurrent inflammation of the nasal mucosa; therefore, rhinosinusitis is a more preferred term, for what is commonly called sinusitis.[3] It can be acute, subacute and chronic, based on the duration of symptoms, and may occur usually due to viral or bacterial infections and very rarely fungal infection.[4,5] Acute sinusitis is a transient inflammation of paranasal sinuses lasting less than 4 weeks, sub-acute sinusitis present for more than four but less than eight weeks and chronic sinus infection/ chronic rhinosinusitis is usually a continuation of unresolved acute sinus infection. Sinusitis is of particular concern because of the anatomical proximity, which may lead to various sequelae and complications involving the brain and the orbit.[6] Many antimicrobial agents (AMAs) including antibacterial, antiviral and antifungal agents, and adjunctive therapies like analgesics, saline nasal irrigation, intranasal corticosteroids, mucolytics, antihistamines and decongestants are used in the treatment and prophylaxis of paranasal sinusitis. The pattern of AMA use may vary from hospital to hospital and in different geographical areas depending on the nature of infections, prevalent strains of pathogens, the pattern of susceptibility/ resistance and cost/availability of antimicrobial agents. The assessment of drug utilization is important for clinical, educational and pharmacoeconomic purposes. Monitoring of prescriptions and study of drug utilization could identify the associated problems and provide feedback to the prescriber so as to create awareness for the rational use of drugs.[7,8] Though there have been several studies and reports in the literature, there are limited and inconsistent data from the Indian population. Hence, there is a need for more systematic studies to generate valid data for improved quality of care and therefore the present study was taken up, to describe the pattern of drugs used in acute, recurrent and chronic bacterial sinusitis and to assess the efficacy and tolerability of the antimicrobials used in the present study.

MATERIALS AND METHODS

This observational study was done to assess the pattern of drugs used in acute, recurrent and chronic bacterial

sinusitis. After approval and clearance from the Institutional Ethics Committee, 50 subjects with sinusitis visiting the Outpatient Department of ENT at Kempegowda Institute of Medical sciences, Hospital and Research Centre, Bangalore were included into the study by the investigator after coordinating and confirming the diagnosis with ENT specialist. (The diagnosis was mainly based on signs, symptoms, duration of illness and clinical examination).[9-11] Study subjects were recruited by purposive sampling method from January 2012 – January 2013. Written informed consent was obtained from all the study subjects after fully explaining the study procedure to their satisfaction, in both English and vernacular language. Subjects fulfilling the inclusion criteria were included into the study; Patients of all age groups above 3 years, from either gender attending the outpatient department of ENT with bacterial sinusitis and willingness of the patients/parents or legal representatives to give the written informed consent and available for follow up (once after AMA therapy). Patients with the following conditions were excluded from the study; Patients already receiving antimicrobial therapy, sinusitis due to viral or fungal infections (based on the signs, symptoms and clinical examination done by ENT specialist. Infectious Disease Society of America (IDSA) guidelines and The Clinical Practice Guidelines of the American College of Physicians guidelines, were followed to distinguish between bacterial and viral sinusitis)[9,12], patients with nasal polyps, deviated nasal septum, allergic rhinitis or traumatic lesions and immunocompromised patients.

Patients were subjected to a detailed history taking including personal history, family history, present and past medical history and drug history. Predisposing or precipitating factors for sinusitis, if any, were also recorded. An examination of the paranasal sinuses and a thorough evaluation done by ENT specialist was documented by the investigator. Details of drug therapy, i.e., the intended purpose of use i.e. prophylaxis or cure, the therapeutic class of AMA used, dose, route, frequency and duration of administration, tolerability and drug interactions were recorded. After the completion of AMA therapy, the efficacy and outcome of the antimicrobial therapy was assessed by clinical examination by the ENT specialist was also documented by the investigator. Only the reported adverse drug reactions were documented after the completion of the AMA therapy. Patient compliance to the prescribed medications was assessed by recovering empty packets/pill count method. It was assessed as compliant (those who didn't miss even a single dose) or non-compliant (those who missed even a single dose).

The data collected was analyzed by using descriptive statistics, namely mean, standard deviation. The results were also depicted in the form of tables and graphs. Microsoft Word and Excel are used to generate graphs and tables.

RESULTS

The demographic data of the study subjects with paranasal sinus infection is presented in the Tables-1. The mean age of the subjects in years was 31.06 ±12.16. Majority of the subjects were in the age group of 16-35 years. Table-2 summarizes the presenting complaints in the study subjects. All the subjects had multiple symptoms. Headache which was mainly frontal or temporal was complained by all the subjects. 90% of the subjects had nasal obstruction and 44% of subjects running nose. Facial pain was complained by 40% of subjects and 18% had fever. The mean duration of the symptoms in days was 8.06±3.59, 90% of the subjects had the symptoms of 6-10 days duration. Except 3 subjects all the others had one or more episodes in the past one year. 11 subjects had more than 4 episodes in the past one year indicating recurrent sinusitis. Only 14 subjects had used the AMAs for the previous episodes which included co-amoxiclav (n=12), cefadroxil (n=1) and cefpodoxime proxetil (n=1), and data was not available in 36 subjects. There was no history of allergic reactions to the AMAs used in the past. The clinical signs (Figure-1) of sinusitis observed were congestion of nasal mucosa and tenderness over the sinuses, in all subjects. Postnasal dripping was observed in 94% of subjects and nasal discharge in 44% of subjects. Enlarged and tender cervical nodes were observed in only 4 subjects and only 1 subject had congestion of pharynx. The provisional diagnosis of the type of sinusitis based on clinical and radiological examination is presented in Figure 2. 72% had acute bacterial sinusitis, 12 subjects had recurrent bacterial sinusitis and only 2 subjects were considered as having chronic bacterial sinusitis since the duration was more than 15 days. Laboratory investigations which included X-ray of the skull (n= 9) subjects and CT scan-PNS (n=4), were done only in subjects with chronic and recurrent sinusitis to confirm the diagnosis. Microbiological examination like culture and sensitivity were not indicated in any subjects. Table -3 summarizes the AMAs used for the paranasal sinus infections. 48 subjects (96%) received the AMAs from beta-lactam group and only 2 subjects from fluoroquinolone group. The beta – lactams

Table-1: Age distribution (n=50)

Age Group (in years)	Number of Patients (%)
3-5	0 (00)
6-10	0 (00)
11-15	5 (10.00)
16-25	15 (30.00)
26-35	14 (28.00)
36-45	8 (16.00)
>45	8 (16.00)
Mean age ± SD = 31.06 ± 12.16	

Table-2: Presenting complaints/symptoms

Symptoms	N (%)
Fever/malaise	18 (36.00)
Cough	1 (2.00)
Headache	50 (100.00)
Running nose	22 (44.00)
Nasal obstruction/congestion	45 (90.00)
Ear pain	0 (0)
Cheek pain/facial heaviness	20 (40.00)
Multiple symptoms*	50 (100.00)

* Multiple symptoms: ≥ 1 symptom

Table-3: AMAs used

AMAs*	Dose	Frequency	Duration	N (%)
Co-amoxiclav	625	BID	5 days	21 (42.00)
Cefpodoxime-clavulanic acid	325	BID	5 days	15 (30.00)
Cefadroxil-clavulanic acid	625	BID	5 days	5 (10.00)
Cefpodoxime proxetil	200	BID	5 days	1 (2.00)
Cefuroxime axetil	250	BID	5 days	4 (8.00)
Cefixime-clavulanic acid	325	BID	5 days	2 (4.00)
Levofloxacin	500	OD	5 days	2 (4.00)

* All medications given as oral formulations as tablets for 5 days irrespective of duration of symptoms

Table-4: Concomitant medications

	Drugs	N (%)
NSAIDs*	Aceclofenac+paracetamol	25 (50.00)
	Diclofenac+paracetamol	14 (28.00)
	Diclofenac	7 (14.00)
	Nimesulide	2 (4.00)
Decongestants*	Cetirizine+pseudoephedrine	3 (6.00)
	Levocetirizine+montelukast	1 (2.00)
	Cetirizine	2 (4.00)
	Levocetirizine	2 (4.00)
	Levocetirizine+pseudoephedrine	4 (8.00)
	Paracetamol+ Phenylephrine +chlorpheniramine	2 (4.00)
	Xylometazoline nasal drops	14 (28.00)
Other drugs	Pantaprazole†	1 (2.00)
	Multivitamins	2 (4.00)

* Used as Adjuvants; † For associated gastritis

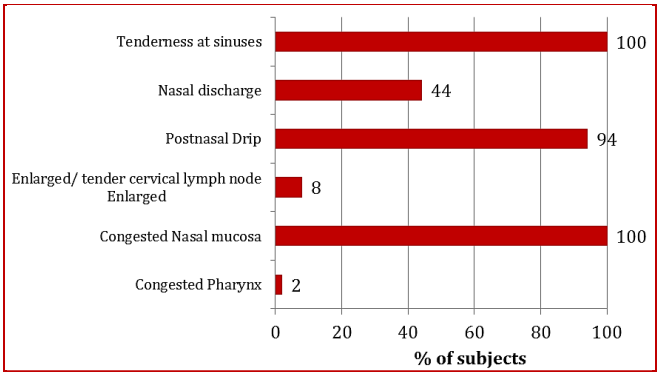

Figure-1: Clinical signs

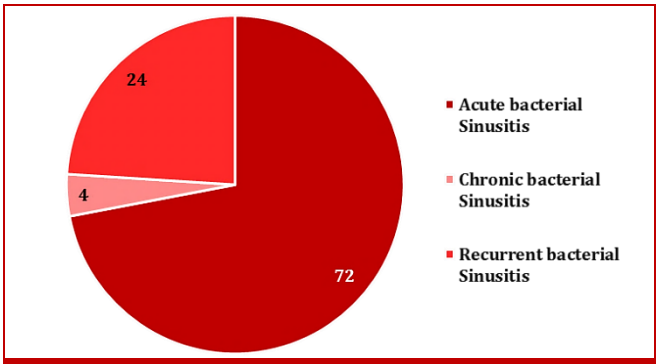

Figure-2: Provisional diagnosis

used were extended spectrum penicillins (co-amoxiclav), 1st generation (cefadroxil), 2nd generation (cefuroxime) and 3rd generation (cefixime, cefpodoxime) cephalosporins and the only fluoroquinolone was levofloxacin. Co-amoxiclav (n=21) and cefpodoxime + clavulanic acid (n=15) were the most commonly used beta-lactams, and levofloxacin was used in 2 subjects with chronic sinusitis with suspected resistance to beta-lactams. All the AMAs were given as oral formulations (tablets) for 5 days irrespective of the type of sinusitis and duration of symptoms. The concomitant medications like NSAIDs and decongestants used in the present study are summarized in Table-4. NSAIDs were mainly used as FDCs of aceclofenac + paracetamol (n=25) and diclofenac + paracetamol (n=14) for 3 days. Various decongestants containing H1-blockers and vasoconstrictors were used to relieve nasal obstruction and were advised for one week. The outcome of treatment as assessed clinically after the completion of 5 days course of AMA therapy. All the subjects showed significant clinical improvement however none of the subjects had complete cure, and some of the symptoms like nasal obstruction, mild frontal headache, and facial heaviness still persisted. The rate of resolution of infection and the clinical improvement was almost similar with all the AMAs. The adverse effects were infrequent, mild and self-limiting and did not require discontinuation or change in therapy. Mild diarrhea was reported in 3 subjects treated with co-amoxiclav, and mild abdominal discomfort in 2 subjects who received cefpodoxime + clavulanic acid. All the patients and their attendants had complied very well to the prescribers instructions regarding the quantity and frequency of administration.

DISCUSSION

In the present study, the pattern of antimicrobial use in acute, recurrent and chronic pharyngitis and paranasal sinus infections, the criteria for their selection, their safety, tolerability and clinical outcome, was assessed in

patients attending the ENT outpatient department in KIMS Hospital and Research Centre, a tertiary care teaching hospital. All the study subjects fulfilled the inclusion and exclusion criteria and were fully compliant with the prescribed medications.

The overall pattern of symptoms showed a good correlation with manifestation of frontal, maxillary and ethmoidal sinusitis, which was consistent with other studies.[5,13] The observed clinical signs corresponded very well with the classical signs of paranasal sinus infection which was consistent with the observations in the other studies.[4,14] The provisional diagnosis of the type of sinusitis was mainly based on clinical examination and in some by radiological examination. According to the IDSA guidelines[12], sinus infection should be considered probably bacterial in cause and antibiotics started only if symptoms last 10 days or more and are not improving (some previous guidelines, including the UK National Health Service (NHS)[15] suggested waiting 7 days), or if symptoms are severe (high fever and purulent nasal discharge or facial pain lasting 3–4 days), or if symptoms get worse. The IDSA guidelines recommend 5–7 days of antibiotics for adult bacterial sinusitis, rather than the 10–14 days in previous guidelines, to discourage development of resistance. Co-amoxiclav was preferred antimicrobial agent because of its good activity against usual pathogens and adequate coverage against beta-lactamase producing *M. catarrhalis* and *H. influenza*. Most guidelines recommend co-amoxiclav as first-line therapy because of good tolerability and cost-effectiveness.[12,17] The combination of clavulanic acid with amoxicillin, cefadroxil, cefpodoxime proxetil and cefixime, may improve the activity against *H. influenzae*, *M. catarrhalis* and certain anaerobes by protecting the antibiotics from bacterial betalactamases[12,14-18], and were considered as alternative for co-amoxiclav non-responders. Combination therapy with a third-generation oral cephalosporin (cefixime or cefpodoxime) plus clindamycin may be used as second-line therapy for children with non–type I penicillin allergy or those from geographic regions with high endemic rates of penicillin-nonsusceptible *S. pneumoniae*.[12] Flouroquinolones were generally reserved for the subjects with history of allergy to beta-lactams.[12,17] NSAIDs were mainly used as fixed dose combinations (FDCs), to alleviate pain and congestion. Several controlled clinical studies have shown that combinations of acetaminophen and NSAIDs provide additive pain-relieving activity, thereby leading to dose-sparing effects and improved safety.[19,20] The use of FDCs of nasal decongestants which mainly include sympathomimetic vasoconstrictors in combination with H_1 blockers seems to be irrational. Continued use of xylometazoline for more than 3 days may result in rebound nasal congestion and rhinitis medicamentosa.[14] As a result, expert guidelines recommend that intranasal decongestant treatment be limited to brief use of less than 10 days with switch to other therapies if symptoms persist after 5 days.[21,22] The outcome of treatment was assessed clinically after the completion of 5 days course of AMA therapy. All the subjects showed significant clinical improvement, both subjective and objective, like relief of fever, headache, malaise, decreased nasal obstruction, running nose, cheek pain, facial heaviness, nasal congestion, tenderness over the frontal, maxillary and ethmoidal sinuses. However none of the subjects had complete cure, and some of the symptoms like nasal obstruction, mild frontal headache, facial heaviness still persisted. The rate of resolution of infection and the clinical improvement was almost similar with all the AMAs. Some studies have shown comparable cure rates with 7-10 days course of treatment with penicillins and cephalosporins.[6] Azithromycin used for 3-6 days achieved a similar cure rate as 10-day therapy with co-amoxiclav.[6] Hence it can be presumed that, though significant clinical improvement is possible with a 5-day course of therapy with empirically chosen AMAs, complete resolution or cure of paranasal sinus infections may require 7-10 day course of therapy. However chronic and recurrent paranasal sinus infections may require definitive therapy with AMAs based on bacteriological studies for an adequate duration of time, apart from correcting any possible underlying anatomical and developmental abnormalities. The adverse effects were infrequent, mild and self-limiting and did not require discontinuation or change in therapy. Other studies also reported good tolerability of the AMAs like co-amoxiclav, cephalosporins, azithromycin and macrolides, only the beta-lactams produced mild abdominal discomfort with occasional diarrhea. Some studies have reported allergic reactions to penicillins only in a few patients.[12,18] There are several limitations to this study: the sample size was less, the treatment was mainly empirical, and the duration of treatment was followed for only five days.

CONCLUSION

Acute, recurrent and chronic bacterial sinusitis can be effectively treated by empirical use of various AMAs. Co-amoxiclav can be considered as the mainstay or primary option because of the proven efficacy, good tolerability and low cost. Other AMAs like cefpodoxime + clavulanic acid, cefadroxil + clavulanic acid, cefuroxime, cefixime +

clavulanic acid and levofloxacin can be considered as alternatives. Though a 5-day course of AMA therapy can produce a significant clinical improvement, the cure rate may be increased by continuing the AMA therapy for 7-10 days. All the AMAs showed good tolerability and patient compliance.

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