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Amoxicillin Vs Amoxicillin-Clavulanate in Sinusitis: A Review of Clinical Outcomes and Resistance Profiles

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ABSTRACT
Sinusitis is a very common chronic illness which can be treated mostly through lifestyle modifications and anti-biotics (only if needed). This reviewed primary focuses on etiology, clinical manifestation, pathophysiology, diagnosis and treatment of the sinusitis. The pathological condition where the transient inflammation of the linings of paranasal sinuses along with the symptoms of nasal congestion, facial pain and difficulty of breathing is known as sinusitis. The major causes of the sinusitis include viruses, bacteria and fungi. The identification of pathogen or causative organism is based on the symptoms. There may be other factors which may increase the risk of developing sinusitis. The pathophysiology of sinusitis is due to obstruction of sinus ostia, ciliary impairment and altered quality and quantity of mucus. The diagnosis majorly involves physical evaluation of the symptoms. An MRI or CT may be rarely prescribed to understand the structural changes. The treatment is based on the symptoms and severity of disease. The primary care includes lifestyle modifications. Amoxicillin with or without clavulanate is the primary first line treatment for sinusitis. The prescription of these drugs is done only during the necessary conditions to promote antimicrobial stewardship.

Key words: *Sinusitis, pathophysiology, diagnosis, amoxicillin-clavulanate, β-lactamase inhibitor.*

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I. INTRODUCTION

Sinusitis also known as “rhinosinusitis” (rhino-nose, sinus-spaces in the body) is the condition which causes inflammation of the linings of the paranasal sinuses and the nose. The location of sinuses is behind the forehead nasal bone, cheeks and eyes. Generally, mucus is formed in the nose and is able to drain out and the free flow of air is observed but during this condition the nasal obstruction is observed causing difficulty in breathing [1-3].

The most common bacterial pathogens of community-acquired acute sinusitis continue to be *Streptococcus pneumoniae* and *Haemophilus influenzae*, accounting for more than 50% of isolates. There is an increased frequency of β-lactamase production by *H influenzae* and *Moraxella (Branhamella) catarrhalis*, penicillin resistance of *Staphylococcus aureus*, and multiple-drug resistance of *S pneumoniae*. The problem of antimicrobial resistance is complicated by bacterial pathogens not being identified in many patients treated for acute bacterial sinusitis. The frequency with which drug-resistant bacteria are isolated and the limited patient-specific identification and susceptibility information available have led to the use of antimicrobial regimens that are effective against a relatively resistant and broad spectrum of pathogens. Consideration must be given to the use of antimicrobial agents that are β-lactamase resistant.

Amoxicillin-clavulanate is a combination product containing the semisynthetic penicillin, amoxicillin, and the β-lactamase inhibitor, clavulanate potassium. The established oral dose regimen for acute bacterial sinusitis in adults is an equivalent of 500 mg of amoxicillin and 125 mg of clavulanate given every 8 h. Since patient compliance is a major factor that determines outcome for outpatient treatment of many infections, it is necessary to determine the most convenient dose regimen that is effective [2,3]

Etiology

Sinusitis is generally of two types based on the symptoms and severity of the disease: Acute sinusitis, Chronic sinusitis and sub-acute sinusitis. The sinusitis caused by viruses or bacteria growing in the sinuses and the symptoms lasting for 4 weeks or less is known as acute sinusitis. When the symptoms and swelling of sinusitis

lasting for 1-3 months is known as sub-acute sinusitis. When the sinusitis is caused by bacteria and fungus and the symptoms and swelling lasting longer than 3 months is known as Chronic sinusitis.

Viral sinusitis include rhinovirus, adenovirus, influenza virus, para-influenza virus and the symptoms may last for less than 10 days and not worsening. Acute bacterial sinusitis caused by Streptococcus pneumoniae, Hemophilus influenza and Moraxella catarrhalis and the symptoms last more than 10 days. Acute fungal which is rare but mostly occurs in immunocompromised patients caused by mucor, Rhizopus, reconductor and aspergillus.

The other factors which may cause the risk of developing sinusitis and make it worse include - Allergic rhinitis (allergy related to inflammation in the nose), Asthma, deviated nasal septum or abnormalities in the nose, increased intake of acetylsalicylic acid while being intolerant to it, weakened immune system and environmental factors such as cigarette smoking or exposure to chemicals [4-6].

Clinical manifestations

Symptoms generally include:

- Stuffy nose and nasal discharge
- Difficulty in breathing
- Reduced sense of smell or bad breath
- Pain and pressure in the face, maxillary dental pain, ear fullness/pressure
- Pyrexia (fever)
- Headache
- Cough, worse during night
- Fatigue
- Sore throat
- Postnasal drip [3,7].

Pathophysiology

The general pathophysiology of sinusitis is related to three factors which are obstruction of sinus ostia (sinus drainage pathway), ciliary impairment and alter mucus quality and quantity.

- Obstruction of sinus ostia: The obstruction of sinus ostia may be due to systemic diseases resulting in decreased mucociliary clearance or mechanical obstruction. Systemic diseases may include cystic fibrosis, respiratory allergies and Kartagener syndrome. Mechanical obstructions include foreign bodies, deviated septa or tumours.
- Impaired ciliary action: The mucociliary transport mechanism is responsible for the drainage pattern where subsequent coordination of ciliated columnar epithelial cells occurs towards sinus contents into natural sinus ostia. The loss of ciliated epithelial cells, increased air flow or other factors results in fluid accumulation within the sinus leading to impairment of mucosal drainage.
- Altered quantity and quality of mucus: The mucous blanket consisting of inner serous layer and outer viscous layer plays important role for normal mucociliary clearance. If the composition of mucous is changed into viscous form due to various factors, it results in retention of mucous within the sinus [8-10].

Diagnosis

The primary diagnosis of sinusitis is a physical evaluation which includes description about the symptoms. The physician may utilize otoscope which is a handheld thin tube consisting of a small light source to take a closer look at the inside of the nose for evaluation of any swelling or deformities. An MRI or CT scan imaging which shows details of sinus and nasal areas may help the physician to check for structural problems, in some cases. Carrying out an allergy test to identify possible triggers is also recommended for further evaluation and treatment. Other evaluation tests include ciliary function test, nasal culture, nasal cytology, ESR and CRP [11,12].

Treatment

The treatment of sinusitis is based on the severity of the symptoms and how long the condition lasts. To treat acute and subacute sinusitis physician primary prescribes antibiotics and for chronic sinusitis the physician may prescribe life style management and few corticosteroids (if needed) to manage the inflammation.

The primary treatment for sinusitis generally includes selfcare at the primary level: To reduce the stuffiness of the sinuses, apply a warm moist cloth to the face, increase the intake of fluids, inhale steam 2-4 times per day and using a humidifier may help improve the symptoms. To reduce the sinus pain or pressure avoiding sudden temperature changes and bending forward with head down may help improve the symptoms. Physician may prescribe acetaminophen, ibuprofen or naproxen for the treatment for sinus pressure and pain. Other treatment also includes immunotherapy, avoiding allergy triggers, steroid nasal sprays, decongesting nasal sprays, oral corticosteroids etc.

Amoxicillin with or without clavulanate are the first line drugs to treat patient suffering from sinusitis, according to American Academy of Otolaryngology guidelines. The dose and duration vary based on the severity of the symptoms, established with risk factors for resistant organisms, comorbidities or age groups [13-16].

Amoxicillin

Amoxicillin is used to treat bacterial sinus infection which cause painful pressure around nose and eyes, with congestion along with mild pyrexia and temporary hyposmia. Amoxicillin is an anti-biotic made from penicillin. It works by preventing the formation of the cell wall by inactivating Penicillin-binding Protein (PBP) 1A, which is essential for the bacteria survival. If the cell wall isn't formed it ultimately leads to death of the bacteria.

Dosage: General dosage for moderate infections is 250mg every 8 h or 500mg every 12 h through oral route of administration and for severe infection 500mg every 8 h or 875mg every 12 h by mouth. The patients with severe kidney impairment, the dosing may range from 250 to 500mg every 12 to 14 h and for patients undergoing haemodialysis the dosing is 250 to 500mg every 24 h.

Adverse events: The adverse events related to amoxicillin is described as follows; diarrhoea, nausea, vomiting, lower GI irritation in gastrointestinal tracts, allergic skin reactions on the skin in few cases. Rare events include dizziness, headache, mucocutaneus candidiasis and rarely hypersensitivity vasculitis [17-20].

Amoxicillin and clavulanate

Amoxicillin and clavulanate is used to treat bacterial sinus infection and belongs to class of penicillin and beta-lactamase inhibitors. Amoxicillin inactivates penicillin-binding protein (PBP) 1A without which peptidoglycan can't be formed leads to bacterial death and clavulanate effects as a suicide inhibitor and activates beta-lactamase, thus becoming more active.

Dosage: General dosage is 125-250mg of amoxicillin and 31.25-62.5mg of clavulanate per 5 ml every 8 h in adults through oral route of administration in the form of chewable tablets or suspensions. In serious infection the dose may be increased to 200-400mg of amoxicillin and 28.5-57mg of clavulanate per 5ml every 12 h.

Adverse events: Diarrhoea, nausea, vomiting, abdominal discomfort in gastrointestinal tract. Rarer complications include prolonged prothrombin time, vasculitis, thrombocytopenia, cholestatic jaundice, hepatitis, hepatotoxicity. Amoxicillin has similar effect to amoxicillin clavulanate with fewer gastro intestinal adverse events. Hence, amoxicillin is widely prescribed in adults to treat sinusitis as first line anti-biotic therapy. But amoxicillin clavulanate is generally prescribed during certain resistance conditions and extreme use of amoxicillin clavulanate can lead to developing of antimicrobial resistance [21-26].

II. CONCLUSION

Sinusitis is the common, chronic, inflammatory disease associated with significant morbidity. It is a self-limiting disease and can resolve on its own through primary care. It is the term used to describe the enlargement or inflammation of the tissue lining the air-filled chambers in the skull known as the sinuses. Genetics, allergies, structural issues blocking the nasal passageways, and bacterial, fungal, or viral infections can all be the reason. To determine the underlying cause of sinusitis and the best course of treatment, a medical professional's precise diagnosis is essential. The disruption of mucociliary clearance results in sinusitis infection caused due to epithelial cell death, the breakdown of the epithelial barrier, and immunological dysregulation. In addition to purulent rhinorrhoea, nasal congestion and blockage, and face pain or pressure, other symptoms may include fever, headache, and/or malaise. Acute sinusitis usually goes away on its own or with treatment, but chronic sinusitis can last longer and need more thorough care. First line drugs primarily include amoxicillin with or without clavulanate. In some cases, clarithromycin or azithromycin may be prescribed. Heat and humidity treatments, glucocorticoid nasal sprays, and decongestants may all aid in sinus drainage and symptom relief. Surgery may be prescribed and is necessary to enhance sinus outflow in cases with recurrent sinusitis. Amoxicillin inactivates penicillin-binding protein (PBP) 1A without which peptidoglycan can't be formed leads to bacterial death and addition of clavulanate effects as a suicide inhibitor and activates beta-lactamase, thus becoming more active.

Although the half-lives of clavulanic acid and amoxicillin are comparable, clavulanic acid is largely metabolized by the liver and is more protein bound and less heat stable than amoxicillin. Surgery is only taken into consideration if all other treatments have failed and you have severe, persistent symptoms. According to treatment guidelines, patients with uncomplicated acute bacterial sinusitis should get an antibiotic regimen for 10–14 days. Depending on the type and severity of the infection, adults, adolescents, and children over 40 kg (88 lbs) should take 250 mg to 500 mg every 8 h or 500 mg to 875 mg every 12 h. Amoxicillin and clavulanate should be taken orally every 12 h (amoxicillin, 875 mg; clavulanate, 125 mg) or every 8 h (amoxicillin, 500 mg; clavulanate, 125 mg). In conclusion, however, first line antibiotics such as amoxicillin or amoxicillin clavulanate is prescribed to treat chronic sinusitis in the view of antimicrobial stewardship.

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