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An Update on Clavulanic Acid (Antibiotic) Drug

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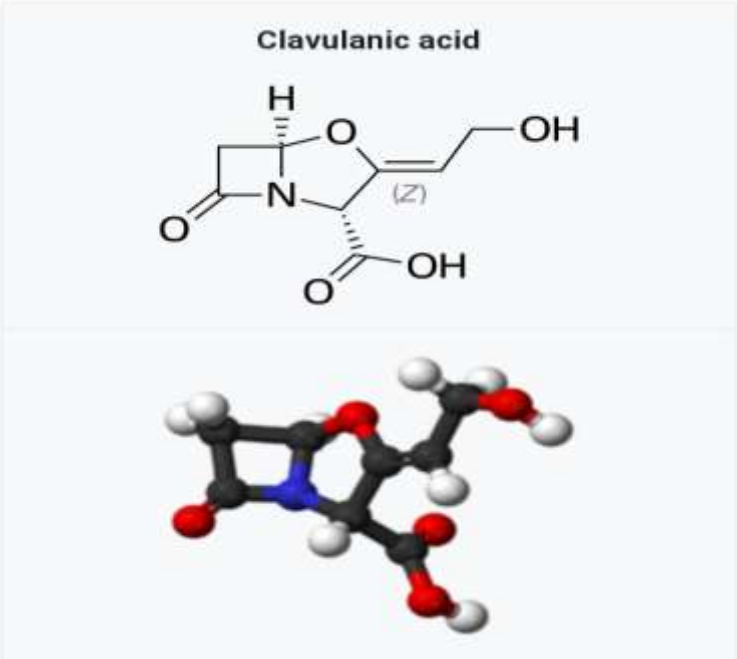
ABSTRACT:
Clavulanic acid is a beta-lactamase inhibitor produced from Streptomyces clavuligerus, which when combined with certain beta-lactam antibiotics extends their activity against bacteria which owe their resistance to the production of beta-lacatamases. In combination with amoxycillin it extends the antibacterial activity of amoxycillin to include beta-lactamase-producing strains, which are otherwise resistant, as well as amoxycillin-resistant species such as Bacteroides fragilis. The addition of clavulanic acid to amoxycillin occasionally extends (but does not decrease) the susceptibility of amoxycillin-sensitive bacteria. Clavulanic acid is adequately absorbed after oral administration and its basic pharmacokinetic characteristics are similar to those of amoxycillin. Preliminary therapeutic trials suggest that amoxycillin plus clavulanic acid is effective in urinary tract infections caused by amoxycillin-resistant organisms and in lower respiratory tract infections unresponsive to previous routine antibiotic therapy, in hospitalised patients. It is generally well tolerated; nausea, vomiting, diarrhoea and skin rash being the most frequently reported adverse effects.

Objectives:
Identifythemechanismofactionofclavulanicacid.
Describethepotentialadverseeffectsofclavulanicacid.
Outlinetheappropriatemonitoringforpatientsreceivingclavulanicacid.
Reviewinterprofessionalteamstrategiesforimprovingcarecoordinationandcommunicationtoadvanceclavulanicacidandimproveoutcomes.

I. INTRODUCTION:

Structure of calvunoic acid :



Clavulanic acid is a β-lactam drug that functions as a mechanism-based β-lactamase inhibitor. While not effective by itself as an antibiotic, when combined with penicillin-group antibiotics, it can overcome antibiotic resistance in bacteria that secrete β-lactamase, which otherwise inactivates most penicillins.

Indications:

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Clavulanic acid, also known by its potassium salt form clavulanate, is FDA approved for clinical use in conjunction with amoxicillin to treat certain bacterial infections. This can be based on the source of the infection, Gram stain, or culture and sensitivity results. The antibacterial activity of amoxicillin is not improved by clavulanic acid when used against bacteria that do not produce beta-lactamase. Therefore, indications for this drug combination only include patients suspected of infection with beta-lactamase-producing bacteria.[1] This combination has demonstrated efficacy in treating infections such as complicated and uncomplicated urinary tract infections, lower respiratory infections, sinusitis, otitis media, and some skin and soft tissue infections caused by organisms such as H. influenzae, M. catarrhalis, and S. aureus. The amoxicillin/clavulanate combination should be considered before ceftriaxone for urinary tract infections to decrease the risk of re-infection and complications.[2] Some off-label uses for amoxicillin/clavulanate include animal bites, impetigo, chronic obstructive pulmonary disease exacerbations, bronchiectasis, and odontogenic infections.

Mechanism of Action:

Clavulanic acid use is always in conjunction with amoxicillin in its salt form clavulanate potassium. Amoxicillin is a beta-lactam antibiotic that disrupts bacterial cell wall synthesis. It binds to penicillin-binding proteins that are present on the inside of the bacterial cell wall, and this inhibits the synthesis of the peptidoglycan layer in the cell wall.[3] This disruption in cell wall synthesis leads to cell lysis and bacterial death. Certain bacterial species produce the enzyme beta-lactamase, which can inactivate beta-lactam drugs by hydrolyzing the beta-lactam ring in the antibiotic compound, leading to drug resistance. Clavulanic acid is an inhibitor of beta-lactamase enzymes. Clavulanic acid contains a beta-lactam ring that binds to the beta-lactamase active site and inactivates the enzyme, thereby enhancing the antibacterial effect of beta-lactam antibiotics, such as amoxicillin. It is provided in a fixed dosage with amoxicillin. Clavulanic acid is classified as a suicide inhibitor of these beta-lactamases because it permanently inactivates the enzyme through chemical reactions at the active site.[1] Clavulanic acid alone has no know antibacterial effect and is always used in combination with amoxicillin.[4]

Administration :

Clavulanic acid alone has been shown to have no antibacterial effects, and administration must accompany amoxicillin. It is available in both solid and liquid forms. For the solid form, the patient must chew the chewable tablets before swallowing, and there are also immediate and extended-release tablets that must be swallowed whole. The oral liquid suspension should be shaken before administration and is the recommended formulation for children who are unable to chew tablets or swallow whole pills. Administration of all forms of the drug should be done at the start of a light meal to enhance oral absorption and avoid gastrointestinal irritation. Clavulanic acid may increase the absorption of amoxicillin. This drug regimen is to be administered twice to three times daily, depending on dosage, at regular time intervals to maintain constant serum concentrations.[5]

Adverse Effects:

Clavulanic acid, when administered with amoxicillin, can cause some mild gastrointestinal adverse effects. These include vomiting, nausea, loose stools, and discomfort. Antibiotic-associated diarrhea due to amoxicillin-clavulanic acid treatment is the most common adverse effect. There is a higher incidence of diarrhea when clavulanic acid is added to amoxicillin compared to amoxicillin alone. Diarrhea is more common in those taking a high dose of the extended-release form of clavulanic acid and amoxicillin.[6] Drug-induced pancreatitis from clavulanic acid and amoxicillin has occurred in a few cases.[7]

When used for the treatment of urinary tract infections, this drug combination can cause candida vaginitis.[8] Amoxicillin, in conjunction with clavulanic acid, is the most common cause of idiosyncratic drug-induced injury, specifically cholestatic liver injury, and this can lead to an increase in alkaline phosphatase and bilirubin levels.[9] Since clavulanic acid administration is always in conjunction with amoxicillin, it is important to consider the adverse effects of amoxicillin alone as well. Hypersensitivity reactions to this drug combination, usually due to amoxicillin, can occur and result in dermatological reactions. Still, none of these allergic reactions are known to be due to clavulanic acid alone.

Contraindications:

All contraindications for clavulanic acid are considered in conjunction with amoxicillin since clavulanic acid is not administered by itself. The drug combination is primarily excreted renally, so caution is necessary when a patient has renal impairment or is on hemodialysis.[1] Patients who have renal disease may need to have their dosages

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adjusted and monitored closely. The liver primarily metabolizes the drug combination, and therefore, caution is necessary when given to patients who have liver damage or disease.[1][10] Amoxicillin/clavulanate should never be given to patients who have had an idiosyncratic drug-induced injury from clavulanic acid or amoxicillin, although there is no evidence that clavulanic acid itself is hepatotoxic.[9] Because clavulanic acid is only administered in conjunction with amoxicillin, it is important to consider the adverse effects of amoxicillin, which is a penicillin-derived antibiotic so caution is necessary for patients who have a known history of penicillin allergy.

II. CONCLUSIONS:

Amoxicillin/clavulanic acid is a well established broad-spectrum antibacterial treatment which is effective and well tolerated in the treatment of AOM in paediatric patients. The high-dose combination should prove valuable in treating AOM caused by penicillin-intermediate and -resistant S. pneumoniae (approved in the US for penicillin MIC < or =2 mg/L). Based on recent recommendations and the available data, high-dose amoxicillin/clavulanic acid can be considered a treatment of choice for recurrent or persistent paediatric AOM (after failure of amoxicillin alone) where involvement of resistant pathogens is suspected.

Amoxicillin/clavulanic acid (875 mg/125 mg) administered twice daily was found to be comparable to clindamycin (150 mg) administered four times daily in achieving clinical success in acute odontogenic infections with or without abscess. It was also found to be well tolerated with a safety profile consistent with the known pharmacologic effects of amoxicillin/clavulanic acid and with that described in the global prescribing information.

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