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Prescription trend of third generation Cephalosporins

Abstract

Cephalosporins are antibiotics which are used to cure gram-negative and gram-positive bacteria and effective as amoxicillin, cefaclor, amoxicillin/clavulanate. Cephalosporins have been linked to alteration of infant's gastrointestinal flora, leading in diarrhoea or thrush, but these impacts not studied thoroughly. It's against Pseudomonas and has very little effect on Staphylococcus aureus and clearance &half-life is 3hr, which allows for twice-daily administration or, in many circumstances, once-daily administration. Cefixime, a novel oral cephalosporin, has a higher antibacterial activity against Enterobacteriaceae than other oral cephalosporins.

Keywords: Cephalosporins, Cefixime, amoxicillin, diarrhea, Enterobacteriaceae

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Introduction

Because their broad host range, clinically demonstrated effectiveness, safety profile, excellent pharmacokinetics, and fewer side effects, 3rd generation cephalosporins are commonly recommended antibiotics (Klein NC, et al. 1999). 3rd cephalosporins are antibiotics which are used to cure gram-negative and gram-positive bacteria (Arumugham VB, et al., 2021).Third cephalosporins outperform other cephalosporins in terms of potency, antimicrobial spectrum, and pharmacologic profile. Escherichia coli, K. pneumoniae, and Proteus strains resistant to aminoglycosides, anti-Pseudomonas amoxicillin, and other cephalosporins are all vulnerable (Donowitz GR, et al., 1989). 3rd cephalosporins are a significant but limited medicinal advance in the arsenal of infectious disease drugs. Their enhanced spectrum of activity, very low MICs for most sensitive organisms, greater price, and to a lesser extent their pharmacokinetic characteristics set them apart from the first and second class cephalosporins (Cunha BA, et al. 1982).

However, practitioners who see the six antibiotics that make up this class as interchangeable face a challenge when choosing third-generation cephalosporins. The antimicrobial spectrum, as well as other criteria like developing resistance and cost, should all be considered when selecting a medicine. The characteristics of parenteral third-generation cephalosporins are the subject of this review. Such discrepancies suggest that the handy "generation" classification scheme for cephalosporin antibiotics should be phased out in favour of a system that facilitates detection of clinically essential aspects of each agent in these diverse classes of antimicrobial agents (Cunha BA.1992)

Ceftriaxone

When taken parenterally and in large dosages, ceftriaxone, a 3rd cephalosporin antibiotic, has been linked to the development of biliary sludge and biliary colic. Ceftriaxone is also linked to rare cases of immunoallergic hepatitis, most commonly cholestatic hepatitis, which is comparable to the harm caused by other cephalosporins (Bethesda 2012).Rocephin is just a brand name for ceftriaxone, which is marketed in a parenteral format.It can be administered intravenously or intramuscularly and is licenced for the treatment of moderate-to-severe bacterial infections caused by pathogenic organisms (Drugs and Lactation Database 2005).

Biliary sludge and hyperbilirubinemia associated with ceftriaxone

Ceftriaxone is a relatively safe antibiotic; nonetheless, rare cases of symptomatic biliary sludge have been observed, the majority of which have included children. Improvements in laboratory indices, such as bilirubin levels, are unusual with ceftriaxone (Bickford CL, et al., 2005)

Cefotaxime

Cefotaxime sodium is an injectable cephalosporin antibiotic that works by inhibiting the formation of bacterial cell walls (Le Frock JL, et al., 19882).Cefotaxime is more effective against Enterobacteriaceae than some other 1st- and 2nd-generation cephalosporins.Although it is more efficient than prior cephalosporins against Pseudomonas aeruginosa and Acinetobacter spp., most bacteria remain resistant (Dudley MN, et al. 1982). Cefotaxime is taken Twice to three times a day, i.v or intramuscular injections, at a dose of 1 to 6 g per day. The usual dose for urinary infections is 1 to 2 g per day, 3 g/day for various mild to serious infections, and higher doses of 6 g/day for life-threatening disorders.The much more suitable regimen for severely susceptible species was 0.5 to 2g each 8–12 hours.The much more suitable regimen for severely susceptible species was 0.5 to 2g each 8–12 hours. In neonates, the dosage is normally 50 mg/kg per day, while in older infants and adolescents, the dosage is 100 to 150 mg/kg per day. For dangerous diseases such as meningitis, newborns up to 7 days of age should receive 150 to 200 mg/kg per day, and older children should receive 200 mg/kg/day. The dosage is normally given twice or three times each day. For the treatment of mild gonorrhoea, any single intramuscular injection of 1g is indicated.For surgery infection protection, a single preoperative dose of one - two gm is recommended, followed by 1–3 doses at 8-hour intervals postoperatively.. In individuals with a creatinine clearance of less than 10 mL/min, the dosage should be reduced by half while the frequency must be maintained (Todd PA, et al. 1990)

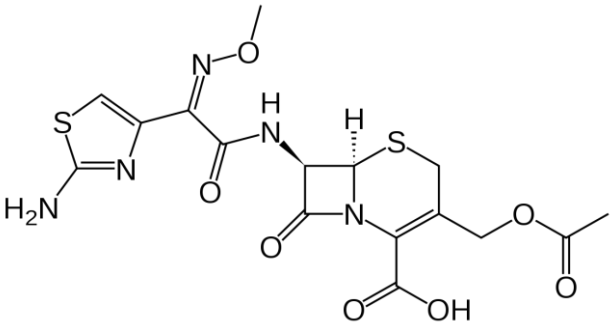

Fig.1. Structure ofCefotaxime

Antibacterial Activity: In vitro, cefotaxime kills the both types of microorganism gram-positive and microorganisms. Cefotaxime is as effective as benzyl penicillin towards Streptococcus pneumoniae and Streptococcus pyogenes, but it is also effective against lactams and multidrug-resistant Streptococcus pneumoniae strains. Cefotaxime, like some other cephalosporins, has weak action against enterococci (including Streptococcus faecalis). Low quantities of cefotaxime suppress beta - lactams and -resistant Staphylococcus aureus strains, however cephalothin and cefamandole are more effective against this species. Cefotaxime is equivalent to cefoperazone against S. aureus, but much more effective than cefoperazone against streptococci in generally, and also more active than moxalactam against any and all Gram-positive bacteria when comparing to other 'third generation' cephalosporins (Carmine AA, et al. 1983)

Pharmacokinetics: Cefotaxime plasma level typically range around 81 and 102 g/ml after a 1000 mg intravenous infusion. Plasma levels of 38 and 200 g/ml are achieved with 500mg and 2000mg dosing, respectively. After receiving 1000mg intravenously and 500mg intramuscular injections for 10 or 14 days, there is no buildup (Carmine AA, et al. 1983).

Cefpodoxime

Cefpodoximeproxetil is a 3rd cephalosporin antibiotic that can be used orally. In vitro efficacy against a wide spectrum of Gram-positive and Gram-negative germs associated with common paediatric diseases has been demonstrated, making it a viable empirical therapeutic option (Fulton B, et al. 2001).Cefpodoxime was proven to be as effective as amoxicillin, cefaclor, amoxicillin/clavulanate, and penicillin in treating respiratory and urinary tract infections in clinical trials. Although no comparison studies have been conducted, it appears to be beneficial in the treatment of skin infections. Cefpodoxime is very well tolerated by toddlers and useful in the therapy of pharyngitis and otitis media. It has a profile of side effects that is comparable to that of other penicillins and cephalosporins, with the most prevalent side effects being gastric ulcer (Chocas EC, et al. 1993)

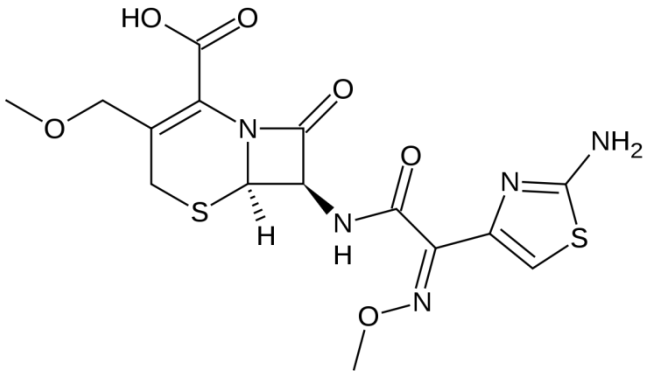

Fig.2. Structure of Cefpodoxime

Ceftazidime

Ceftazidime-avibactam (Zavicefta®) is a combo of ceftazidime, a third cephalosporin, and avibactam, a novel non-lactam-lactamase blocker, administered intravenously (Shirley M. et al., 2018).

According to the limited information available, ceftazidime creates minimal quantities in milk that are unlikely to cause harm to breastfed babies. Cephalosporins have been linked to alteration of the infant's gastrointestinal flora, leading in diarrhoea or thrush, but these impacts have not been thoroughly studied. Ceftazidime is safe to take when breastfeeding (Drugs and Lactation Database 2006)

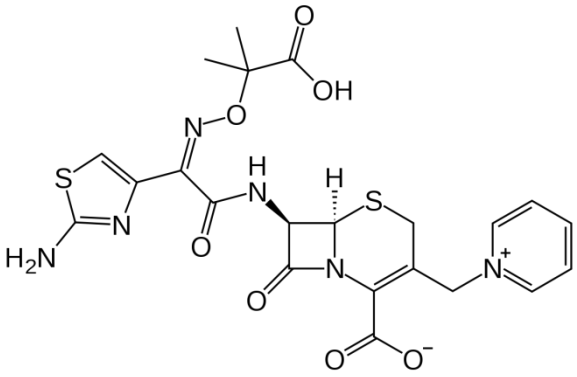

Fig.3. Structure of Ceftazidime

Ceftibuten

Ceftibuten is a 3rd cephalosporin that is orally active and has strong microbiologic action againstmicroorganisms that are gram-negative and gram-positive.It can withstand extended-spectrum beta-lactamases induced by plasmids. Ceftibuten has been demonstrated to be effective in the treatment of upper and lower respiratory utis, as well as complex and simple infections in both adults and children, despite the fact that these are not recognized indications. After oral treatment, it is rapidly absorbed (75-90 percent), with peak serum levels of 17 microg/ml in healthy volunteers.Healthy volunteers have a ½ of 2.5 hours, while older people

have a half-life of 3.2 hours.Dose must be changed if creatinine clearance decreases below 50 ml/minute. The medicine has a positive safety profile that is equal to that of most some cephalosporins (Owens RC, et al. 1997)

Ceftibuten, an oral expanded-spectrum cephalosporin, is efficient against a wide range of bacteria, both gram-positive and gram-negative, including Streptococcus pneumoniae, Streptococcus pyogenes, Moraxella catarrhalis, and Haemophilusinfluenzae. Most common beta-lactamases are unable to hydrolyze ceftibuten. Ceftibuten is swiftly and almost totally absorbed from the gastrointestinal tract, it is the majority of it is eliminated unaltered in the kidneys. Ceftibuten has a half-life of little more than 2 hours in the body (Guay DR, et al. 1997)

In clinical studies, 1312 paediatric patients were given ceftibuten suspension at a dose of 9 mg/kg per daily, with a maximum daily dose of 400 mg. In 1152 people, negative emotionality were gathered by voluntarily reports from clinicians based on direct inspections, parental and/or patient comments. In addition to volunteer reports, gastrointestinal unpleasant events were elicited from 160 participants at each visit (Reidenberg BE. 1995)

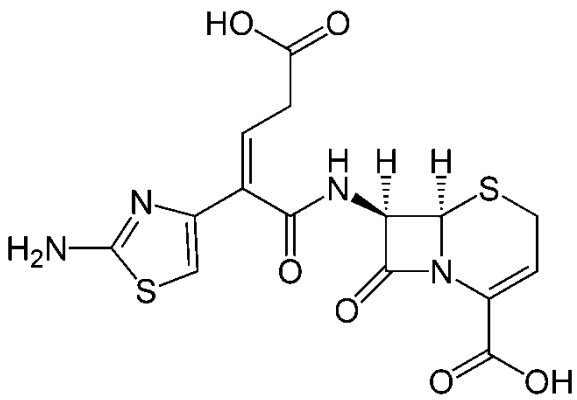

Fig.4. Structure of Ceftibuten

Ceftibuten is detected in breast milk at low doses and is unlikely to damage breastfed infants. Cephalosporins have been linked to alteration of the infant's gut flora, leading in diarrhoea or thrush, but these impacts have not been thoroughly studied. Ceftibuten is safe to take during nursing (Drugs and Lactation Database, 2021)

Ceftizoxime

Ceftizoxime is a third-generation cephalosporin that is administered intravenously. Ceftizoximenot performs invitroactivity against gram-negative bacteria. Richards DM, et al. 1985). Apart from Streptococcus faecalis, most Enterobacteriaceae and streptococcal organisms are inhibited by a concentration of less than or equal to 1 microgram/ml. By 3-8 micrograms/ml, methicillin-resistant Staphylococcus aureus is repressed, whereas methicillin-resistant Staphylococcus aureus is tolerant. Bacteroides fragilis is suppressed at a

concentration of 16-64 micrograms/ml. At commonly accessible quantities, it inhibits Pseudomonas aeruginosa (Neu HC, et al. 1984)

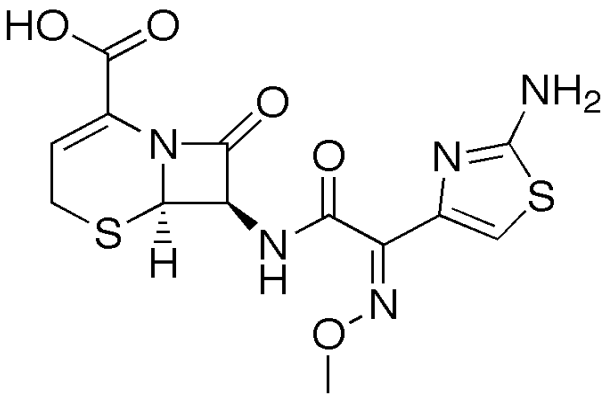

Fig.5. Structure of Ceftizoxime

It is excreted by the kidneys and has a half-life related to ceftizoxime, cefoperazone, as moxalactam. Ceftazidime has the same effectiveness and safety as that of the rest of the carbapenems, and it hasn't been found to affect prothrombin or cause the disulfuram response asmoxalactam and cefoperazone (Yost RL, et al. 1985)

Cefixime

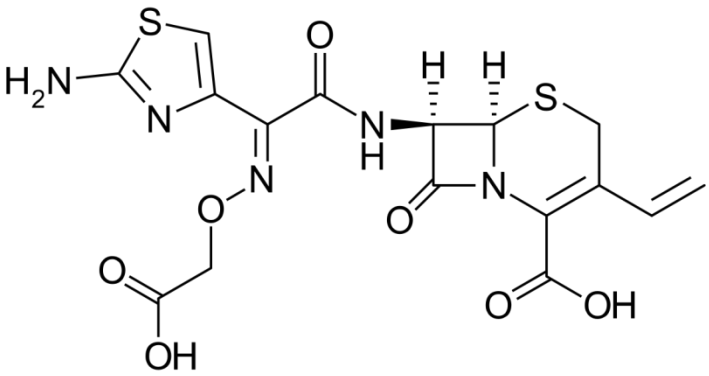

Fig.6. Structure of Cefixime

Cefixime, a novel oral cephalosporin, has a higher antibacterial activity against enterobacteriaceae than other oral cephalosporins. The kidneys discharge around 20% of the medication as active drug. As a result, cefixime medication for (UTI) may be a viable option (Naber KG, et al. 1990)

It's quite good at fighting H. influenzae and other Enterobacteriaceae. It is present in Streptococcus pyogenes, Streptococcus pneumoniae, and Branhamellacatarrhalis and is resistant to digestion by various beta-lactamases. Cefixime is inert against Pseudomonas and has very little effect on Staphylococcus aureus.Cefixime is distinguished by its three-hour excretion half-life, which allows for twice-daily administration or, in many circumstances, once-daily administration.Cefixime 200 to 400 mg per day, given as a single dose or in two divided doses, has clinical and microbiological efficacy comparable to various daily dosages of co-trimoxazole or amoxycillin, as well as amoxycillin, amoxycillin/clavulanic acid, and cefaclor in acute uncomplicated utility (Brogden RN, et al. 1989)

In comparison studies, cefixime was found to be as effective as amoxicillin +/- clavulanic acid, cefaclor, cefalexin, cefuroxime axetil, and clarithromycin. Preliminary data from trials evaluating the efficacy of cefixime as an oral component of an iv to orally changeover treatment have been positive, but further well-conducted trials are needed (Markham A, et al. 1995)

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