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Cefotaxime Induced Macular Rash

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Case Report

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Abstract: Cefotaxime is a 3rd Generation Cephalosporin and mainly acts by binding to penicillin-binding proteins and inhibits final transpeptidation step of peptidoglycan synthesis, resulting in cell-wall death; resists degradation by beta-lactamase; proper dosing and appropriate route of administration are determined by condition of patient, severity of infection, and susceptibility of microorganism. Indicated in the various conditions like Gonococcal Urethritis/Cervicitis, Gonorrhea, Rectal, Infections Caused by Susceptible Organisms, Prophylaxis of surgical infection. A child of 5 years old of male patient came to pediatrics department with chief complaints of seizures and admitted in pediatrics department-II and his treatment chart was phenytoin 100mg PO BD and valproic acid 200mg – 200 mg – 300 mg Po OD. During his second of treatment child developed fever of 102^0F and to reduce the condition physician prescribed cefotaxime 500mg BD IV on 4^{th} day of treatment child developed macular rash all over the body. Better vigilance is necessary for implementation of safe and effective treatment for each individual patient.in order to prevent serious adverse drug reactions of this drug,close monitoring drug treatment course, creating awareness, recognition of the problem and careful management of all the patients who receive medication are essential, because use of cefotaxime causes Colitis, Diarrhea, Elevated blood urea nitrogen (BUN) and creatinine, Elevated hepatic transaminases, Eosinophilia, Fever, Injection site pain, Nausea, Pruritis, Rash, Thrombocytopenia, Transient neutropenia, Vomiting.
Keywords: Cefotaxime, adverse drug reaction, Erthrocyte sedimentation rate, Bilateral airway entrance, Focal neurological deficit

INTRODUCTION

Cefotaxime was discovered in 1976 and came into commercial use in 1980. It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. It is a broad-spectrum antibiotic with activity against numerous gram-positive and gram-negative bacteria.

Given its broad spectrum of activity, cefotaxime is used for a variety of infections, including:

- Lower respiratory tract infections - e.g. Pneumonia (most commonly caused by S. Pneumoniae)
- Genitourinary system infections - urinary tract infections (e.g. E. Coli, S. Epidermidis, P. Mirabilis) and cervical/urethral gonorrhea
- Gynecologic infections - e.g. Pelvic inflammatory disease, endometritis, and pelvic cellulitis
- Bacteremia/septicemia – secondary to Streptococcus spp., S.Aureus, E.Coli, and Klebsiella spp.
- Intra-abdominal infections - e.g. Peritonitis
- Bone and joint infections - S. Aureus, Streptococcus spp.
- CNS infections - e.g. Meningitis/ ventriculitis secondary to N. Meningitis, H. Influenzae, S. Pneumonia

Although cefotaxime has demonstrated efficacy in these infections, it is not necessarily considered to be the first-line agent. In meningitis, cefotaxime crosses the blood–brain barrier better than cefuroxime

Spectrum of activity

As a β-lactam antibiotic in the third-generation class of cephalosporins, cefotaxime is active against numerous Gram-positive and Gram-negative bacteria, including several with resistance to classic β-lactams such as penicillin. These bacteria often manifest as infections of the lower respiratory tract, skin, central nervous system, bone, and intra-abdominal cavity. While regional susceptibilities must always be considered, cefotaxime has typically been effective against these organisms (in addition to many others):

- Staphylococcus aureus (not including MRSA) and S. Epidermidis

- Streptococcus pneumoniae and S. Pyogenes
- Escherichia coli
- Haemophilus influenzae
- Neisseria gonorrhoeae and N. Meningitis
- Klebsiella spp.
- Burkholderia cepacia
- Proteus mirabilis and P. Vulgaris
- Enterobacter spp.
- Bacteroides spp.
- Fusobacterium spp.

Notable organisms against which cefotaxime is not active include Pseudomonas and Enterococcis. As listed, it has modest activity against the anaerobic Bacteroides fragilis.

The following represents MIC susceptibility data for a few medically significant microorganisms:

- H. Influenzae: ≤0.007 - 0.5 µg/ml
- S. Aureus: 0.781 - 172 µg/ml
- S. Pneumoniae: ≤0.007 ─ 8 µg/ml

Historically, cefotaxime has been considered to be comparable to ceftriaxone (another third-generation cephalosporin) in safety and efficacy for the treatment of bacterial meningitis, lower respiratory tract infections, skin and soft tissue infections, genitourinary tract infections, and bloodstream infections, as well as prophylaxis for abdominal surgery. The majority of these infections are caused by organisms traditionally sensitive to both cephalosporins. However, ceftriaxone has the advantage of once-daily dosing, whereas the shorter half-life of cefotaxime necessitates two or three daily doses for efficacy. Changing patterns in microbial resistance suggest cefotaxime may be suffering greater resistance than ceftriaxone, whereas the two were previously considered comparable. Considering regional microbial sensitivities is also important when choosing any antimicrobial agent for the treatment of infection [1].

Absorption of cefotaxime is rapid and reaches peak plasma concentration within 30 min. Widely distributed to body tissues and fluids, including aqueous humor, ascetic and prostatic fluids, bone, penetrates CSF when meninges inflamed. Partially metabolized in liver.

Metabolite: Desacetylcefotaxime (active), Elimination Half-life: Parent drug, 1-1.5 hr; active metabolite, 1-1.9 hr Excreted through urine [2] .

CASE REPORT

A child of 5 years old of male patient came to pediatrics department with chief complaints of seizures and admitted in pediatrics department-II and his treatment chart was phenytoin 100mg (2+2) BD and valproic acid 200mg OD. During his second of treatment child developed fever of 102^0F and to reduce the condition physician prescribed cefotaxime 500mg BD IV on 4th day of treatment child developed macular rash all over the body. On general examination, patient was drowsy and coherent. on physical examination PR-79/min,RR:20/min,spo_2: 96% with RA, No FND, Resp: BAE+, CVS: S_1 S_2 +. On laboratory examination shows Hb: 8.5gm, total count: 5,6000, differential count: $P_{61}L_{51}E_3$, ESR:30, Platelets: 30,000, sodium: 156meq/lit, chlorides: 110meq/lit, serum creatinine: 0.6mg/dl, widal test: < 1:20 dilutions, smear for MP : Negative and treatment was given as follows phenytoin 100mg PO BD and valproic acid 200mg – 200 mg – 300 mg Po OD. During his second of treatment child developed fever of 102^0F and to reduce the condition physician prescribed cefotaxime 500mg BD IV. Based on the above information here we have suspected it as probable ADR(Macular rash). Patient was referred to dermatology department to confirm the ADR. On analysis compared to all other drugs prescribed, cefotaxime pharmacology and literature support the occurrence of rash. In order to confirm the relationship between the effect and drug we have also done dechallenge test i.e. drug was withdrawn from treatment regimen, and prescribed Tab. chlorphenaramine maleate 4mg OD and candid powder TID.

CAUSALITY ASSESSMENT

To evaluate the relationship between the drug and reaction, we performed causality assessment by using scales like WHO causality assessment scale, Naranjo's scale and observed ADR (Table-1 & 2).

Table-1: causality assessment of suspected ADR

ADR SCALE	WHO – UMC	NARANJO'S
ASSESSMENT	PROBABLE	PROBABLE

Table-2: Analysis of observed ADR

SEVERITY ASSESSMENT	MODERATE LEVEL – 4(A)
PREVENTABILITY	Probably preventable
PREDICTABILITY	Type - A

DISCUSSION

A maculopapular rash is made of both flat and raised skin lesions. The name is a blend of the words "macule," which are flat discolored skin lesions, and "papule," which are small raised bumps. These skin lesions are usually red and can merge together. Macules that are bigger than 1 centimeter are considered patches, while papules that are merged together are considered plaques [3] .

A maculopapular rash is a marker for many diseases, allergic reactions, and infections. Most of the time, the cause is a viral infection, more than one symptom may also appear. These include: fever, headache, vomiting, breathing troubles, muscle pain, dry skin. This may be a sign of an infection, which may be potentially contagious. Proposed mechanism of pathogenesis of DRESS has been failure of drug detoxification pathways leading to accumulation of harmful metabolites which in turn activate CD4 + CD8 + T-cells. These cells release interleukin-5 which activates eosinophils and sets up an inflammatory cascade [4].

During treatment course as a clinical pharmacist we have identified adverse drug reactions as follows, the patient was under the medication with inj. Cefotaxime based upon the literature reviews and based on local examination and other investigations we have concluded that this condition is due to the drug cefotaxime and performed casuality assessment, severity, preventability, predicatability. After the identification we have immediately withdrawn the drug cefotaxime and provided appropriate treatment.

CONCLUSION

Better vigilance is necessary for implementation of safe and effective treatment for each individual patient. In order to prevent serious adverse drug reactions of this drug, close monitoring drug treatmentcourse, creating awareness, recognition of the problem and careful management of all thepatients who receive medication are essential, because by use of cefotaxime causes Colitis, Diarrhea, Elevated blood urea nitrogen (BUN) and creatinine, Elevated hepatic transaminases, Eosinophilia, Fever, Injection site pain, Nausea, Pruritis, Rash, Thrombocytopenia, Transient neutropenia, Vomiting.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

Abbreviations:

WHO – World health organization
CSF- Cerebro Spinal fliud
FND- functional neurological disorder
OD- once a day
BD- Twice a day

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