



Coagulopathy Induced by Cefoperazone/Sulbactam in a Geriatric Patient

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Abstract

Cefoperazone, which is a third generation cephalosporin, has a broad spectrum activity. In clinical studies, only a few adverse effects of this agent have been reported, and these effects are similar to those seen with other cephalosporins. An 86 year-old man was admitted to emergency department with complaints of high fever, cough and weakness. On his physical examination; the patient was alert and had a limited orientation, as well as a reduced general condition. After our investigations, the coagulation disorder was bonded with C/S treatment and we stopped administration of Cefoperazone/Sulbactam(C/S). The bleeding was controlled with intravenous vitamin K and fresh frozen plasma and coagulation tests were recovered to normal values. His antibiotherapy was changed with meropenem. Unfortunately, the patient died due to the progression of respiratory and renal failure. In conclusion, the clinician should keep in mind this complication while administrating this agent. Therefore, close follow-up of coagulation parameters is crucial.

Keywords: Cefoperazone, sulbactam, coagulopathy

Rec.Date: Jan 25, 2015

Accept Date: Apr 20, 2015

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Introduction:

Cefoperazone, which is a third generation cephalosporin, has a broad spectrum activity. In clinical studies, only a few adverse effects of this agent have been reported, and these effects are similar to those seen with other cephalosporins. Prolonged prothrombin time with clinical bleeding bonded with other cephalosporins such as moxobactam and cefamandole. Vitamin K deficiency may occur rarely in patients who are treated with cefoperazone. We report the occurrence of coagulopathy related with Cefoperazone/Sulbactam(C/S) use in a geriatric patient.

Case presentation:

An 86 year-old man was admitted to emergency department with complaints of high fever, cough and weakness. On his physical examination; the patient was alert and had a limited orientation, as well as a reduced general condition. His body temperature was 38 C, heart rate: 112/min, arterial blood pressure: 130/70 mmHg, respiratory rate: 24/min and intensified breathing sounds were audible in the left middle field of his lungs. The patient was hospitalized in the department of internal medicine with diagnosis of pneumonia and acute renal failure. We commenced IV Ertapenem 1x500 mg, but due to the progression of his respiratory symptoms, his treatment altered with IV Cefoperazone/Sulbactam (C/S) 2x1 gr and the patient was started to be followed in the intensive care unit (ICU). The renal failure of the patient was progressed and the patient started to get hemodialysis. On his following-up in ICU, bleeding at the catheter insertion site was observed on the fourth day after initiating C/S treatment. Prothrombin time, activated partial thromboplastin time, and INR were found to be 27.3 sec, 73.6 sec, and 2.57 respectively. Laboratory markers including liver enzymes, d-dimer, thrombocyte, fibrinogen were normal. Patient's blood culture and hepatitis markers were negative. Warfarin and heparin weren't being used. He had no liver disease, obstructive jaundice or other diseases disrupting intestinal absorption of vitamin K. After our investigations, the coagulation disorder was bonded with C/S treatment and we stopped administration of C/S. The bleeding was controlled with intravenous vitamin K and fresh frozen plasma and coagulation tests were recovered to normal values. His antibiotherapy was changed with meropenem. Unfortunately, the patient died due to the progression of respiratory and renal failure.

Discussion and Conclusion:

In the absence of vitamin K, the carboxylation and activation of clotting factors II, VII, IX and X are impaired. Clinically, this is manifested as functional deficiencies of these factors. Antibiotic use, plays a major role in vitamin K deficiency. It causes depletion of intestinal bacterial source of vitamin K, thereby leading to hypoprothrombinemia [1]. Antibiotics known to cause clotting factor deficiencies include cefoperazone and those with N-methyl-thiotetrazol(NMTT) side chains [2,3]. These have been reported to reduce the levels of reduced forms of vitamin K and prolong PT by inhibiting vitamin K epoxide reductase [4]. Reports on the association between C/S use and coagulation disorders are scant in the current literature [5-7]. Therefore, according to the best of our knowledge, there is no literature about the coagulation effect of sulbactam. Administration of C/S to renal failure patients may lead to C/S associated coagulopathy [8,9]. We did not perform a vitamin K assay in this case, however the prolonged coagulation time and positive response to vitamin K supplementation are highly suggestive of vitamin K deficiency. In a previous study researchers proposed that routine use of vitamin K in patients who are on short term treatment with cefoperazone but without a perceptible bleeding risk was unnecessary [10]. Our patient had adequate dietary vitamin K intake and no liver impairment; yet, he was being followed in ICU and had inadequate nutrition. The rapid development of clotting derangement after cefoperazone therapy suggested that antibiotics with an NMTT side chain should be exercised cautiously even in patients who are considered at “low risk” of developing bleeding complications. The clotting profile should be monitored, and a vitamin K supplement may be required to prevent hemorrhagic complications.

In conclusion, the clinician should keep in mind this complication while administering this agent. Therefore, close follow-up of coagulation parameters is crucial.

Conflict of interests statement

We have no competing interests to declare.

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