Clinical Microbiology and Infectious Diseases

Short Commentary ISSN: 2398-8096

From bench to bedside: Colistin nephrotoxicity and vitamin E

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Introduction

By increasing the prevalence of infections caused by multi-drug resistance gram negative bacillus bacteria and mortality due to hospital acquired infections, we are using an old but not forgotten antibiotic called colistin [1-3]. Based on previous studies it was reported that about half of the isolated gram negative bacillus bacteria or even more are resistant to most of the antibiotics in our country and we are facing some problems in controlling and managing them [4,5]. Colistin, a polymyxin structured antibiotic is sometimes our only option. It was first discovered in 1949. By increasing bacterial cell membrane permeability by acting like a cationic detergent in gram negative bacteria colistin could have its bactericidal effect [6-8]. It is eliminated from kidney by renal tubular secretion, and also 80% of secreted medication reabsorbed in tubules [9]. Colistin nephrotoxicity as a serious adverse drug reaction which is mostly reversible but sometimes irreversible need special attention [10]. The exact mechanism of this reaction is not fully understood but, data from clinical studies suggest that oxidative stress and cell apoptosis play a role in acute tubular necrosis due to colistin consumption and this oxidative stress increase activity of Endothelial Nitric Oxide Synthase and Inducible Nitric Oxide Synthase which could lead to apoptosis and necrosis [11,12]. It also causes cellular permeability control dysfunction which could lead to cell lysis and acute tubular necrosis [13,14]. Although the exact mechanism is not recognized yet, it seems Reactive Oxygen Species (ROS) play an important role in tubular cells apoptosis [15]. In animal studies, it was shown before that using an antioxidant like N-acetyl cysteine or ascorbic acid could decrease ROS level an apoptosis [12,16-18]. Using ascorbic acid by dose of 3000 milligrams daily concomitantly by colistin may lead to lower acute kidney injury [11]. Vitamin E as a nutrient which approved to be used by human by Food and Drug Administration in 1969 is a fat-soluble vitamin has antioxidant effect and could decrease cellular damage by oxidant agents [19,20]. Alpha-tocopherol which possess most anti-oxidant activity amongst different vitamin E forms acts as a radical scavenger could protect unsaturated fatty acid in the structure of cell membrane from oxidative agent damage [21]. In an animal study it is shown that alpha-tocopherol could effect on colistin nephrotoxicity due to its antioxidant effect and radical scavenging when used concomitantly by colistin [22]. In an animal study, which considered to examine the effect of vitamin E on colistin nephrotoxicity, vitamin E as alpha-tocopherol initiated before colistin initiation with the dose of 200mg per day and vitamin E showed its protective properties and rodents which received vitamin E had lower serum creatinine level. They started vitamin E before colistin initiation with this rational that the animal stabled in a good antioxidant serum level. This effect is also proven by pathologic data from another animal study [22,23]. Alpha tocopherol also were effective in reducing renal damage induced by other agents such as aminoglycoside which oxidative stress have a role [24,25]. Based on these data we thought to conduct a randomized trial to assess alpha-tocopherol effect on colistin nephrotoxicity in Loghman-Hakim hospital, a referral tertiary teaching medical center. Patients who are candidate to receive colistin to treat infections caused by multi-drug resistance gram negative bacillus are randomly assigned to receive 400 mg vitamin E in form of alpha tocopherol per day concomitantly by colistin or receive colistin alone. The trial is registered in the Iranian Registry on Clinical Trials by the code of IRCT20130917014693N8. After finishing of the study results will be published.

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Received: July 31, 2019; **Accepted:** August 19, 2019; **Published:** August 22, 2019

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