Letter

The significance of different formulations of aerosolized colistin

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We thank Dr Mubareka and Dr Rubinstein for their thoughtful commentary [1] related to our recent publication on aerosolized colistin for the treatment of nosocomial pneumonia due to multidrug-resistant Gram-negative bacteria in patients without cystic fibrosis [2]. We would like to provide some additional clarifications related to the formulation of colistin used in our study because the commentators state that "… it is not clear why the more toxic form of colistin was chosen over the better-tolerated colistin sulphamethate".

There are two different forms of colistin available for clinical use. Colistin sulfate is administered orally for bowel decontamination and is administered topically as a powder for the treatment of bacterial skin infections; and colistimethate sodium (also called colistin methanesulfate, pentasodium colistimethanesulfate, colistin sulfamethate, and colistin sulfonyl methate) is administered intravenously and intramuscularly [3]. It is obvious that the terminology regarding the different formulations of colistin may be confusing. Colistimethate sodium is produced by a sulfomethylation reaction of colistin in which the primary amine groups of L-α-γ-diaminobutyric acid are reacted with formaldehyde followed by sodium bisulfite [4].

Both formulations of colistin (colistin sulfate and colistimethate sodium) have been used for aerosol treatment. However, colistimethate sodium is associated with fewer adverse effects such as chest tightness, throat irritation, and cough compared with colistin sulfate [5]. The formulation of colistin that was administered to our patients was therefore colistimethate sodium (i.e. the less toxic form of the drug), not colistin sulfate. In fact, the exact trade names of colistin that were administered to our patients are stated in our paper [2].

Authors' response

S Mubareka and E Rubinstein

We would like to thank the authors for their response to our editorial [1]. We acknowledge that colistimethate may be better tolerated from a respiratory point of view. What remains unknown, however, is the systemic absorption of inhaled colistin in critically ill patients, particularly in those with pneumonia in whom the barrier between the alveolar cell layer and the vascular system may be damaged. It is appreciated that this parameter may not be determined in a retrospective study, and these preliminary results suggest that further research is called for.

High-pressure liquid chromatography has been used to measure serum levels of colistin in humans [6]. Appreciable limitations of bioassays exist, particularly where more than one antimicrobial is administered in the same patient. Since the publication of this study by Michalopoulos and colleagues, a retrospective study of 80 adults who received nebulized, parenteral, and intrathecal colistin has been published [7]. The use of intrathecal colistin in two patients highlights its expanding use and reinforces the need to further our understanding of the pharmacodynamics of this drug.

Although microbial eradication has been demonstrated in some patients receiving colistin, the contribution of other antimicrobials given concomitantly must be considered. We agree with the authors' conclusions that monotherapy with aerosolized colistin, particularly in this patient population, is unlikely to be sufficient [2].

Circumstances where colistin is the only feasible therapy are likely to increase in frequency. These would include infections with multidrug-resistant *Acinetobacter baumanii*, *Pseudomonas*

spp. and other non-fermenting Gram-negative rods. Nevertheless, the broader microbiological picture must also be considered where nosocomial infection with methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Entercococcus* spp. is already well established and continuing to spread. Without the judicious use of antimicrobials, including colistin, the risk of perpetuating these organisms and other emerging resistant pathogens will only increase, particularly in high-risk areas such as intensive care units.

Competing interests

The author(s) declare that they have no competing interests.

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