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LETTER TO THE EDITOR

Cost-effectiveness analysis of low versus high dose colistin in the treatment of multi-drug resistant pneumonia: a comment

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To the editor

We read with great interest the article by Cara et al. [1] in a recently published issue of the International Journal of Clinical Pharmacy. This study was conducted to evaluate cost-effectiveness of high dose versus low dose colistin (HDC vs. LDC) in treatment of nosocomial pneumonia (NP) due to multidrug resistant gram-negative bacteria (MDR-GNB). The authors concluded that LDC is as effective as and less nephrotoxic than HDC and could be considered as a cost-effective treatment for MDR-GNB NP. The study topic is important; however we faced issues in the study methodology and interpretation of results that need to be highlighted.

A major concern arises from considering LDC as a previously proven approach in treatment of MDR-GNB NP. In this study, doses less than 2.5 mg/kg were considered as LDC and doses above 2.5 mg/kg were defined as HDC. Three studies were cited in the paper as the basis for proven efficacy of LDC. The first citation belongs the study by Kalin et al. [2] in which low doses was determined in according to creatinine clearance referring to another study. In none of the above mentioned studies doses less than 2.5 mg/kg/day were used. In another cited study which was conducted retrospectively, 30 days mortality and MIC were compared in two groups of patients (bacterial cure vs. bacterial failure) who received colistin doses less than 2.5 mg/kg/day [3]. The study results revealed that MIC was an independent predictor of bacterial cure and the values were significantly higher in the bacterial failure group. In spite of observed reasonable bacterial cure rate following low dose of colistin in this study, authors concluded that decisions to use such doses should be made considering institutional bacterial MICs. This is while bacterial MIC and microbiological cure were not reported by Cara et al. Although, they conducted this study in the same hospital with aforementioned study, the time span and the infection sites were different between them.

Another important point is about definition of effectiveness in this study. Effectiveness of colistin was evaluated using clinical cure with definition of white blood cells under 12,000 cells/ml and absence of fever for 72 h. However, resolution of other signs and symptoms of pneumonia including respiratory secretions and radiographic findings was not taken into account. Considering that nearly one-third of study patients were critically ill, measurement of APACHE or SOFA score might have been important to determine frequency of severe cases and assess clinical response. Moreover, time to clinical stability, mortality, development of complications during treatment, median stay in intensive care unit and days of intubation, persistent bacteremia, and emergence of antibiotic resistance in the causative organism are among other recommended criteria for evaluating pneumonia cure in studies [4].

We faced an ambiguity about the body weight that was used by Cara et al. in calculating received daily dose in obese patients. It has been recommended to calculate colistin dose in obese patients using ideal body weight (IBW). However, it was not clear in the paper that either IBW or actual body weight (ABW) was used to convert received daily doses into mg/kg/day in obese patients. Significantly higher mean weight of patients in LDC group was explained as selection bias in the limitations of the study. The authors also added that this observation might be attributed to physicians' practice and prescribing lower than needed doses for obese patients. Regardless of body weight that had been used by physicians in determining prescribed colistin doses, it seems that ABW was used instead of IBW in conversion of prescribed daily doses into mg/kg/day in this study. Hence,

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this calculation resulted in low doses for obese patients and consequently led to their entrance into LDC group. Probably, more patients could have entered to HDC, if IBW had been used in calculations.

The last point is about the evaluation of costs and interpretation of cost-effectiveness results in this study. Determined cure and defined effectiveness called question into robustness of considered cost-effectiveness model. Moreover, colistin cost per patient was significantly higher in LDC group in spite of similar duration of colistin therapy between two groups. On the other hand, conducted sensitivity analysis revealed that incremental costs were mostly affected by costs of staff physician visits, ICU days and general wards day. In other words, cost of colistin was not a determinant source of changes in incremental costs. Hence, concerns remain regarding concluded cost-effectiveness of LDC.

Conflicts of interest The authors have nothing to declare.

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