Variability Within Investigations of Intravenous Colistin: The Scope of the Problem

To the Editor—We are encouraged by the correspondence by Nation et al [1] and support recommendations to decrease confusion and promote the optimal use of colistin through establishing consistent terminology for product and dosing conventions. Attention to current dose conversion is particularly important [1, 2], because misinterpretation of data may lead to medication errors [3].

1 million international units (IU) $\approx$ 30 mg of colistin base activity (CBA) $\approx$ 80 mg of colistimethate sodium (colistin methanesulfonate [CMS]).

An accurate understanding of this last-line antibacterial drug is essential as clinicians worldwide care for patients infected by drug-resistant organisms. Unfortunately, although concerns exist, the full magnitude and range of discrepancies within this area of research have not been well described. The purpose of this letter is to provide objective data detailing the extensive variability in current colistin literature as it relates to study populations, endpoint selection, and other reporting practices.

We searched Scopus (www.scopus.com/home/url) and PubMed (www.ncbi.nlm.nih.gov/pubmed) using the Medical Subject Heading terms “colistin” and “colistimethate” along with the operator “OR” to identify human research published in English between January 1990 and July 2013 with an abstract available. Publications reporting original research or outcomes data for a cohort of adult (age >18 years) patients who received intravenous colistin were included. Of the 1695 identified studies, 51 (3%) articles met inclusion criteria and were evaluated for this descriptive report.

Included studies ranged from 1999 to 2013, with two-thirds published after 2008. Prospective studies composed 35% of the sample. Studies originated from 21 unique countries, with the United States and Greece being most frequent at 22% and 20% of publications, respectively. Of the articles reporting doses in milligrams of CBA, two-thirds were from North America, whereas none of the articles reporting in international units of CMS originated from this region.
In regard to outcomes, 24 unique nephrotoxicity definitions were utilized by 40 studies, with 9 employing the RIFLE (risk, injury, failure, loss, end-stage renal disease) criteria to assess kidney injury. Ten multivariate analyses identified 20 different independent risk factors for colistin-associated nephrotoxicity. For mortality, 8 unique clinical endpoints were employed by 41 studies. In addition, 9 multivariate analyses identified 11 different independent risk factors for colistin-associated mortality.

These data clearly reflect a concerning picture in the scope of inconsistency within current colistin literature that limits the interpretation of dosing, efficacy, and toxicity between studies. Inconsistency with current conversion recommendations is particularly concerning. As antimicrobial resistance progresses and the role of colistin in therapy expands, it is essential that confusion be avoided to ensure that toxicity is limited while efficacy is maximized. It is the responsibility of researchers, clinicians, and peer reviewers to follow the direction of international leaders in this field such as Nation et al [1] to ensure that future literature is tailored to address the needs of the global medical community.

**Note**

Potential conflicts of interest. All authors: No reported conflicts.

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**References**


