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Review

Systemic colistin use in children without cystic fibrosis: a systematic review of the literature

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ABSTRACT

The increasing incidence of multidrug-resistant (MDR) Gram-negative infections necessitates the use of neglected antibiotics such as colistin, even in the paediatric field. The objective of this review was to evaluate the available clinical evidence regarding the effectiveness and safety of systemic colistin in children without cystic fibrosis (CF). Relevant articles were identified from PubMed, Cochrane and Scopus databases. Ten case series and fifteen case reports, including a total of 370 children, were eligible for inclusion in this systematic review. Only 17 of the children were included in studies published after 1977. A total of 326 children received colistin for the treatment of infections and 44 for surgical prophylaxis or prophylaxis of infections in burns patients. Regarding the clinical outcome, 271 of 311 children included in the identified cases series were evaluable. From these 271 children, 235 (86.7%) were cured of the infection, 10/271 (3.7%) improved, 6/271 (2.2%) deteriorated and 20/271 (7.4%) died. Fourteen (70%) of the 20 deaths were attributed to the infection. No infection occurred in the 44 reported children with burns or surgical morbidity who received colistin for prophylaxis. Of these 44 children, 9 (20.5%) died; all deaths were attributed to co-morbidity. Nephrotoxicity occurred in 10/355 (2.8%) of the evaluable children in cases series included in this review. Most of the identified relevant case reports focused on treatment complications. The available evidence, mainly from old case series, suggests that systemic colistin is an effective and acceptably safe option for the treatment of children without CF who have MDR Gram-negative infections.

1. Introduction

The current literature provides evidence of an increasing incidence of infections caused by multidrug-resistant (MDR) Gram-negative bacteria [1–5]. This has necessitated a resurgence in the use of neglected antimicrobial agents such as the polymyxins (colistin and polymyxin B) [6,7].

The effectiveness and safety of colistin in adult populations has been reported in a significant number of studies. These reports refer mainly to patients in the critical care setting [8–12]. With regard to paediatric populations, data from published experience primarily address the effectiveness and safety of colistin in the treatment of MDR infections in children with cystic fibrosis (CF) [13–22]. In addition, data regarding the role of either oral or local colistin treatment in other types of paediatric pathologies are also provided from a significant number of studies, mainly with reference to patients with infectious diarrhoea [23–28], otitis (chronic or external) [29–36] or ophthalmic infections [37–39], and children with malignancies with specific infections [40–43]. However, there is a scarcity of data regarding the role of systemic colistin treatment in paediatric populations without CF.

In this regard, in an era of increasing incidence of infections due to MDR Gram-negative pathogens even in paediatric populations, we aimed to review systematically the available published evidence regarding the effectiveness and safety of systemic colistin treatment in children without CF.

2. Methods

2.1. Data sources

The studies included in this review were retrieved from searches performed in PubMed, Cochrane and Scopus databases assessed at 9 July 2008, 16 July 2008 and 11 September 2008, respectively. Bibliographies of relevant articles were also hand-searched. The search strategy applied on PubMed was (colistin OR colistimethate

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sodium) AND (children OR child OR pediatric OR infant OR infants). The search strategy applied on both the Cochrane and Scopus database was (colistin OR colistimethate sodium) AND (child OR children).

2.2. Selection criteria

A study was considered eligible for inclusion in this review if it provided data regarding the use of intravenous (i.v.), intrathecal (i.t.), intramuscular (i.m.) or intraventricular colistin in paediatric patients for the treatment of infections caused by colistin-susceptible pathogens or for prophylaxis. All or the majority of patients involved in each individual study should not have CF in order for the study to be regarded as eligible for inclusion. Studies that focused on colistin use in paediatric patients with CF were excluded since there are considerable differences between paediatric patients with and those without CF. These differences mainly refer to the volume of distribution, drug metabolism, dosing and the frequency of use of concomitant antibiotic treatment. In addition, studies reporting the use of oral colistin or the use of colistin for topical treatment in paediatric patients were excluded. Abstracts in scientific conferences or studies published in languages other than English, Spanish, French, German, Italian or Greek were also excluded from the review.

2.3. Data extraction

The data extracted from each of the studies included the number and demographic characteristics of the included children, any underlying disease and/or intervention, the characteristics of the infection (type, causative pathogen and site of isolation), antibiotic treatment prior to colistin, the characteristics of colistin treatment, concomitant treatment to colistin, the clinical outcome of each patient and any reported adverse event. Two reviewers (EKV and PIR) independently performed data extraction of the included articles.

2.4. Definitions

Causative pathogens of the infection were defined as any pathogen isolated from the patient's biological fluids that was regarded as responsible for the index infection. Concomitant treatment was defined as any antibiotic agent or any other medication administered concomitantly with colistin. Clinical outcome was

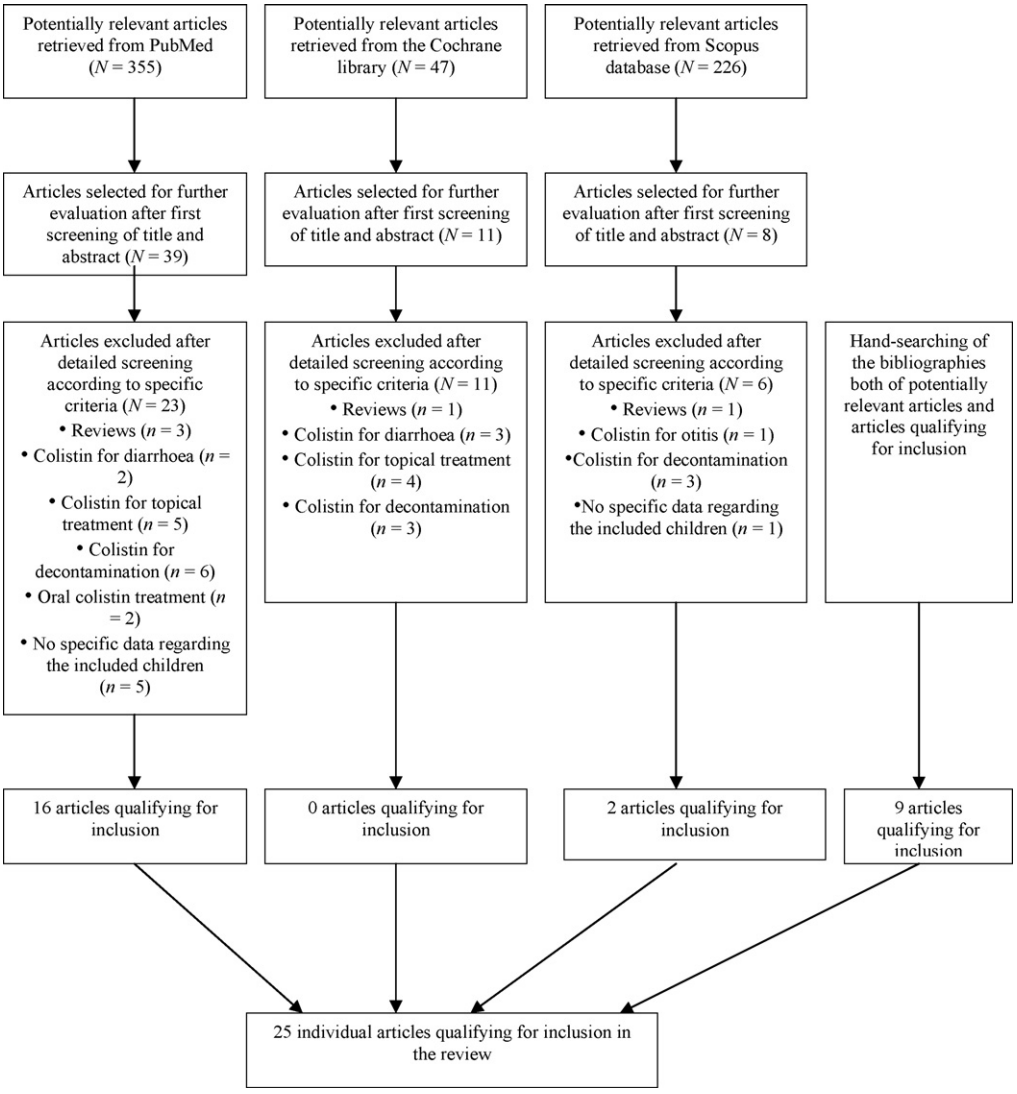

Fig. 1. Flow diagram of the detailed process of selection of articles for inclusion in the review.