Pelargonium sidoides for acute bronchitis: A systematic review and meta-analysis

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Abstract

Objective: To critically assess the efficacy of *Pelargonium sidoides* for treating acute bronchitis.

Data sources: Systematic literature searches were performed in 5 electronic databases: (Medline (1950 – July 2007), Amed (1985 – July 2007), Embase (1974 – July 2007), CINAHL (1982 – July 2007), and The Cochrane Library (Issue 3, 2007) without language restrictions. Reference lists of retrieved articles were searched, and manufacturers contacted for published and unpublished materials.

Review methods: Study selection was done according to predefined criteria. All randomized clinical trials (RCTs) testing *P. sidoides* extracts (mono preparations) against placebo or standard treatment in patients with acute bronchitis and assessing clinically relevant outcomes were included. Two reviewers independently selected studies, extracted and validated relevant data. Methodological quality was evaluated using the Jadad score. Meta-analysis was performed using a fixed-effect model for continuous data, reported as weighted mean difference with 95% confidence intervals.

Results: Six RCTs met the inclusion criteria, of which 4 were suitable for statistical pooling. Methodological quality of most trials was good. One study compared an extract of *P. sidoides*, EPs®7630, against conventional non-antibiotic treatment (acetylcysteine); the other five studies tested EPs®7630 against placebo. All RCTs reported findings suggesting the effectiveness of *P. sidoides* in treating acute bronchitis. Meta-analysis of the four placebo-controlled RCTs suggested that EPs®7630 significantly reduced bronchitis symptom scores in patients with acute bronchitis by day 7. No serious adverse events were reported.

Conclusion: There is encouraging evidence from currently available data that *P. sidoides* is effective compared to placebo for patients with acute bronchitis.

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Keywords: Acute bronchitis; Bronchitis Symptom Score; EPs®7630; *Pelargonium sidoides*; Umckaloabo

Introduction

Acute bronchitis refers to the acute or sub-acute onset of productive cough with no history of chronic pulmonary disease and without evidence of pneumonia or sinusitis (Gonzales and Sande, 1995). It is one of the most common diagnoses in primary care (Knutson and Braun, 2002), affecting 44 adults in every 1000 (>16 years old) each year in the UK, with 82% of the episodes occurring in autumn or winter (Macfarlane et al., 2001). Hueston and Mainous (1998) reported that viruses are the most common cause of this condition. However, non-viral agents (bacteria and allergens) play a role in its etiology in less than 10% of cases (Niroumand and

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Grossman, 1998). Surprisingly, prescription of antibiotics for acute bronchitis is still wide-spread even though their efficacy is limited to bacterial infections (Bent et al., 1999; Hueston and Mainous, 1998; Orr et al., 1993).

Perhaps due to the limited success of antibiotics, substantial cost, associated adverse effects and antibiotic resistance as a result of overuse and misuse (Bent et al., 1999) more attention is now focused on alternative treatments for acute bronchitis and other upper respiratory tract infections; hence the search for effective herbal options (Kligler et al., 2006). *Pelargonium sidoides* is an herbaceous perennial that is popular in South African traditional medicine for the treatment of infectious respiratory diseases (Watt and Breyer-Brandwyk, 1962). *Pelargonium* containing phytopharmaceuticals are currently widely used in Europe to treat respiratory tract infections (Matthys et al., 2003).

The aim of this systematic review was to assess available evidence from rigorous clinical trials on the efficacy and/or effectiveness of *Pelargonium sidoides* for the treatment of acute bronchitis.

Methods

Search strategy

Systematic literature searches were conducted in 5 electronic databases: (Medline (1950 – July 2007), Amed (1985 – July 2007), Embase (1974 – July 2007), CINAHL (1982 – July 2007), and The Cochrane Library (Issue 3, 2007) without language restrictions. The search strategy was structured as "search terms for condition" AND "search terms for intervention". Both MeSH terms and text terms were searched for the condition as well as the intervention. The MeSH term for the condition was acute bronchitis and for the intervention were *Pelargonium* OR *sidoides* OR Umckaloabo OR EPs®7630. We also searched the reference lists of all retrieved articles. We contacted 4 manufacturers of commercial preparations of *Pelargonium sidoides* for further information, particularly unpublished materials.

Inclusion and exclusion criteria

Only randomized clinical trials (RCTs) testing monopreparations of *P. sidoides* as sole or adjunctive treatment administered orally against a control intervention (placebo or conventional therapy), in patients of any age or sex with acute bronchitis and assessing clinically relevant outcomes were included. Trials including patients with pre-existing chronic bronchitis or other infectious diseases were excluded.

Data extraction and assessment of methodological quality

All titles and abstracts identified by the literature search were initially assessed against the inclusion criteria to decide if the full text article should be obtained (TBA). The retrieved full text papers were independently assessed by two reviewers (TBA and RG) to decide on inclusion. Disagreements were resolved by discussion between the two reviewers and by seeking the opinion of a third reviewer (EE) when necessary. Data concerning the details of study design, quality of the study, participants, intervention, outcomes and adverse events were independently extracted by two reviewers (TBA and RG) using a pre-designed data extraction sheet.

The methodological quality of all included studies was assessed independently by two reviewers (TBJ and RG) using the 5-point Jadad score (Jadad et al., 1996). We also assessed allocation concealment and the use of intention to treat analysis. Discrepancies were resolved by discussion between the two authors.

Data analysis

Included trials were categorised by the type of control interventions and the following comparisons were made: (a) herbal medicine *versus* placebo and (b) herbal medicine *versus* conventional therapy.

Meta-analysis was carried out using Review Manager Software (version 4.2.10 2007, Cochrane Collaboration and Updated Software). We quantitatively combined the results of four studies that were suitable for statistical pooling. We calculated weighted mean differences (WMD) and 95% confidence intervals (CI) for continuous data using fixed-effect model. The chi-square test for homogeneity was performed to determine whether the distribution of results was compatible with the assumption that differences between trials were due to chance variation alone. To evaluate potential publication bias we constructed a funnel plot for the primary outcome of change in Bronchitis Severity Scores (BSS) score, using effect size as a measure, and visually examined it for asymmetry.

Results

The literature searches identified 295 potentially relevant titles and abstracts. We also identified two unpublished trials (Kieser, 2007a, b). Initial screening of the titles and abstracts identified 16 relevant references for which full texts were retrieved for further evaluation. Ten references were subsequently excluded for the following reasons: eight references as they were