Device selection and outcomes of aerosol therapy: evidence-based guidelines

CRD summary
This review assessed the efficacy and safety of nebulisers, pressurised metered-dose inhalers and dry powder inhalers as delivery systems for beta-agonists, anticholinergic agents and corticosteroids. The authors concluded that the delivery devices can be equally effective. Given the risk of studies being underpowered and the limited consideration of quality, the robustness of the authors' conclusions is somewhat unclear.

Authors' objectives
To compare the efficacy and safety of nebulisers, pressurised metered-dose inhalers (MDIs) with or without a spacer or holding chamber, and dry powder inhalers (DPIs) as delivery systems for beta-agonists, anticholinergic agents and corticosteroids.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched for English language articles. The search terms were reported though the dates of the searches were unclear.

Study selection
Specific interventions included in the review
Studies comparing the same drug delivered using two different inhaler devices were eligible for inclusion. Studies comparing devices of the same type were excluded, as were studies comparing oral or parenteral therapy with aerosol therapy. The delivery systems compared in the included studies were: MDI with DPI; nebuliser with MDI plus spacer or holding chamber; DPI with MDI plus spacer or holding chamber; DPI with nebuliser; MDI with nebuliser; and intermittent with continuous nebuliser. The medications delivered were mainly beta2-agonists, though there were some studies of corticosteroid and anticholinergic agents.

Participants included in the review
Inclusion criteria for the participants were not specified. The included studies were of adults and children with asthma and adults with chronic obstructive pulmonary disorder (COPD). The studies were conducted in acute care, out-patient and clinical laboratory settings.

Outcomes assessed in the review
Inclusion criteria for the outcomes were not specified. Studies were excluded if they did not have useable data or comparable outcomes (further details were not provided). The outcome of interest were forced expiratory volume in 1 second (FEV1), peak flow, mechanics, symptoms and physical findings, forced vital capacity, forced expiratory flow 25-75%, blood gas, adrenergic use, technique or preference, and heart rate, blood-pressure and electrocardiograph. A combined end point of FEV1, peak flow and specific airway conductance was also used for some of the comparisons. Details of the order of preference of measures used to evaluate these outcomes were reported.

How were decisions on the relevance of primary studies made?
Two investigators independently assessed studies for relevance.

Assessment of study quality
The authors did not state that they assessed validity.
Data extraction
The authors did not report how the data were extracted. Mean scores and standard deviations were extracted for individual studies and used to calculate the weighted mean difference and 95% confidence interval. Where an outcome was assessed at more than one time point, the most recent time point was used. Where more than one outcome was assessed, the outcome that was highest in the specified hierarchy (ranging from FEV1 at the top of the hierarchy to heart rate, pulse rate and increase in heart rate at the bottom) was used.

Methods of synthesis
How were the studies combined?
The studies were pooled in a meta-analysis for the various device comparisons and different outcomes, and based on whether the studies were of adult or paediatric populations. The details of the specific method used for pooling were not reported. The level of evidence for each intervention was graded on the basis of study design using the hierarchy of evidence described by the Health and Sciences Policy Committee of the American College of Chest Physicians: strong evidence from good RCTs or meta-analyses; fair evidence from other controlled trials or RCTs with minor flaws; low evidence from non-randomised, case-control or other observational studies; and expert opinion based on consensus.

How were differences between studies investigated?
In addition to pooling the results separately based on the devices being compared and the outcome being assessed, the studies were also stratified based on the intended purpose and design of the study. The following groups of studies were considered separately: studies that assessed the delivery devices in a real world setting such as an emergency department; studies where device performance was assessed in the clinical laboratory setting (emergency department, out-patient and in-patient settings were pooled separately); studies that analysed differences in response variables such as comparing mean increases in lung function values; and studies estimating differences in clinical potency by establishing dose-response curves. The chi-squared test was used to assess statistical heterogeneity.

Results of the review
Fifty-nine RCTs were included (n not reported).
Over 20 separate meta-analyses were conducted across the different populations and settings for the various delivery devices. There were no statistically significant differences between delivery devices in any of the meta-analyses conducted. The authors stated that there was very little heterogeneity in any of the analyses (data were not reported).

Authors’ conclusions
The various devices used for the delivery of bronchodilators and steroids can be equally efficacious. There is no clear basis for selecting one device over another.

CRD commentary
The review addressed a defined review question. The review question was broad and only inclusion criteria for the interventions of interest and study design were specified. Some relevant electronic databases were searched. Details of the search terms were provided though the search dates were not. No attempts were made to locate unpublished studies and only English-language studies were included; there is therefore a risk of publication and language bias. Two reviewers were involved in selecting studies, which helps minimise error and bias, though it was unclear how the data were extracted.

The statistical pooling was probably appropriate as the authors stratified studies based on the devices being compared, study population and setting. The authors stated that there was no significant heterogeneity, though this data and details of the method of pooling were not reported. Individual studies were not quality assessed. The quality of the evidence was graded, but this was based primarily on study design and the criteria that were used to distinguish the quality of the RCTs were unclear. Many of the studies were small and the authors pointed out that many might have been underpowered to detect an effect. In addition, many of the studies conducted in a laboratory setting were designed to be equivalence studies. Given the risk of the studies being underpowered and the limited consideration of quality, the
robustness of the authors' conclusions is somewhat unclear.

Implications of the review for practice and research
Practice: The authors stated that several factors should be considered when selecting a delivery device for individuals with asthma and COPD. In particular, the availability of the device; the clinical setting; the age of the patient and their ability to use the device appropriately; the use of multiple medications; costs and reimbursement; drug administration time; convenience and durability; and patient and physician preference. Further recommendations about specific devices and settings were made.

Research: The authors did not state any specific implications for research. However, they did highlight the lack of information in the included studies on who is likely to use specific devices properly, patient preference, and other factors that are important in choosing a delivery device. This may be a useful area for future research.

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Other publications of related interest
This additional published commentary may also be of interest. Horner SD. Review: various devices for delivery of aerosol treatment can be equally efficacious. Evid Based Nurs 2005;8:106.

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