Review: pressurised metered dose inhalers are as effective as other hand held inhalers for delivering corticosteroids in stable asthma

Brocklebank D, Wright J, Cates C, et al, on behalf of the National Health Technology Assessment Inhaler Review Group. *Systematic review of clinical effectiveness of pressurised metered dose inhalers versus other hand held inhaler devices for delivering corticosteroids in asthma. BMJ 2001 Oct 20;323:896-900.*

QUESTION: In patients with stable asthma, is the standard chlorofluorocarbon (CFC) containing pressurised metered dose inhaler (PMDI) as effective as other hand held inhaler devices for delivering corticosteroids?

Data sources

Studies published from 1966 to July 1999 were identified by searching the Cochrane Airways Group trials database and by reviewing bibliographies of relevant studies. Pharmaceutical companies that manufacture inhaled asthma drugs were contacted for further studies.

Study selection

Studies in any language were selected if they were laboratory, hospital, or community based randomised controlled trials of children or adults with stable asthma that lasted ≥ 4 weeks and compared a single drug delivered by a standard PMDI (with or without a spacer device) with any other hand held inhaler. Trials comparing different doses of the same drug were also included.

Data extraction

2 reviewers independently extracted data on study design, patient characteristics, details of the intervention, study duration, outcomes, and quality. Outcomes included lung function, quality of life measures, symptom scores, drugs for additional relief, acute

exacerbation, days off work or school, treatment failure, patient compliance, patient preference, adverse effects, bronchial hyper-reactivity, and systemic bioavailability.

Main results

24 articles describing 29 studies met the selection criteria. 14 studies compared PMDIs with dry powder inhalers: PMDIs were less effective than dry powder inhalers for improving forced expiratory volume in 1 second, morning peak expiratory flow rate, and use of additional relief drugs (table). However, these differences disappeared after adjusting for baseline variables or were within clinically equivalent limits. 11 studies compared CFC PMDIs with hydrofluoroalkane PMDIs: 10 of these studies used beclomethasone and 1 study used fluticasone. No differences in treatment effects were found. 1 study compared breath actuated PMDIs with standard PMDIs and found no differences for any of the outcomes. 3 studies of children were identified, but meta-analysis could not be done because of study differences. None of the studies of children found any differences in pulmonary function between devices. However, 1 study found a reduction in use of relief drugs of 1 puff per week (95% CI 0.35 to 1.96) in the Turbohaler group compared with PMDI.

Conclusion

In patients with stable asthma, the standard chlorofluorocarbon containing pressurised metered dose inhaler is as effective as other hand held inhaler devices for delivering corticosteroids.

Source of funding: NHS Research and Development Health Technology Assessment Programme.

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A modified version of this abstract appears in ACP Journal Club.

Pressurised metered dose inhaler v dry powder inhaler for delivering corticosteroids to patients with stable asthma (parallel studies only)*

Outcomes at ≥ 4 weeks	Number of studies (n)	Standardised mean difference (95% CI)
FEV ₁	7 (1404)	-0.14 (-0.25 to -0.03)
Morning peak expiratory flow rate	7 (1389)	-0.14 (-0.25 to -0.04)
Use of additional relief drugs	6 (967)	-0.18 (-0.31 to -0.05)

*Meta-analyses were done using a fixed effects model. FEV₁ = forced expiratory volume in 1 second.

COMMENTARY

The 2 systematic reviews by Brocklebank *et al* and Ram *et al* assess an important, and perhaps overlooked, area of asthma care — the effectiveness of various inhaler devices for delivering short acting bronchodilators and corticosteroids. These papers are based on reviews found in the *Cochrane Library*; given that the mandate of the Cochrane Collaboration is the conduct of high quality systematic reviews of healthcare interventions, we can be confident about the methodological rigour of these reviews. It is unlikely that studies were missed because the authors conducted thorough searches for published and unpublished studies reported in any language. Studies were identified through electronic databases (Medline, CINAHL, EMBASE/Excerpta medica), online respiratory websites, manual searches of pertinent journals, review of references of retrieved articles, and review of proceedings of respiratory societies. The investigators also contacted pharmaceutical companies to identify additional studies. Studies included in the reviews involved children and adults with mild to moderate asthma who were followed up in a broad range of practice settings. Unfortunately, many of the studies could not be included in the meta-analyses because of inconsistencies across studies in the type of outcomes measured, the methods used to measure various outcomes, and because of lack of extractable data.

The results of the 2 reviews are applicable to nurses working with patients who have asthma and their families. The reviews highlight the importance of considering the characteristics of inhaler devices for delivering asthma medications. The reviews compared CFC containing PMDIs to other hand held inhaler devices for delivering short acting β_2 agonists and corticosteroids, and concluded that CFC PMDIs are as effective as alternative types of inhalers. The reviews did not identify a superior inhaled delivery device for asthma medications.

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Review: pressurised metered dose inhalers are as effective as other hand held inhalers for delivering β_2 agonist bronchodilators in stable asthma

Ram FSF, Wright J, Brocklebank D, et al, on behalf of the National Health Technology Assessment Inhaler Review Group. *Systematic review of clinical effectiveness of pressurised metered dose inhalers versus other hand held inhaler devices for delivering β_2 agonist bronchodilators in asthma. BMJ 2001 Oct 20;323:901-5.*

QUESTION: In patients with stable asthma, is the standard chlorofluorocarbon containing pressurised metered dose inhaler (PMDI) as effective as other hand held inhaler devices, including chlorofluorocarbon-free PMDIs, for delivering short acting β_2 agonist bronchodilators?

Data sources

Studies published from 1966 to December 2000 were identified by searching the Cochrane Airways Group trials database, Medline, EMBASE/Excerpta Medica, CINAHL, and 17 online respiratory websites. Bibliographies of relevant studies were reviewed, and pharmaceutical companies that manufacture inhaled asthma drug were contacted for further studies.

Study selection

Studies in any language were selected if they were laboratory, hospital, or community based randomised controlled trials of children or adults with stable asthma that compared delivery of short acting β_2 agonist bronchodilators by standard PMDI (with or without a spacer device) with any other hand held inhaler. Trials comparing different doses of inhaled drugs and those that used challenge testing were also included.

Data extraction

2 reviewers independently extracted data on study design, patient characteristics, details of the intervention, study duration, outcomes, and quality. Outcomes included lung function, quality of life measures, symptom scores, drugs for additional relief, steroid requirement, nocturnal awakening, acute exacerbation, days off work or school, treatment failure, patient compliance, patient

preference, adverse effects, bronchial hyper-reactivity, and systemic bioavailability.

Main results

89 articles describing 84 studies met the selection criteria. 71 trials involved adults and 13 involved children. Most trials involved patients with mild to moderate asthma (baseline forced expiratory volume in 1 second [FEV₁] > 50% of predicted). Meta-analyses were done using a fixed effects model as long as statistical heterogeneity did not exist. In both adults and children, standard PMDIs did not differ from any of the other 10 hand held inhaler devices (Turbohaler, Diskhaler, hydrofluoroalkane PMDI, Rotahaler, Spiros, Easyhaler, multidose powder inhaler, Clickhaler, Gentlehaler, and Autohaler) for FEV₁, forced vital capacity, peak expiratory flow rate, area under the curve for FEV₁, blood pressure, symptoms, bronchial hyper-reactivity, systemic bioavailability, inhaled steroid requirement, serum potassium concentration, or use of additional relief bronchodilators.

Conclusion

In patients with stable asthma, the standard chlorofluorocarbon containing pressurised metered dose inhaler is as effective as other hand held inhalers, including chlorofluorocarbon free pressurised metered dose inhalers, for delivering short acting β_2 agonist bronchodilators.

Source of funding: NHS Research and Development Health Technology Assessment Programme.

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Much global attention is focused on the use of CFCs because of their ozone depleting nature. As a result of the recognition of CFCs as an ozone depleting substance, the Montreal Protocol was signed by Canada, the UK, the USA, and several other countries to develop a national transition strategy to phase out the use of CFCs used in PMDIs. In Canada, the first step of the phase out schedule became effective January 1, 2002.

As a result of the Montreal Protocol and the international recognition of CFCs as an ozone depleting substance, our attention must focus on determining the effectiveness of non-CFC containing inhaler delivery devices for individuals with asthma. We need to ensure that safe, effective, easy to use, desirable, and suitable alternatives exist for patients with asthma. In most countries, non-CFC containing inhaler delivery devices have existed for several years. Some of these alternative inhalers were included in the studies reviewed by Brocklebank *et al* and Ram *et al*. Examples include the Turbohaler, Diskhaler, and hydrofluoroalkane based PMDIs. It is expected that as a result of the phase out of CFC containing PMDIs, several new inhaler devices will be developed and marketed. It is important for nurses to be familiar with the schedule of phase out for CFC PMDIs in their countries, to inform patients of the phase out schedule and how it will affect them, and to work with patients to identify a suitable replacement. If a replacement inhaler is required, nurses need to ensure that the patients are aware of the appropriate dosing and timing of medication, that they are able to accurately provide a return demonstration of the replacement device, and that they are knowledgeable about the care of the inhaler and whether a spacer device is needed.

In summary, the clock is ticking towards the phase out of CFC based PMDI devices. Several viable replacements are currently available and more will be forthcoming. These devices are not bioequivalent and it is the responsibility of nurses and other healthcare providers to assist individuals with asthma in their choices of replacement devices and to provide instructions for their proper use.

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