

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Asthma Treatments for Acute Asthma: Clinical Effectiveness, Cost Effectiveness, and Guidelines

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Research Questions

1. What is the comparative clinical effectiveness of metered dose inhalers with spacers versus nebulizers for acute asthma treatment?
2. What is the comparative cost effectiveness of metered dose inhalers with spacers versus nebulizers for acute asthma treatment?
3. What are the evidence-based guidelines regarding treatments for acute asthma?

Key Findings

Two systematic reviews, and two randomized controlled trials were identified regarding the comparative clinical effectiveness of metered dose inhalers with spacers versus nebulizers for acute asthma treatment. In addition, two evidence-based guidelines were identified regarding treatments for acute asthma. No relevant economic evaluations were identified regarding the comparative cost effectiveness of metered dose inhalers with spacers versus nebulizers for acute asthma treatment.

Methods

A limited literature search was conducted by an information specialist on key resources including Medline, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were metered dose inhalers, nebulizers and asthma. No filters were applied to limit retrieval by study type for questions 1 and 2. A methodological filter was used to limit retrieval to guidelines for question 3. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2015 and January 3, 2020. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients experiencing acute asthma (i.e., asthma attack, asthma exacerbation)
Intervention	Q1-2: Metered dose inhalers with spacers Q3: Treatments for acute asthma (e.g., metered dose inhalers with or without spacers, Salbutamol, nebulizers, ipratropium, education)
Comparator	Q1-2: Nebulizers Q3: No comparator
Outcomes	Q1: Clinical effectiveness (e.g., change in asthma symptoms, respiratory symptoms, morbidity, mortality, O ₂ saturation, adverse events) Q2: Cost effectiveness (e.g., cost per hospitalization avoided, cost per quality adjusted life years increase) Q3: Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines.

Two systematic reviews^{1,2}, and two randomized controlled trials^{3,4} were identified regarding the comparative clinical effectiveness of metered dose inhalers with spacers versus nebulizers for acute asthma treatment. In addition, two evidence-based guidelines^{6,7} were identified regarding treatments for acute asthma. No relevant health technology assessments, non-randomized studies or economic evaluations were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Two systematic reviews,^{1,2} and two randomized controlled trials (RCTs),^{3,4} were identified regarding the comparative clinical effectiveness of metered dose inhalers (MDI) with spacers versus nebulizers for acute asthma treatment. The authors of the systematic review¹ found that both MDI with spacers and nebulizers achieved a similar result in heart rate, respiratory rate, O₂ saturation, and asthma score. Alternatively, the authors of the second systematic review² found that MDI with a spacer, also known as a valved holding chamber (VHC), significantly reduced hospital admission rates, improved clinical score, reduced emergency department admission, and reduced adverse events when compared to nebulizers. The authors of an RCT³ found that bronchodilators administered to children via MDI with VHC significantly lowered rate of hospital admission and significantly improved oxygen saturation compared to a nebulizer administering the same medication. However, authors of a second randomized controlled trial⁴ did not find a significant difference between the two devices with regards to heart rate, respiratory rate, oxygen saturation or ease of use when bronchodilators were administered to preschool children in the pediatric emergency department.

Guidelines by the Scottish Intercollegiate Guidelines Network (SIGN) for the management of asthma recommend that pressurized MDI and spacers are the preferred method of delivery of β_2 agonists and inhaled corticosteroids in young children. Until a child can breathe reproducibly using the spacer mouth piece, a face mask is required. If this is not effective, then a nebulizer may be required.⁵

Guidelines from the Global Initiative for Asthma (GINA) recommends that asthma treatment begin with repeated administration of short-acting beta₂-agonist (SABA) administered via a pressurized MDI and spacer, early introduction of oral corticosteroids, and controlled flow of oxygen, if available.⁶ Ipratropium bromide is recommended only for severe exacerbations and intravenous magnesium sulfate should be considered for patients with severe exacerbations that do not respond to initial treatment.⁶ Response of symptoms, oxygen saturation and lung function should be reviewed after one hour.⁶ The guideline also states the preferred device for children aged 0 to 5 is a pressurized MDI with a dedicated spacer and face mask. If an alternative device is required, a nebulizer with a face mask should be considered for children aged 0 to 3, and a nebulizer with a face mask or a mouthpiece should be considered for children aged 4 to 5 years.⁶

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Roncada C, Andrade J, Bischoff LC, Pitrez PM. Comparison of two inhalational techniques for bronchodilator administration in children and adolescents with acute asthma crisis: a meta-analysis. *Rev Paul Pediatr*. 2018 Jul-Sep;36(3):364-371. [PubMed: PM29995144](#)
2. Castro-Rodriguez JA, Rodrigo GJ, Rodriguez-Martinez CE. Principal findings of systematic reviews of acute asthma treatment in childhood. *J Asthma*. 2015;52(10):1038-1045. [PubMed: PM26303207](#)

Randomized Controlled Trials

3. Iramain R, Castro-Rodriguez JA, Jara A, et al. Salbutamol and ipratropium by inhaler is superior to nebulizer in children with severe acute asthma exacerbation: randomized clinical trial. *Pediatr Pulmonol*. 2019 04;54(4):372-377. [PubMed: PM30672140](#)
4. Mitselou N, Hedlin G, Hederos CA. Spacers versus nebulizers in treatment of acute asthma - a prospective randomized study in preschool children. *J Asthma*. 2016 Dec;53(10):1059-1062. [PubMed: PM27186989](#)

Non-Randomized Studies

No literature identified.

Economic Evaluations

No literature identified.

Guidelines and Recommendations

5. British guideline on the management of asthma. Edinburgh (UK): Scottish Intercollegiate Guidelines Network (SIGN); 2019: <https://www.sign.ac.uk/sign-158-british-guideline-on-the-management-of-asthma.html>. Accessed 2020 Jan 16
See: 2.6 Inhaler Devices, page 8
6. Global strategy for asthma management and prevention. Fontana (WI): Global Initiative for Asthma; 2019: <https://ginasthma.org/wp-content/uploads/2019/06/GINA-2019-main-report-June-2019-wms.pdf>. Accessed 2020 Jan 16
See: Choice of inhaler device, page 144; Box 6-7 Choosing and inhaler device for children 5 years and younger, page 110; Management of Exacerbations, page 102

Appendix — Further Information

Previous CADTH Reports

7. Edge R, Butcher R. Vibrating mesh nebulizers for patients with respiratory conditions requiring nebulization: clinical effectiveness, cost-effectiveness, and guidelines. (*CADTH rapid response report: summary with critical appraisal*). Ottawa (ON): CADTH; 2019:
<https://www.cadth.ca/sites/default/files/pdf/htis/2019/RC1145%20Vibrating%20Mesh%20Nebulizer%20Final.pdf>. Accessed 2020 Jan 16.
[PubMed: PM31553547](#)
8. Hafizi D, MacDougall D. Salbutamol administration via nebulizer versus metered-dose inhalers: clinical effectiveness and cost-effectiveness. (*CADTH rapid response report: summary of abstracts*). Ottawa (ON): CADTH; 2019:
<https://www.cadth.ca/sites/default/files/pdf/htis/2019/RB1367%20Salbutamol%20Nebulizer%20vs%20MDI%20Final.pdf>. Accessed 2020 Jan 16

Systematic Reviews – Alternative Population

9. van Geffen WH, Douma WR, Slebos DJ, Kerstjens HA. Bronchodilators delivered by nebuliser versus pMDI with spacer or DPI for exacerbations of COPD. *Cochrane Database Syst Rev*. 2016 Aug 29(8):CD011826.
[PubMed: PM27569680](#)

Randomized Controlled Trials – MDI without Spacer

10. Snider MA, Wan JY, Jacobs J, Kink R, Gilmore B, Arnold SR. A randomized trial comparing metered dose inhalers and breath actuated nebulizers. *J Emerg Med*. 2018 07;55(1):7-14.
[PubMed: PM29716819](#)

Non-Randomized Studies – Alternative Outcome

11. Dilts JJ, Humiston SG, Lee BR, Allen NH, Michael JG. Effect of an asthma guideline in 2 pediatric emergency departments and an urgent care center. *Pediatr Emerg Care*. 2018 Oct;34(10):729-735.
[PubMed: PM28169982](#)
12. Breuer O, Shoseyov D, Kerem E, Brooks R. Implementation of a policy change: replacement of nebulizers by spacers for the treatment of asthma in Children. *Isr Med Assoc J*. 2015 Jul;17(7):421-424.
[PubMed: PM26357717](#)

Clinical Practice Guidelines – Methodology Not Specified

13. Otiz-Alvarez O, Mikrogianakis A, Canadian Paediatric Society, Acute Care Committee. Managing the paediatric patient with an acute asthma exacerbation. Ottawa (ON): Canadian Paediatric Society; 2017:
<https://www.cps.ca/en/documents/position/management-acute-asthma-exacerbation>.

14. Asthma in adults - recognition, diagnosis and management. Victoria (BC): Government of British Columbia; 2015: <https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/asthma-adults-fullguideline.pdf>. Accessed 2020 Jan 16

Position Statements

15. FitzGerald JM, Lemiere C, Loughheed MD, et al. Recognition and management of severe asthma: a Canadian Thoracic Society position statement. *Can J Respir Crit Care Sleep Med*. 2017;1(4):199-221. Available from: <https://doi.org/10.1080/24745332.2017.1395250> Accessed 2020 Jan 16
16. Ducharme FM, Dell SD, Radhakrishnan D, et al. Diagnosis and management of asthma in preschoolers: A Canadian Thoracic Society and Canadian Paediatric Society position paper. *Can Respir J*. 2015 May-Jun;22(3):135-143. [PubMed: PM25893310](#) Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4470545/pdf/crj-22-135.pdf> Accessed 2020 Jan 16

Review Articles

17. Hon KLE, Leung AKC. Medications and recent patents for status asthmaticus in children. *Recent Pat Inflamm Allergy Drug Discov*. 2017;11(1):12-21. [PubMed: PM28137226](#)