Commentary on: Craig SS, Dalziel SR, Powell CVE, Graudins A, Babl FE, Lunny C, Interventions for escalation of therapy for acute exacerbations of asthma in children: an overview of Cochrane Reviews (Review) *Cochrane Database of Systematic Reviews* 2020 Issue 8

Title: Treatment escalation for children with exacerbations of asthma – what works? An overview of Cochrane Reviews.

Implications for practice and research:

- The authors acknowledge a lack of comparative studies regarding treatment options therefore recommendations to change practice should be applied with caution. Intravenous magnesium sulphate appears to reduce length of inpatient stay.
- No evidence that any treatments reduce risk of intensive care admission.
- Need to develop internationally agreed outcome measures for future trials.
- Need multi-centred trials on second-line therapies with separate focus on pre-school children with wheeze.

Context

Exacerbation of asthma is one of the most common reasons for children to attend an emergency department. Children generally respond well to first line treatments such as inhaled short-acting beta-agonists and systemic corticosteroids. For the minority requiring second line therapies the availability of numerous interventions has led to inconsistency in management. This overview of Cochrane reviews has sought to identify high certainty evidence from existing reviews regarding current interventions.

Methods

The primary outcome of the review[1] was to identify efficacy and safety of second line therapies for children with acute exacerbation of asthma. The relatively new approach of systematically reviewing systematic reviews, known as an overview or umbrella review was used[2]. Secondary outcomes focused on gaps in evidence for future research and to identify outcome measures/scores. Data collected from the Cochrane database included randomised and non-randomised clinical trials covering all types of comparison studies such as drug vs placebo with identified primary and secondary outcomes. GRADE[3] (Grading of Recommendations, Assessment, Development and Evaluations) was used to measure the quality of the data, while ROBIS (risk of bias in systematic reviews) assessed it for bias.

Findings

From the 13 systematic reviews included the findings were grouped into one of the three interventions identified: inhaled bronchodilators, parenteral bronchodilators, and interventions to reduce the work of breathing. Although there was low certainty evidence of the use of inhaled bronchodilators regarding admission to hospital or intensive care, there was moderate-certainty evidence that adding inhaled anticholinergic agents with the inhaled beta2-agonists did reduce risk of hospital

admission. There was high certainty evidence that intravenous magnesium sulphate reduced the length of stay in hospital and could also reduce admission to hospital. However, the evidence for using inhaled Heliox to assist in respiratory effort and reduce risk of admission to hospital was of low certainty.

Commentary

Systematic reviews are valued for the high-quality evidence they produce however the increasing number of published reviews makes it difficult for healthcare staff to keep up to date[5]. Overviews such as this support clinical decision making and guideline development[2].Managing acute exacerbations of asthma in children is challenging; the increasing number of treatments available and the variation in approaches across departments and countries challenges us further. The high certainty evidence from this review[1] supporting the use of intravenous (IV) magnesium sulphate in reducing length of stay for children is reassuring. However, the high certainty evidence supporting IV magnesium sulphate as a means of avoiding admission is at odds with established guidance. British Thoracic Society/SIGN[6] guidance recommend its use where first line inhaled therapy has failed, indicating a child in the moderate to severe category. This group of children would be admitted for ongoing treatment and not discharged directly from an emergency department.

This review[1] is helpful for those developing local and national guidelines as it will strengthen current practice regarding the use of intravenous magnesium sulphate. For the healthcare professional assessing and treating a child with acute exacerbation of asthma, recognising that the evidence base for much of the current interventions is unclear or of low certainty is not reassuring. However, it should be recognised that this reflects a lack of quality research rather than a lack of safe and effective treatments.

References:

1. Craig SS, Dalziel SR, Powell CVE, Graudins A, Babl FE, Lunny C, Interventions for escalation of therapy for acute exacerbations of asthma in children: an overview of Cochrane Reviews (Review) *Cochrane Database of Systematic Reviews* 2020 Issue 8

2. Hunt H, Pollock A, Campbell P, Estcourt L, Brunton G, An introduction to overviews of reviews: planning a relevant research question and objective for an overview *Systematic Reviews* 2018 **7** 39

3. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations *BMJ* 2008; **336** :924

4. Whiting P, Savović J, Higgins JPT, Caldwell DM, Reeves DC, Shea B, Davies P, Kleijnen J, Churchill R, ROBIS: A new tool to assess risk of bias in systematic reviews was developed *Journal of Clinical Epidemiology* 2016 **69**, 225-234.

5. Smith V, Devane D, Begley CM, Clarke M, Methodology in conducting a systematic review of systematic reviews of health care interventions *BMC Medical Research Methodology* 2011 **11** 15

6. British Thoracic Society/SIGN (Scottish Intercollegiate Guidelines Network) *British Guideline on the management of asthma* 2019 Available at: https://www.brit-thoracic.org.uk/quality-improvement/guidelines/asthma

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Conflict of interest: None