Interventions for managing asthma in pregnancy

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RHL summary

Key Findings

- Magnesium sulfate in addition to usual treatment may reduce frequency of exacerbations in acute asthma.
- No clear difference in risk of acute exacerbations was shown when using inhaled beclomethasone in addition to standard maintenance therapy, or in comparisons of inhaled beclomethasone to oral theophylline for maintenance therapy.
- Use of a fraction of exhaled nitric oxide (FENO)-based algorithm significantly reduced asthma exacerbations, had fewer neonatal hospitalisations, had some improvement in quality of life scores, and showed improved use of pharmacological therapies. Pharmacist-led management improved asthma control scores at 6 months, improved lung function and quality of life measures.

Evidence included in this review

Eight trials were included in this review involving 1181 mothers and their babies. Five trials assessed pharmacological agents while three trials assessed non-pharmacological interventions.

Quality assessment

Overall, the trials were of moderate quality. Two trials were determined to be of low risk of bias, two of unclear risk and four of moderate risk of bias.

Clinical implications

There is a limited body of evidence on effects of interventions for managing asthma during pregnancy. Trials of pharmacological interventions could not provide clear evidence of benefits or harms to support or refute current practices. Magnesium sulphate was shown to reduce acute exacerbation of asthma, but this was in a small trial of unknown quality. FENO-based algorithms are not yet appropriate for implementation due to unknown effects on perinatal outcomes. Similarly, outcomes surrounding pharmacist-led management are still inconclusive.

Further research
There is a limited evidence base to draw conclusions about the most effective and safe interventions. Future trials need to be well designed and powered to allow differences in outcomes for mothers and babies to be determined.

**Cochrane review**


**Abstract**

Asthma is the most common respiratory disorder complicating pregnancy, and is associated with a range of adverse maternal and perinatal outcomes. There is strong evidence however, that the adequate control of asthma can improve health outcomes for mothers and their babies. Despite known risks of poorly controlled asthma during pregnancy, a large proportion of women have sub-optimal asthma control, due to concerns surrounding risks of pharmacological agents, and uncertainties regarding the effectiveness and safety of different management strategies.

To assess the effects of interventions (pharmacologic and non-pharmacologic) for managing women's asthma in pregnancy on maternal and fetal/infant outcomes.

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (2 June 2014) and the Cochrane Airways Group's Trials Register (4 June 2014).

Randomised and quasi-randomised controlled trials comparing any intervention used to manage asthma in pregnancy, with placebo, no intervention, or an alternative intervention. We included pharmacological and non-pharmacological interventions (including combined interventions). Cluster-randomised trials were eligible for inclusion (but none were identified). Cross-over trials were not eligible for inclusion.

We included multi-armed trials along with two-armed trials. We also included studies published as abstracts only.

At least two review authors independently assessed trial eligibility and quality and extracted data. Data were checked for accuracy.

We included eight trials in this review, involving 1181 women and their babies. Overall we judged two trials to be at low risk of bias, two to be of unclear risk of bias, and four to be at moderate risk of bias.

Five trials assessed pharmacological agents, including inhaled corticosteroids (beclomethasone or budesonide), inhaled magnesium sulphate, intravenous theophylline, and inhaled beclomethasone verus oral theophylline. Three trials assessed non-pharmacological interventions, including a fractional exhaled nitric oxide (FENO)-based algorithm versus a clinical guideline-based algorithm to adjust inhaled corticosteroid therapy, a pharmacist-led multi-disciplinary approach to management versus standard care, and progressive muscle relaxation (PMR) versus sham training.

The eight included trials were assessed under seven separate comparisons.

Primary outcomes: one trial suggested that inhaled magnesium sulphate in addition to usual treatment could reduce exacerbation frequency in acute asthma (mean difference (MD) -2.80; 95% confidence interval (CI) -
3.21 to -2.39; 60 women). One trial assessing the addition of intravenous theophylline to standard care in acute asthma did not report on exacerbations (65 women). No clear difference was shown in the risk of exacerbations with the use of inhaled beclomethasone in addition to usual treatment for maintenance therapy in one trial (risk ratio (RR) 0.36; 95% CI 0.13 to 1.05; 60 women); a second trial also showed no difference, however data were not clearly reported to allow inclusion in a meta-analysis. No difference was shown when inhaled beclomethasone was compared with oral theophylline for maintenance therapy (RR 0.88; 95% CI 0.59 to 1.33; one trial, 385 women). None of these trials reported on neonatal intensive care admissions.

Secondary outcomes: inhaled magnesium sulphate in acute asthma was shown to improve lung function measures (one trial, 60 women); intravenous theophylline in acute asthma was not associated with benefits (one trial, 65 women). No clear differences were seen with the addition of inhaled corticosteroids to routine treatment in three trials (374 women). While inhaled beclomethasone, compared with oral theophylline, significantly reduced treatment discontinuation due to adverse effects in one trial (384 women), no other differences were observed, except for higher treatment adherence with theophylline. Four of the five trials did not report on adverse effects.

Primary outcomes: in one trial, the use of a FENO-based algorithm was shown to significantly reduce asthma exacerbations (RR 0.61; 95% CI 0.41 to 0.90; 220 women); and a trend towards fewer neonatal hospitalisations was observed (RR 0.46; 95% CI 0.21 to 1.02; 214 infants). No exacerbations occurred in one trial assessing pharmacist-led management; this approach did not reduce neonatal intensive care admissions (RR 1.50; 95% CI 0.27 to 8.32; 58 infants). One trial (64 women) assessing PMR did not report on exacerbations or neonatal intensive care admissions.

Secondary outcomes: the use of a FENO-based algorithm to adjust therapy led to some improvements in quality of life scores, as well as more frequent use of inhaled corticosteroids and long-acting ?-agonists, and less frequent use of short-acting ?-agonists (one trial, 220 women). The FENO-based algorithm was associated with fewer infants with recurrent episodes of bronchiolitis in their first year of life, and a trend towards fewer episodes of croup for infants. Pharmacist-led management improved asthma control scores at six months (one trial, 60 women); PMR improved lung function and quality of life measures (one trial, 64 women). No other differences between comparisons were observed.

Based on eight included trials, of moderate quality overall, no firm conclusions about optimal interventions for managing asthma in pregnancy can be made. Five trials assessing pharmacological interventions did not provide clear evidence of benefits or harms to support or refute current practice. While inhaled magnesium sulphate for acute asthma was shown to reduce exacerbations, this was in one small trial of unclear quality, and thus this finding should be interpreted with caution. Three trials assessing non-pharmacological interventions provided some support for the use of such strategies, however were not powered to detect differences in important maternal and infant outcomes. While a FENO-based algorithm reduced exacerbations, the effects on perinatal outcomes were less certain, and thus widespread implementation is not yet appropriate. Similarly, though positive effects on asthma control were shown with PMR and pharmacist-led management, the evidence to date is insufficient to draw definitive conclusions.

In view of the limited evidence base, further randomised trials are required to determine the most effective and safe interventions for asthma in pregnancy. Future trials must be sufficiently powered, and well-designed, to allow differences in important outcomes for mothers and babies to be detected. The impact on health services requires evaluation. Any further trials assessing pharmacological interventions should assess novel agents or those used in current practice. Encouragingly, at least five trials have been identified as planned or underway.

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