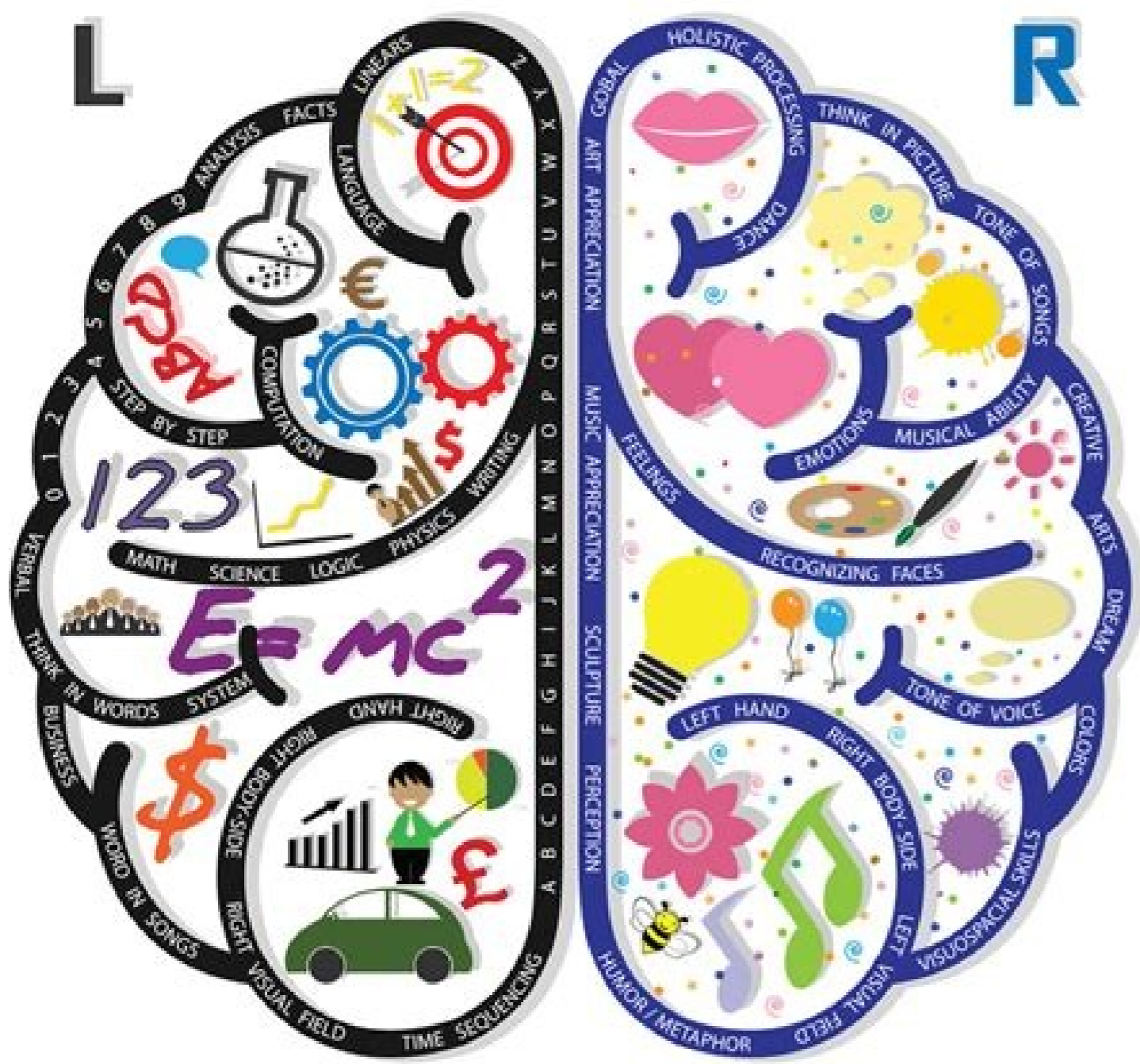


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your pregnancy, don't stop without talking to your doctor first. During the delivery of your baby, it will be important to have asthma medication available. If discussing the availability of your healthcare team, this can be added to your birthing plan. Pregnancy asthma during pregnancy requires expecting mothers to carefully monitor their symptoms, avoid asthma triggers and take asthma medicines as directed by their doctor. Suddenly stopping asthma medicines could be harmful to you and your baby. It's important to continue to follow-up with your asthma care provider throughout your pregnancy and get your annual flu shot, which is safe for pregnant women. Labor and DeliveryTalk with your healthcare providers about your labor and delivery plan. With a diagnosis of asthma, your healthcare team will choose medicines that are safe for you and your baby. For example, in the event of an emergency cesarean delivery, your healthcare team may select general anesthesia that promotes dilation of the airways.Belly breathing exercises for relaxation will come in handy during labor and delivery. The Lung Association has an instructional video to help you practice and be prepared. Belly breathing is a great skill for people with asthma to have on hand during pregnancy or anytime who may experience difficulty breathing.Asthma Medication and BreastfeedingThere are many health benefits that your baby gets from breast milk. Talk to your doctor about continuing to use your asthma medicines while breastfeeding and list any concerns that you may have. Asthma medications are generally safe for breastfeeding babies. This systematic review aimed to assess the effects of interventions (pharmacologic and non-pharmacologic, including self-management interventions) for managing women's asthma in pregnancy on maternal and fetal/infant outcomes. Eight trials (randomising 1181 women and their babies), at a moderate risk of bias overall, were eligible for inclusion, and were assessed under seven different comparisons in the review. Five of the trials assessed pharmacological agents, including inhaled magnesium sulphate (Badawy 2012) and intravenous theophylline (Wendel 1996) for women following acute asthma exacerbations; and inhaled corticosteroids (beclomethasone and budesonide) (Caramez 1998; Silverman 2005; Wendel 1996), including versus oral theophylline (Dombrowski 2004) for maintenance therapy. The other three trials assessed non-pharmacological interventions for asthma management during pregnancy, including a validated fractional exhaled nitric oxide (FENO)-based algorithm versus a clinical guideline-based algorithm to adjust asthma therapy (Powell 2011), a pharmacist-led multi-disciplinary approach to asthma management versus standard care (Lim 2012), and progressive muscle relaxation (PMR) versus sham training (Nickel 2006).Considering primary review outcomes, relatively few differences were seen across the seven comparisons for the trials that reported on these outcomes. For women following acute asthma exacerbations, inhaled magnesium sulphate in addition to standard treatment in Badawy 2012 (60 women) was shown to significantly reduce the frequency of acute exacerbations before birth. The Badawy 2012 trial was however judged to be at an unclear risk of bias overall; thus this result must be interpreted with caution. In the Wendel 1996 trial (65 women), which assessed the addition of intravenous theophylline to standard treatment in acute asthma, asthma exacerbations were not reported. An inhaled corticosteroid (beclomethasone) in addition to usual treatment for maintenance therapy, did not have a clear effect on asthma exacerbations in two trials (of largely unclear methodological quality) (Caramez 1998; Wendel 1996) (155 women); and when inhaled beclomethasone was compared to oral theophylline in the Dombrowski 2004 trial for maintenance therapy (385 women), no clear difference was shown in the rate of exacerbations. None of the five trials assessing pharmacological interventions reported on the neonatal primary outcome of neonatal intensive care unit admissions.In regards to non-pharmacological interventions, the use of a validated FENO-based treatment algorithm (compared with a clinical guideline-based algorithm) to adjust asthma therapy (FENO used to adjust dose of inhaled corticosteroids; and Asthma Control Questionnaire score used to adjust dose of long-acting β2 agonist) was shown to reduce exacerbations in Powell 2011 (220 women), and a trend towards reduced neonatal intensive care unit admissions was also shown. No women in Lim 2012 (60 women) (assessing a pharmacist-led multi-disciplinary approach to maternal asthma management) had exacerbations, and no difference was shown in the risk of admission to the neonatal intensive care unit in this trial. In Nickel 2006 (64 women), comparing PMR with sham training, asthma exacerbations and neonatal intensive care unit admissions were not reported.Similarly, across the seven comparisons, there were few differences observed for secondary review outcomes. In the Wendel 1996 trial, intravenous theophylline in addition to usual treatment following acute exacerbations was not associated with differences in maternal or infant outcomes (discontinuation due to adverse effects, stillbirth, neonatal death, preterm birth, length of hospitalisation). The addition of inhaled magnesium sulphate compared to routine treatment following acute exacerbations in Badawy 2012, was however shown to improve lung function (as measured by FEV1, FVC, FEV1/FVC, FEF25-75 and PEF) compared to routine treatment alone. No difference was seen for caesarean birth (the only other outcome reported in the Badawy 2012 trial).When inhaled corticosteroids in addition to usual treatment were compared with no additional treatment for maintenance therapy (Caramez 1998; Silverman 2005; Wendel 1996), no differences were seen for the secondary outcomes reported (including: caesarean birth, compliance with the intervention, abortion, stillbirth, neonatal death, preterm birth, birthweight, Appgar score less than seven, congenital malformations). When inhaled beclomethasone was compared with oral theophylline for maintenance therapy in one trial (Dombrowski 2004), no differences were seen for a range of maternal and infant outcomes (maternal: asthma symptoms, medication requirements, measures of lung function, pre-eclampsia, caesarean birth, postpartum haemorrhage, chorioamnionitis, self-reported compliances) (infant: perinatal mortality, gestational age at birth, preterm birth, birthweight, low birthweight, small-for-gestational age, sepsis, major congenital malformations) (health services: antenatal hospital admissions, emergency department visits). While women receiving beclomethasone did not experience significantly fewer adverse effects overall (nausea, nervousness, insomnia, tremor, palpitations, heartburn), they were shown to have a significantly lower risk of discontinuing the intervention because of adverse effects, compared with women receiving oral theophylline (Dombrowski 2004).In addition to significantly reducing asthma exacerbations, the FENO-based treatment algorithm in Powell 2011, was shown to improve some measures of quality of life (mental summary scores on the SF-12). The use of the FENO-based algorithm was also shown to influence treatment profile, with more women in this group receiving inhaled corticosteroids (though at a non-significantly lower equivalent dose) and long-acting β-agonists, and fewer women in this group receiving short-acting β-agonists. No differences were seen with the use of FENO-based management for the other maternal and infant outcomes reported by the trial (maternal: symptoms, lung function, pregnancy-induced hypertension, pre-eclampsia, gestational diabetes, caesarean birth, antepartum or postpartum haemorrhage, ruptured membranes, hyperemesis) (infant: stillbirth, gestational age at birth, preterm birth, birthweight, low birthweight, small-for-gestational age, jaundice, congenital malformations) (Powell 2011). At 12-month follow-up in Powell 2011, infants born to mothers in the FENO group were shown to have a significantly reduced risk of recurrent bronchiolitis, and a trend towards a reduced risk of recurrent croup.When a pharmacist-led multi-disciplinary approach to management of maternal asthma was compared with standard care in Lim 2012, significant improvements in asthma control at six months were observed (which were not observed at three months). No other differences were seen in this trial for the maternal or infant secondary review outcomes that were reported (maternal: hypertension in pregnancy, gestational diabetes) (infant: gestational age at birth, preterm birth, birthweight, small-for-gestational age, Appgar scores, congenital malformations).Finally, in Nickel 2006, when PMR was compared with sham training, improvements were seen in measures of lung function (FEV1 and PEFR) and in some measures of quality of life (five of eight domains on the SF-36 (role physical, vitality, social functioning, role emotional, mental health), and two of five scales on the State-Trait Anger Expression Inventory (State-Anger, Trait-Anger)).The five trials in this review assessing pharmacological interventions did not provide clear evidence of benefits or harms to support or refute current practice (Badawy 2012; Caramez 1998; Dombrowski 2004; Silverman 2005; Wendel 1996), which varies, but commonly follows a 'step-wise approach', guided by randomised evidence from non-pregnant populations and observational data from pregnancy studies (Dombrowski 2008; NAEPP 2005; Schatz 2009). Short-acting bronchodilators (particularly short-acting inhaled β-agonists such as albuterol (salbutamol) have been recommended for symptom relief in women with mild, intermittent asthma; in mild persistent asthma, a daily low-dose inhaled corticosteroid has been recommended (with budesonide, with the greatest amount of safety data in pregnancy, preferred to beclomethasone, which was the inhaled corticosteroid assessed in three trials in this review (Caramez 1998; Dombrowski 2004; Wendel 1996)). Low-dose inhaled corticosteroids are favoured over methylxanthines, such as theophylline (which was the focus of two trials in this review (Dombrowski 2004; Wendel 1996)), mast cell stabilisers (such as cromolyn) and leukotriene-receptor antagonists. For moderate and severe persistent asthma, the combination of a low-dose inhaled corticosteroid with a long-acting β-agonist (such as salmeterol or formoterol) or an increased dose of the inhaled corticosteroid has been recommended. For the use of a combination of pharmacological agents including short-acting inhaled β-agonists, inhaled anticholinergic agents (ipratropium bromide), and oral/intravenous systemic corticosteroids, has been supported (Dombrowski 2008; NAEPP 2005; Schatz 2009); the addition of inhaled magnesium sulphate for exacerbation management, which showed some benefits in one trial in this review (Badawy 2012), is not currently recommended in practice.Three trials included in this review provide promise for the optimisation of asthma management in pregnancy with the use of non-pharmacological interventions (Lim 2012; Nickel 2006; Powell 2011). Though positive effects on asthma control were observed in this review with PMR (one trial: Nickel 2006), and a pharmacist-led, multi-disciplinary approach to management (with the provision of education and regular review) (one trial: Lim 2012), this evidence is unlikely to be sufficient to support clinical practice recommendations. Similarly, while the use of an algorithm incorporating FENO to adjust inhaled corticosteroid dose and asthma symptoms to adjust β-agonist dose showed reductions in exacerbations during pregnancy, and changes in maintenance pharmacologic therapy (with more frequent use of inhaled corticosteroids at lower daily doses), this evidence is unlikely to be sufficient to recommend universal implementation into the antenatal care setting (Powell 2011). The benefits and/or harms for perinatal outcomes are as yet, uncertain; further, there is a need to consider and evaluate the resource implications of such a management strategy, given that FENO measurement devices are not routinely available in many clinical settings. Though the randomised evidence for non-pharmacological interventions for asthma management in pregnancy accumulated to date is unlikely to be sufficient for widespread practice change, the need for such strategies to be incorporated into the management of a woman's asthma during pregnancy is increasingly being recognised. Clinical practice guidelines have highlighted the need to ensure that pregnant women have access to education about asthma and its relationship with pregnancy, and have the opportunity to develop the skills necessary for asthma management (such as correct inhaler technique, ability to self-monitor and follow a long-term management plan, and knowledge of how to promptly handle signs of worsening asthma) (Dombrowski 2008; NAEPP 2005).There is currently a lack of randomised evidence in this area, with only eight trials completed to date. The largest trial included almost 400 women (Dombrowski 2004), however, in five of the included trials, the sample sizes were of less than 100 women (Badawy 2012; Caramez 1998; Lim 2012; Nickel 2006; Wendel 1996). Encouragingly, at least five further trials are currently planned or underway (ACTRN12613000202763; ACTRN12613000244707; ACTRN12613000301763; ACTRN12613000800729; ("type":"clinical-trial","attrs":{"text":"NCT01345396","term_id":"NCT01345396"})NCT01345396).The scarcity of data for the management of asthma during pregnancy was evident, not only in the limited number of completed trials, but also in the small number of outcomes evaluated in some of the included trials. Considering primary outcomes, only five of the eight included trials reported on asthma exacerbations (Badawy 2012; Caramez 1998; Dombrowski 2004; Lim 2012; Powell 2011), and only two trials reported on neonatal intensive care unit or special care nursery admissions (Lim 2012; Powell 2011). For the majority of outcomes, data were reported by less than half of the included trials; the most commonly reported secondary review outcomes were lung function, stillbirth, birthweight, congenital malformations (each reported by four trials), preterm birth and caesarean birth (both reported by five trials). Only one (Powell 2011) of the eight included trials completed to date has reported on follow-up outcomes of the infants (Powell 2011 has reported on the outcomes of bronchiolitis and croup).Clinical heterogeneity of the data and also of the study designs (with a variety of different interventions and comparisons assessed across the eight trials), meant that very little data could be pooled in meta-analysis, making interpretation difficult. Different methods of measuring outcomes, such as lung function, and different outcome definitions across trials, such as for asthma exacerbations, also made comparisons between trials difficult. At present there is no commonly accepted definition for asthma exacerbations. A further drawback of definitions for exacerbations is that they are currently based on retrospective criteria; prospective criteria for the definition of asthma exacerbations, including in pregnancy, would be desirable.Two of the eight included trials assessed xanthines for asthma management in pregnancy: intravenous aminophylline was assessed for acute asthma (Wendel 1996), and oral theophylline for maintenance treatment of asthma (Dombrowski 2004). These agents are, however, now infrequently used in clinical practice, particularly outside of the United States and developing world (Giles 2013), with the risk-benefit balance shown to be unfavourable (Nair 2012; Seddon 2006; Tee 2007). If oral theophylline is to be used in pregnancy, careful titration of the dose and regular monitoring to maintain the recommended serum theophylline concentration are required, due to the potential for serious toxicity from excessive dosing (NAEPP 2005).Three included trials evaluating inhaled corticosteroids for maintenance treatment utilised beclomethasone (Caramez 1998; Dombrowski 2004; Wendel 1996). While inhaled corticosteroids are currently recognised as the preferred preventative medication for managing asthma in pregnancy, it is important to note that agents such as fluticasone and budesonide (as utilised in the later Silverman 2005 and Powell 2011 trials), rather than beclomethasone, have been regarded as 'preferred' inhaled corticosteroids for use in pregnancy, with the most gestational safety data for budesonide (George 2012; NAEPP 2005).The Powell 2011 trial, which revealed benefits of a FENO-based algorithm to adjust asthma therapy, included only non-smoking pregnant women. As a proportion of pregnant women (including pregnant asthmatic women) continue to smoke during pregnancy, it is important that the effects of this intervention in the smoking pregnant population are assessed.This systematic review is the first Cochrane review to assess the effectiveness of both pharmacological and non-pharmacological interventions for managing asthma during pregnancy.In relation to non-pharmacological interventions, our findings are consistent with a recently published review of randomised trials of healthcare interventions for improving asthma in pregnant women (Zairina 2014). This review similarly concluded that while non-pharmacological interventions were associated some significant improvements in maternal asthma control and neonatal outcomes, that firm conclusions could not be drawn, due to the limited number of reported studies, the clinical heterogeneity of the interventions, variations in outcome measures and limitations in study designs (Zairina 2014).While a Cochrane review of tailoring asthma interventions based on FENO (in comparison to clinical symptoms) in children and adults did not show clear benefits to recommend the use of FENO for clinical practice (Petsky 2009), the findings of the Powell 2011 trial, provide some promise for the use of a FENO-based algorithm to adjust asthma therapy in pregnant women. In contrast to the findings of the Petsky 2009 review, which showed that FENO did not significantly reduce exacerbations, and may be associated with higher doses of inhaled corticosteroids in children and adolescents, in Powell 2011, exacerbations for pregnant women were reduced with the use of FENO to adjust inhaled corticosteroid dose, and while more women in the FENO group were treated with inhaled corticosteroids, their mean daily dose was in fact lower (though not significant).In Lim 2012 and Powell 2011, women were also provided with education on asthma self-management skills (inhaler technique, knowledge and action plans) and adherence was assessed and optimised. For Lim 2012, asthma education, monitoring, feedback and follow-up were integral components of the monthly intervention, and asthma action plans were recommended by the trial pharmacist, drafted alongside a respiratory physician and signed off by a family physician. Asthma education programs and self-management plans that enable individuals to adjust therapy based on written action plans have been proven to be effective in improving health outcomes in the general asthmatic population in randomised trials and systematic reviews (Gibson 2002); observational studies have also suggested benefits of asthma education and self-management skill development for pregnant women (Murphy 2005a). Previous studies have supported the utility of pharmacist-led or community pharmacy-based programs in asthmatic patients (Basheti 2007; Mehuys 2008), as was shown to be of potential benefit for pregnant women in Lim 2012; this topic will be the focus of an upcoming Cochrane review of pharmacy programs for all patients (Ryan 2013).The use of relaxation therapies in the general asthmatic populations was the focus of a systematic review by Huntley 2002. In this review, five of the 15 included trials assessed PMR (as was the focus of the Nickel 2006 trial included in this review), and the authors concluded that while there is currently a lack of evidence for the efficacy of relaxation therapies in asthma management, largely due to the poor methodology of the studies, and inherent problems of conducting such trials, there is some evidence that muscular relaxation can improve lung function of patients with asthma (Huntley 2002); similar to the findings of the Nickel 2006 trial.While many reviews in non-pregnant populations have strongly supported the use of inhaled corticosteroids such as inhaled beclomethasone (Adams 2005) and budesonide (Adams 1999), the benefits and potential harms for pregnant women have been less certain. Our review findings are in line with those of a recent, comprehensive systematic review of the safety of regular preventative asthma medications during pregnancy (Lim 2011b). This review similarly highlighted the lack of randomised evidence in this area, however concluded that while some negative outcomes of preventative asthma medications have been reported, that no clear, direct association with medication use in most of these cases has been shown. In this review, the use of inhaled corticosteroids was not shown to be associated with any particular adverse event (Lim 2011b).When inhaled corticosteroids have been compared with oral xanthines (such as theophylline) in previous reviews, such as in children, it has been shown that while xanthines are an effective preventative treatment, they may be less effective than inhaled corticosteroids, with a less favourable side-effect profile (Seddon 2006). In this review, while the Dombrowski 2004 trial did not show oral theophylline to be less effective than inhaled beclomethasone, a higher rate of discontinuation due to adverse effects with oral theophylline was seen.In regards to the use of inhaled magnesium sulphate in addition to routine treatment in the management of acute asthma, a recent Cochrane review (Powell 2011) did not show a significant improvement in lung function overall, as was suggested for pregnant women in the Badawy 2012 trial. This review, however acknowledged the considerable between-study heterogeneity, and noted that individual results from three of the included trials showed possible improvements in lung function with inhaled magnesium sulphate in those with severe asthma exacerbations (Powell 2012). The Badawy 2012 trial, however, was judged to be at an unclear risk of bias overall, with a lack of methodological information provided to confidently assess trial quality; thus the results of this trial should be interpreted with caution.

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