Pregnancy and asthma

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Educational aims

- To provide information on the management of asthma during pregnancy
- To emphasize that benefits of asthma medication outweigh the risks
- To highlight the importance of a multidisciplinary approach in the care of a pregnant asthmatic

Key words
asthma, pregnancy, inhaled corticosteroids, β_2-agonists, exacerbation, complications

Abstract

Asthma is the most common chronic condition encountered in pregnancy. Due to lack of evidence on the adverse effects of asthma medication during pregnancy, there is persistent concern regarding use of asthma-related medication throughout the pregnancy, management of exacerbations and asthma management during labour. Several respiratory-related physiological changes are said to occur during pregnancy which could possibly worsen or improve asthma, and asthma as well as its treatment can affect pregnancy outcomes. The aim of this paper is to summarize current literature findings on clinical management issues encountered in this cohort of patients.

Introduction

Asthma is a chronic inflammatory disease of the airways that is characterized by increased airway responsiveness to multiple stimuli. It is considered to be the most common chronic condition encountered in pregnancy.[1] The prevalence of asthma during pregnancy in Europe has been estimated to be between 4% and 8%.[2] Asthma-related morbidity and mortality rates during pregnancy are comparable to those in the general population. Mortality from asthma in the United States is calculated to be 2.1 persons per 100,000 population.[1] No local or European data has been identified in the literature regarding mortality. Many physiological and anatomical changes of pregnancy affect the respiratory system. These changes often affect the presentation and management of the various respiratory illnesses in pregnancy, including asthma,[3] and asthma and its treatment can affect pregnancy outcomes.[4] Pregnancy can have a variable impact on asthma, and there is no general rule to predict in whom it is going to be better, stable or worse.[5] The National Asthma Education and Prevention Program (NAEPP) "Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment—Update 2004" emphasizes that maintaining adequate control of asthma during pregnancy is important for the health and well-being of both the mother and her baby.[6]

Differential Diagnosis

A number of conditions that can mimic symptoms of asthma in pregnant patients include the following:

- **Amniotic fluid embolism[1]**
  Amniotic fluid embolism is a rare event which is precipitated when amniotic fluid is able to breach the physical barrier between the maternal and foetal environments as a result of uterine trauma. It can take a variety of clinical presentations but a classical presenting sign is dyspnoea, which in the acute situation can mimic an acute exacerbation of asthma, particularly in patients who are known to suffer from asthma.[7]
- **Acute congestive heart failure, secondary to peripartum cardiomyopathy[1]**
  Peripartum cardiomyopathy is an uncommon disorder associated with pregnancy in which the heart dilates and weakens, leading to symptoms of

heart failure. This condition may be difficult to diagnose because symptoms of heart failure can mimic those of pregnancy as well as other respiratory conditions such as asthma.[8]

- **Physiologic dyspnoea of pregnancy**[1] Dyspnoea is commonly reported by 70% of healthy pregnant women during their daily living activities, starting from the very first trimester of gestation. Possible explanations could be an increased awareness of the new sensation of the physiological hyperventilation associated with pregnancy or an increased central perception of respiratory discomfort or a combination of these two. This should be a diagnosis of exclusion after pulmonary and cardiac causes for the dyspnoea have been excluded.[9]

Pathophysiology

Asthma control often changes during pregnancy; in approximately one-third of women asthma symptoms worsen, in one-third they improve, and in the remaining one-third they remain unchanged.[10] Pregnancy has a significant effect on the respiratory physiology of a woman. While the respiratory rate and vital capacity does not change in pregnancy, tidal volume, minute ventilation (40%), and minute oxygen uptake (20%) increase, with a resultant decrease in functional residual capacity and residual volume of air as a consequence of the elevated diaphragm. In addition, airway conductance is increased and total pulmonary resistance is reduced, possibly as a result of the influence of progesterone. The consequence of these physiologic changes is a hyperventilatory picture as a normal state of affairs in the later half of pregnancy. This results in the picture of a chronic respiratory alkalosis during pregnancy, with a decreased partial pressure of carbon dioxide (pCO_2), decreased bicarbonate, and increased pH. A normal pCO_2 in a pregnant patient may signal impending respiratory failure. The increased minute ventilation and improved pulmonary function in pregnancy promote more efficient gas exchange from the maternal lungs to the blood. Therefore, changes in respiratory status occur more rapidly in pregnant patients than in non-pregnant patients.[1]

Non-pharmacological management

Non-pregnant asthmatics

Asthmatic patients should be strongly advised to quit smoking and smoking cessation advice given as necessary. Weight loss in overweight patients has many health benefits, and should be supported in people with asthma since, if successful, it may lead to improvements in asthma symptoms. Allergen avoidance and elimination of exposure to trigger factors is of optimal importance. The practitioner must also ensure that the patient is adherent with existing therapies. Inhaler technique should also be checked and explained as necessary. The use of a spacer should be strongly encouraged.

Pregnant asthmatics

Non-pharmacological management is very similar to non-pregnant patients. Pharmacologic as well as cognitive interventions should be offered to pregnant women to assist in smoking cessation, in view of the known risks associated with cigarette smoking.[3] Avoidance of exposure to allergens as well as any situation which could potentially trigger asthma symptoms should be avoided. The importance of a good inhaler technique and spacer use should be emphasized.

Pharmacological management

Non-pregnant asthmatics

Before initiating asthma medication, practitioners should address non-pharmacological measures. A short acting β_2-agonists (SABA) is recommended for symptom relief, on an as needed basis, in the mildest cases of asthma. Inhaled corticosteroids (ICS) are the recommended preventer drug for adults for achieving overall treatment goals. If asthma symptoms remain uncontrolled, add-on therapy to ICS in adults is an inhaled long-acting β_2- agonist (LABA), which should be considered before going above a dose of 400 micrograms beclomethasone or equivalent per day and certainly before going above 800 micrograms. If asthma control remains suboptimal after the addition of LABA, then the dose of ICS should be increased to 800 micrograms/day, if not already on these doses. A leukotriene receptor antagonist should also be considered at any stage after initiation of an ICS. Theophyllines might also be considered at times.[4]

Pregnant asthmatics

There is much concern amongst pregnant asthmatic patients regarding the use of their asthma medications. In fact lack of adherence to therapy is a frequent occurrence, because such patients are worried about medication effects on the foetus.[1] Current available literature shows that the management of asthma remains largely unchanged compared to the non-pregnant state.[3] Differences were found in the prevalence of prescribing of asthma medications during and surrounding pregnancy in Europe from data recorded in seven European population-based databases. Inhaled β_2-agonists and ICS were, however, the most popular therapeutic regimens in all databases.[2]

According to the BTS guidelines, the following drugs should be used as normal during pregnancy: SABA, LABA, ICS, oral and intravenous theophyllines. They also recommend that systemic corticosteroids should also be used as normal when indicated during pregnancy for severe asthma. If leukotriene receptor antagonists are required to achieve adequate control of asthma then they should not be withheld during pregnancy.[4] ICS prevent exacerbations of asthma during pregnancy, and their cessation during pregnancy is a significant risk factor for exacerbations.[10] ICS are the preferred treatment for long-term control medication. Budesonide is the preferred ICS because more data is available on using budesonide in pregnant women than is available on other ICS, and the data is reassuring. However, no data indicates that the other ICS preparations are unsafe during pregnancy. Garne et al also concluded that the use of ICS during the first trimester of pregnancy seems to be safe in relation to the risk for a range of specific major congenital anomalies.[11] It has also been recommended that a low priority should be placed on stepping down treatment (however guided) until after delivery.[10] There is minimal published data on the use of leukotriene receptor antagonists during pregnancy; however, animal safety data submitted to the Food and Drug Administration (FDA) is reassuring.[6] Treatment to control symptoms and hence minimize adverse outcomes from exacerbations using recommended asthma medications is considered of utmost importance.

Acute exacerbations

During pregnancy, exacerbations of asthma which require medical intervention occur in about 20% of women, with approximately 6% of women requiring hospitalization. Severe asthma appears to be the biggest risk factor for exacerbations during pregnancy

Table 1: Adverse perinatal outcomes that have been associated with uncontrolled asthma during pregnancy

Adverse perinatal outcomes
Pre-eclampsia
Pregnancy-induced hypertension
Uterine haemorrhage
Preterm labour
Premature birth
Congenital anomalies
Intra-uterine growth restriction
Low birth weight
Breech presentation
Neonatal hypoglycemia
Neonatal seizures

although some have noted that respiratory viral infections are also a common cause. Pregnant women appear also to be particularly susceptible to the effects of viral respiratory infections, including influenza.[10] This could be explained by the changes in cell-mediated immunity during pregnancy which may lead to exacerbations of asthma.[12] Non-adherence to asthma treatment could also be an important cause. It is safer for pregnant women who have asthma to be treated with asthma medications than to have asthma symptoms and exacerbations. Monitoring and making appropriate adjustments in therapy may be required to maintain lung function and, hence, blood oxygenation that ensures oxygen supply to the fetus.[6] Exacerbations are common in pregnancy, particularly in the second trimester. Exacerbations and poor asthma control during pregnancy may be due to mechanical or hormonal changes, or to cessation or reduction of asthma medications due to concerns by the mother. Exacerbations and poor symptom control are associated with worse outcomes, as described below, for both the baby and the mother.[10]

The British Thoracic Society (BTS) guidelines recommend that during an exacerbation, pregnant mothers should be administered drug therapy as for non-pregnant patients.[4] Acute severe asthma in pregnancy is an emergency situation and should be treated aggressively with nebulized SABA, oxygen and early administration of systemic corticosteroids.[10] Asthma exacerbation during pregnancy is not associated with adverse pregnancy outcomes while managed appropriately with systemic corticosteroids.[13] Magnesium sulphate can also be administered if necessary. Delivery of high flow oxygen immediately to maintain oxygen saturations of 94 to 98% is recommended together with continuous foetal monitoring,[4] so as to avoid foetal hypoxia. Respiratory infections should be monitored and managed appropriately during pregnancy.[10] Infectious respiratory illness, including pneumonia and tuberculosis, are similarly managed in pregnancy with antibiotics, although special attention may be needed for antibiotic choices with more pregnancy safety data.[3]

When mechanical ventilation is necessary, consideration should be given to the maternal haemodynamics of pregnancy and foetal oxygenation. Maintaining maternal oxygen saturation above 95% is recommended to sustain optimal foetal oxygenation.[3]

It is also recommended that there should be close liaison between the respiratory physician and obstetrician, with early referral to critical care physicians for women with acute severe asthma.[4] Prevention of exacerbations is essential to reduce the risk of complications and poor outcome.[14]

Management during labour

During labour and delivery, usual controller medications should be taken, with a SABA, such as salbutamol, if needed.[10] Acute exacerbations during labour and delivery are uncommon,[4] but bronchoconstriction may be induced by hyperventilation during labour, and should be managed with SABA. Neonatal hypoglycemia may be seen, especially in preterm babies, when high doses of beta$_2$-agonists have been given within the last 48 hours prior to delivery. If high doses of SABA have been given during labour and delivery, blood glucose levels should be monitored in the baby (especially if preterm) for the first 24 hours.[10]

If anaesthesia is required, regional blockade is preferable to general anaesthesia. In the absence of an acute severe asthma attack, caesarean section should be reserved for the usual obstetric indications. Prostaglandin F2α should be used with caution because of the risk of inducing bronchoconstriction.[4]

Women receiving steroid tablets at a dose exceeding prednisolone 7.5 mg per day for more than 2 weeks prior to delivery should receive parenteral hydrocortisone 100 mg 6–8 hourly during labour.[4]

Monitoring

Pregnancy profoundly affects asthma-related health care use.[13] It is recommended that pregnant asthmatics should be monitored closely, particularly those patients with moderate or severe asthma to keep their asthma well controlled.[4] Monthly evaluations of asthma history and pulmonary function (spirometry is preferred, but measurement with a peak flow meter is generally sufficient) are recommended.[6] Regular evaluation will allow the opportunity to step-up treatment as necessary.

Outcomes and complications

Although women with mild asthma are unlikely to have problems, patients with severe asthma are at greater risk of deterioration. The deterioration risk is highest in the last portion of a pregnancy. In fact, severe and/or poorly controlled asthma has been associated with numerous adverse perinatal outcomes as per Table 1.[1,5,6,14,15]

This risk of giving birth to a small or preterm infant appears to be small and may be minimized by good control of asthma. Studies have indicated that low-birth-weight infants are more common in women with daily symptoms or low expiratory flow than in women without asthma.[1]

Table 2: Adverse maternal outcomes have been associated with uncontrolled asthma during pregnancy

Adverse outcomes in pregnant asthmatics
Respiratory failure +/- mechanical ventilation
Barotrauma
Complications of systemic corticosteroid use
Mortality

Table 3: Recommended interventions by health care professionals to pregnant asthmatics
Dispel any fears/misconceptions about use of asthma medication
Emphasize the importance of adherence to therapy
Highlight the risk of non-adherence to therapy for mother and foetus
Arrange regular follow-ups to identify symptoms of uncontrolled asthma
Monitor inhaler technique
Emphasize the importance of using a spacer
Advise smoking cessation as necessary
Offer smoking cessation techniques as necessary
Provide the patient with an asthma self-management plan

Asthma can also lead to complications in pregnant women as per table 2.[1]

According to Blais *et al*, only severe asthma exacerbations were found to significantly increase the risk of congenital malformations in this representative study.[16] However, it is uncertain whether this risk is associated with the exacerbation itself or the treatment given.[2] Being able to identify complications associated with asthma during pregnancy is of great importance in providing appropriate asthma management and medical care to these pregnant women, which may have lifelong consequences for their offspring.[15] Hence the importance of advising adherence with asthma medications, with the aim of achieving the best asthma control possible.

Breastfeeding

Asthmatic women should be encouraged to breastfeed. Asthma medications should be taken as normal during lactation.[4]

General advice

- Women should be advised about the importance of maintaining good control of their asthma during pregnancy to avoid problems for both mother and baby.
- Pregnant asthmatics should be advised that poorly controlled asthma, and exacerbations, provide a much greater risk to their baby than do asthma medication.
- Smokers should be advised about the dangers for themselves and their babies and should be given appropriate smoking cessation advice.
- Table 3 highlights a list of recommended interventions by health care professionals to pregnant asthmatics.

Conclusion

The management of asthma during pregnancy remains mainly unchanged compared to a non-pregnant patient. The advantages of achieving asthma control and avoiding exacerbations appear to outweigh the potential risks related to asthma medication. Stepping down of treatment during pregnancy should be reserved for the post-partum period. In case of an exacerbation, this should be treated aggressively.

Key points

- The management of asthma during pregnancy remains largely unchanged compared to a non-pregnant patient
- For both the mother and baby, the advantages of achieving asthma control and avoiding exacerbations appear to outweigh the potential risks related to asthma medication
- Stepping down of treatment should be reserved for the post-partum period.
- In the case of an asthma exacerbation during pregnancy, this should be treated aggressively
- Pregnant women should be advised that an acute asthma attack is rare in labour but if this occurs, they should continue their usual asthma medications throughout labour

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