Management of Asthma: Facing the Challenges in Special situations (Pregnancy, Surgery)

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1. ASTHMA IN PREGNANCY

DURING pregnancy about one third of asthma patients experience an improvement in their asthma, one third experience a worsening of symptoms and one third remain the same[1]

In a large cohort study the most severe symptoms were experienced by patients between the 24th and 36th week of pregnancy thereafter symptoms decreased significantly in the last four weeks and 90% had no asthma symptoms during labour or delivery. Of those who did, only two patients required anything more than inhaled bouchochilators[2]

Uncontrolled asthma is associated with many maternal and fetal complications including hyperemesis, hypertension, pre-eclampsia, vaginal haemorrhage, complicated labour, intrauterine growth restriction, preterm birth increase perinatal mortality and neonatal hypoxia [3,4]

A large Swedish population-based study using record linkage data demonstrated increased risks for preterm birth, low birth weight, prenatal mortality and pre-eclampsia in women with asthma. The risks for prematurity and low birth weight were higher in women with more severe asthma necessitating admission [5]. In contrast, if asthma is well controlled throughout pregnancy there is little or no increased risk of adverse maternal or fetal complications [6,7] Pregnancy should therefore be an indication to optimise therapy and maximise lung function in order to reduce the risk of acute exacerbation.

Management of Acute Asthma in pregnancy

Oxygen should be delivered to maintain saturation above 92% in order to prevent maternal and fetal hypoxia. Drug should be given as for a non-pregnant patient with acute asthma including repeated doses of inhaled $ß_2$ agonists and early administration of steroid tablets [3,6,7,8,9]. In severe cases intravenous aminophylline or intravenous $ß_2$ agonists can be used as indicated. Continuous fetal monitoring should be performed when asthma is uncontrolled or severe or when fetal assessment is not reassuring. For women with poorly controlled asthma during pregnancy there should be close liaison between the respiratory physician and Obstetrician.

Drug therapy in pregnancy

In general, the medicine used to treat asthma are safe in pregnancy[10]. The risk of harm to the fetus from severe or chronically under-treated asthma outweighs any small risk from the medications used to control asthma.

$ß_2$ Agonists

No significant association has been demonstrated between major congenital malformations or adverse perinatal outcome and exposure to $ß_2$ agonists [10,11].

A prospective study of 259 pregnant patients with asthma who were using bronchodilators compared with 101 pregnant patients with asthma who were not and 295 control subjects found no differences in perinatal mortality, congenital abnormalities, prematurity mean birth weight, apgar scores or labour/delivery complications[12]. Evidence from prescription event monitoring suggests that salmetorol is also safe in pregnancy [13]

Inhaled Steroid

No significant association has been

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demonstrated between major congenital malformation or adverse perinatal outcome and exposure to inhaled steroids [12,13,14]. Inhaled anti-inflammatory treatment has been shown to decrease the risk of an acute attack of asthma in pregnancy[8] and the risk of readmission following exacerbation[7]

Theophyllines

No significant association has been demonstrated between major congenital malformation or adverse perinatal outcome and exposure to methylxanthines [10,15]. For women requiring therapeutic levels of theophylline to maintain asthma control (oral and intravenous) measurement of theophylline levels is recommended. Since protein binding decreases in pregnancy, resulting in increased free drug levels, a lower therapeutic range is probably appropriate [16].

Steroid tablets

The balance of evidence suggests that steroid tablets are not teratogenic [3,10,17]. Date from many studies have failed to demonstrate as association between first trimester exposure to steroid tablets and oral clefts[17]. Although one meta-analysis found an increased risk[18], a prospective study by the same group found no difference in the rate of major birth defects in prednisolone-exposed and control babies[18]. one case control study that may have influenced the finding of the meta-analysis found a significant association between exposure to steroids in the first trimester and an increased risk of cheft lip[19] although this increase is not significant if only paired controls are considered.

Even if the association is real, the benefit to the mother and the fetus of steroids for treating a life-threatening disease justify their use in pregnancy[3] .Pregnant women with acute asthma exacerbation are less likely to be treated with steroid tablets than non-pregnant women[20]. This failure to administer steroid tablets when indicated increases the risk of ongoing exacerabation and therefore the risks to the mother and her fetus

Some studies have found an association between steroid tablets use and pregnancy-induced hypertension or pre-eclampsia and preterm labour[20] but severe asthma may be a confounding variable.

In summary use steroid tablets as normal when indicated during pregnancy for severe asthma. Steroid tablets should never be withheld because of pregnancy.

Leukotriene Receptor antagonists

Data regarding the safety of leukotriene antagonists in pregnancy are extremely limited. Animal studies and post marketing surveillance for zafirlukast and montelukast are reassuring. Animal data raise concern in case of zileuton .[22]

Leucotriene antagonists should not be commenced in pregnancy. They may be continued in women who have demonstrated significant improvement in asthma control with these agents prior to pregnancy not achievable with other medications.

Management during labour

Acute attacks of asthma are very rare in labour due to endogenous steroid production. In women receiving steroid tablets there is a theoretic risk of maternal hypothalamic-pituitary-adrenal axis suppression. Women with asthma may safely use all forms of pain relief in labour.

Data suggest that the risk of postpartum exacerbation of asthma is increased in women having caesarean sections[23]. This may relate to the severity of their asthma rather than to the caesarean section or to factors such as postoperative pain with diaphragmatic splinting, hypoventilation and atelectasis. Prostaglandin E2 may safely be used for labour inductions[16] while prostaglandin F2á (Carboprost/hemobate®) used to treat postpartum haemorrhage due to uterine atony may cause bronchospasm[16]. Although ergometrine may cause bronchospasm particularly in association with general anaesthesia,[16] this is not a problem encountered when syntometrine(syntocinon/ergometrine) is used for postpartum haemorrhage prophylaxis.

Although suppression of the fetal hypothalamic pituitary-adrenal axis is a theoretical possibility with maternal systemic steroid therapy, there is no evidence from clinical practice or the literature to support this [24]

Women are advised to continue their usual asthma medications in labour and informed that asthma exacerbation is rare in labour. Women receiving steroid tablets at a dose exceeding prednisolone 7.5mg per day for more than two weeks prior to delivery should receive parenteral hydrocortisone 100mg 6 - 8 hourly during labour [25].

In the absence of acute severe asthma, caesarean section should be reserved for the usual obstetric indications. If anaesthesia is required regional blockade is preferable to general anaesthesia.

Drug Therapy in Breast Feeding Mothers

The risk of atopic disease in the offspring of women with asthma is increased up to three-fold. This risk is reduced by breast-feeding [26,27]. The medicines used to treat asthma, including steroid tablets, have been shown to be safe to use in nursing mothers[28]. Less than 1% of the maternal dose of theophylline is excreted into breast mild [28].

Prednisolone is secreted in breast milk, but concentrations of prednisolone are only 5-25% of those in the serum[29]. The proportion of an oral or intravenous dose of prednisolone recovered in the breast milk is less than 0.1%[29-31]. For maternal doses of at least 20mg once or twice daily the nursing infant is exposed to minimal amounts of steroid with no clinically significant risk [29-31].

2. BRONCHIAL ASTHMA AND SURGERY

Patients with asthma are at increased risk of specific complications during and after surgical operations such as acute bronchospasm triggered by intubation, hypoxemia and possible hypercapnia, impaired effectiveness of cough, atelectasis and respiratory infection due to airway hyper responsiveness (AHR)[32]. Therefore preoperative evaluation of the state of asthma and systemic administration of corticosteroids to maintain pulmonary function at its best are important precautions to reduce the risk during the perioperative period[33]. However, corticosteroid administration increases the likelihood of respiratory infections, wound infection, difficulties in wound healing, complications of adrenal insufficiency, therefore, its dosage preoperatively must be carefully evaluated.

The National Institutes of Health has established the following guideline: "For patients who have received systemic corticosteroids during the past 6 months, give 100mg hydrocortisone every 8 hours intravenously during the surgical period and reduce the dose rapidly within 24 hours following surgery"[33] Corticosteroids treatment reduces AHR and prevents perioperative attacks of asthma by suppressing the production of inflammatory cytokines (IL-5 and TNF-á)[34]

If anaesthesia is required, regional blockade is preferable to general anaesthesia especially in patients with severe asthma. The choice of epidural anaesthesia for patients with bronchial asthma is controversial. Epidural anaesthesia produced by 1% or 2% lidocaine or mepivacaine without epinephrine did not induce asthmatic attack in any of the patients in a series[35]. After the epidural block, general anaesthesia was induced with midazolam and vecuronium. Operative procedures can also be performed under general anaesthesia (GA) using nitrous oxide-oxygen-seroflurane anaesthesia [35,36].

Some Basic Principles of Treatment of Acute Asthma in Adult

These should be followed in acute exacerbation of asthma in pregnancy, labour and in perioperative periods.

1. Correction of hypoxaemia: this should be corrected urgently using high concentration of inspired oxygen (usually 40-60%). The oxygen saturations (Sao_2) should be at least 92%.
2. Bronchodilate your patients: $ß_2$ agonists are used as first line agents in acute asthma and nebulised route (oxygen-driven) is recommended. Repeated doses of $ß_2$ agonists should be given at 15-30 minutes intervals or continuous nebulization of salbutamol at 5-10mg/hr. In acute asthma, the use of IV aninophylline is not likely to result in any additional bronchodilation compared with standard care using inhaled bronchodilators and steroids. IV aminophylline should only be used after consultation with a pulmonologist.

Some individual patients with near fatal asthma or life threatening asthma with a poor response to initial therapy may gain additional benefit from IV aminophylline (5mg/kg loading dose over 20 minutes, then infusion of 0.5-0.7mg/kg/hr)

3. Give anti-inflammatory agent: Steroid tablets reduce mortality, relapses, subsequent hospital admissions and requirement of $ß_2$ agonist therapy. The earlier they are given in acute attacks the better the outcome. Doses of predinisolone at 40-50mg daily or parenteral hydrocortisone 100mg six hourly are as effective as higher doses. Continue prednisolone 40-50mg daily for at least five days or until recovery

Referral to Intensive Care Unit (ICU)

Indications for admission into intensive care facilities include patients requiring ventilatory support and those with severe or life threatening asthma who are failing to respond to therapy, as evidenced by

- Persisting or worsening hypoxia
- Hypercapnea
- Arterial blood gas analysis showing fall in PH or rising H^+ concentration
- Exhaustion, feeble respiration
- Drowsiness, confusion
- Coma

In conclusion, management of asthma in special situations of pregnancy can be very challenging. However mortality can be reduced significantly through effective and intensive monitoring, as well as judicious use of drugs.

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