

Asthma in Pregnancy

Background

1. General information

- Prevalence
 - 4-8% of pregnancies
 - Most common medical condition in pregnancy
- Increased morbidity
 - Mild or well-controlled moderate asthma can have excellent outcomes
 - Moderate/severe or poorly-controlled asthma - assoc w/signif increased risk of:
 - Preterm delivery
 - Cesarean delivery
 - Pre-eclampsia
 - Growth restriction
 - Gestational diabetes

Pathophysiology

1. Changes in pulmonary physiology during pregnancy

- Progesterone induces an increase in minute ventilation, leading to a compensated respiratory alkalosis
- Normal pregnancy arterial blood gas: higher pO₂ (100-106mmHg), lower pCO₂ (28-30 mmHg)
- Diaphragm raised 4cm by enlarging uterus
- FRC reduced
- No change in FVC, PF, FEV₁

2. Effects of pregnancy on asthma:

- 1/3 of patients get worse
- 1/3 improve
- 1/3 no change
- Exacerbation rate: 12-50% of pts
- Exacerbations most common in weeks 17-24
- Hospitalization rate: 2-27% of pts
- Course of symptoms during pregnancy
 - Asthma usually less severe in last 4 weeks of pregnancy
 - In pts with improvement, it was gradual
 - In pts with worsening, got worse between weeks 29-36
 - Significant symptoms rare during labor & delivery
 - Course of asthma in successive pregnancies were similar

3. Effects of asthma on pregnancy

- Very inconsistent data regarding specific maternal and perinatal outcomes
- Strong data show that excellent symptom control minimizes poor outcomes
- Strongest prospective studies suggest:
 - Well-controlled mild or moderate asthma can have excellent outcomes
 - Possible increase in preterm delivery with severe asthma and/or oral steroids
 - Possible increase in preeclampsia, cesarean delivery, gestational diabetes, and SGA with moderate / severe asthma

Diagnostics

1. See Asthma Diagnostics (Adult)

Differential Diagnosis

1. Key DDx
2. Special considerations
 - New onset asthma is unusual during pregnancy
 - Physiologic dyspnea of pregnancy – shortness of breath at rest or with mild exertion

Therapeutics

1. General principles
 - Safer to treat with meds than leave untreated and experience uncontrolled symptoms and exacerbations
 - Strongly supported by literature
 - Stepwise approach – use the least amount of drug necessary to control symptoms
 - Goals - maintain adequate fetal oxygenation by preventing maternal hypoxia
 - Inhaled corticosteroids are preferred treatment for all levels of persistent asthma in pregnancy
2. **Acute exacerbation management**
 - Goal during exacerbation – PF or FEV1 >70% of predicted
 - Oxygen
 - IV fluids
 - Minimum rate 100mL/hr
 - Rest seated, rather than supine
 - Continuous fetal monitoring
 - Beta2-agonists
 - Home management
 - Albuterol MDI 4-8 puffs every 20 min up to 4 hours
 - Seek medical attention if this does not improve symptoms
 - Hospital management
 - Albuterol nebulizer w/ oxygen (2.5-5mg q20min x 3 doses, then 2.5-10mg q1-4hrs prn, or 10-15mg/h continuously)
 - Corticosteroids
 - Oral burst indicated if beta2 agonists insufficient
 - Prednisone/ Methylprednisolone/ Prednisolone - same doses
 - Outpatient "burst":
 - 40-60 mg in single or 2 divided doses x3-10 days, with or without taper x7-10 days
 - Inpatient:
 - IV/PO 120-180 mg/day in 3-4 divided doses x 48 hrs; then 60-80 mg/day until PF reaches 70% of predicted or personal best
 - Anticholinergics
 - Incomplete data
 - Ipratropium felt to be safe
 - Should only be used as adjunctive therapy in nebulizer with beta2-agonists
 - Ipratropium dose: 0.5 mg q30min x3 doses then q2-4 hrs prn

- Terbutaline
 - Use if nebulizer not effective due to insufficient air movement
 - Concentration: 1 mg/mL
 - Dose: 0.25 mg q15-20 min x 3doses SQ
- Magnesium sulfate
 - Bronchodilator
 - Consider as adjunctive treatment with inhaled beta2-agonists and IV corticosteroids, esp. in pts with HTN or preterm contractions
- Epinephrine
 - Use only for anaphylaxis
 - Theoretical concern for vasoconstriction in uteroplacental circulation
 - Concentration:
 - 1:1000 (1 mg/mL)
 - Dose:
 - 0.3-0.5 mg q20 min x3 doses SQ
- Aminophylline
 - Not recommended
 - In combination with inhaled beta2-agonists, may cause increased side effects

3. Maintenance strategy

- Goal: PF or FEV1 >80% of predicted
- **Step 1: Mild Intermittent Asthma**
 - Albuterol inhaler
- **Step 2: Mild Persistent Asthma**
 - Recommended:
 - Daily low-dose inhaled corticosteroid
 - Alternatives:
 - Cromolyn, leukotriene modifiers, theophylline
- **Step 3: Moderate Persistent Asthma**
 - Option 1:
 - Low-dose inhaled corticosteroid + long-acting inhaled beta2-agonist, OR
 - Option 2:
 - Increasing dose of inhaled corticosteroid to medium dose range
- **Step 4: Severe Persistent Asthma**
 - Increase inhaled corticosteroids to high-dose range
 - Budesonide preferred
 - Consider oral steroids

4. Maintenance medications

- Inhaled corticosteroids
 - Preferred management for all levels of asthma in pregnancy
 - May decrease rate of exacerbations
 - No evidence suggesting increased rate of adverse perinatal outcomes or congenital malformations
 - Budesonide is preferred (class B; best data); all others are class C
 - If pt already stable on med other than budesonide, reasonable to continue on that med
- Oral corticosteroids
 - Extensive research, but conflicting evidence

- First trimester use may increase risk for cleft lip/palate
- May be associated with increased risk of preeclampsia, preterm delivery, low birth weight
- Benefits of controlling severe asthma still outweigh potential risks
- Maintenance dose for severe asthma: 7.5-60 mg qAM or qod
- Dose for exacerbations (see Acute management above)
- Inhaled beta-agonists
 - Recommended for all levels of asthma in pregnancy
 - Albuterol is preferred: considered safe; excellent data; no correlation with adverse outcomes
 - Short-acting: albuterol (see Acute management above)
 - Long-acting
 - Salmeterol preferred due to longer duration of use in US
 - Salmeterol: MDI 2puffs q12 hrs; DPI 1 blister q12 hrs
 - Formoterol: DPI 1 capsule q12 hrs
- Combined medication
 - Fluticasone/Salmeterol (Advair): DPI 100, 250, or 500 mcg/50 mcg
 - 1 inhalation bid, depending on asthma severity
- Cromolyn
 - Alternative treatment for mild persistent asthma
 - Excellent safety profile; virtually no significant side effects
 - May be less effective than inhaled corticosteroids
 - MDI: 2-4 puffs tid-qid
 - Nebulizer: 1 ampule tid-qid
- Theophylline
 - Alternative treatment for mild persistent asthma
 - Adjunctive treatment for moderate/severe asthma
 - Chronic therapy only, not acute
 - Monitor drug levels for toxicity
 - Safe serum concentration range 5-12 mcg/mL
 - Long duration of action 10-12 hrs
 - Useful for nocturnal Sx
 - Frequent side effects:
 - Jitteriness in mothers/neonates, tachycardia, palpitations, vomiting, insomnia, heartburn
 - Drug interactions:
 - May potentiate inhaled corticosteroids
 - Frequent interactions with other drugs can raise theophylline levels and cause toxicity
 - Dose: 10 mg/kg/day up to 300 mg max, usual max 800 mg/day
- Leukotriene modifiers
 - Alternative treatment for mild persistent asthma
 - Adjunctive treatment for moderate/severe asthma
 - Minimal safety/efficacy data during pregnancy (class B)
 - Montelukast (Singulair): 10 mg po qhs
 - Zafirlukast (Accolate): 20 mg po bid

5. Allergic rhinitis treatment

- Intranasal corticosteroids preferred
- Decongestants

- Oral decongestant use in first trimester associated with gastroschisis
- Inhaled decongestants (oxymetazoline, nasal corticosteroids) are preferred
- Antihistamines – loratadine (Claritin) and cetirizine (Zyrtec) are recommended

6. Immunotherapy

- Considered safe during pregnancy; should be continued in patients already receiving it with good results
- Avoid initiating during pregnancy due to risk of anaphylaxis

7. Labor and delivery

- Postpone elective delivery if patient having exacerbation
- Oxytocin is drug of choice for induction of labor, post-partum hemorrhage
- Prostaglandins
 - E1/E2 (cervidil / cytotec / misoprostol) – no reported bronchospasm, can be used
 - F2-alpha – can cause bronchoconstriction, should not be used
- Carboprost (Hemabate) – may cause bronchospasm
- Methylergonovine (methergine) – may cause bronchospasm
- Ergot derivatives – may cause bronchospasm; avoid use
- Indomethacin – may cause bronchospasm in aspirin-sensitive patient
- Magnesium sulfate – bronchodilator (see Acute management above)
- Calcium-channel blockers – no reported effects of bronchospasm
- Corticosteroids
 - If systemic corticosteroids have been used in previous 4 weeks, give IV corticosteroids to prevent adrenal crisis
 - Hydrocortisone 100 mg q8h during labor and 24hr post-partum
- Anesthesia
 - Regional anesthesia reduces maternal oxygen consumption and minute ventilation
 - 2% incidence of bronchospasm with regional anesthesia
 - Meperidine, morphine – cause histamine release, but rarely associated with bronchospasm
 - Fentanyl – may be preferred to meperidine
 - General anesthesia:
 - Ketamine preferred, can prevent bronchospasm

8. Breastfeeding

- Only small amounts of asthma medications enter breast milk
- No contraindications for
 - Prednisone, beta2 agonists, antihistamines, beclomethasone, cromolyn, theophylline
- Theophylline may cause toxic neonatal effects, including jitteriness, vomiting, feeding difficulties, arrhythmias

Follow-Up

1. Monitoring

- Frequency of visits
 - Perform spirometry at initial prenatal assessment
 - Monthly asthma evaluations are recommended in addition to regular prenatal visits

- Assess spirometry/peak flow as well as symptom control, exacerbations, hospital/ER visits, medications
 - Pulmonary function testing
 - Spirometry (FEV1) – preferred if available
 - Peak flow testing easier, more economical
 - Consider daily or twice daily peak flow monitoring in moderate/severe asthma
 - Fetal monitoring – consider in moderate/severe asthma
 - Establish dates with first-trimester ultrasound if possible
 - Consider serial ultrasounds starting at 32 weeks to monitor fetal well-being, growth in suboptimally-controlled moderate/severe asthmatics
 - Consider ultrasound after severe exacerbation
 - Continue trigger avoidance, patient education
2. Referral to specialist
- Inadequate control
 - Concomitant allergies
 - PFTs
 - Severe disease
3. Hospital admission criteria
- Maternal
 - See Asthma (Adult)
 - Fetal distress

Prognosis

1. Use the least amount of drug necessary to control symptoms
2. See pathophysiology

Prevention

1. See Primary Care Therapeutics

References

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