South Australian Perinatal Practice Guidelines

Cystic Fibrosis in Pregnancy

Cystic fibrosis (CF)

- Found primarily in Caucasian populations, CF is inherited as an autosomal recessive trait, caused by cystic fibrosis gene defect leading to dysfunction of the cystic fibrosis transmembrane conductance regulator (CFTR) protein (Gillet et al. 2002)
- Approximately 1 in 25 people are carriers of the CF gene. Carriers of the CF gene do not have any symptoms of the condition
- There are currently 300 people with CF in South Australia, with approximately 7 newborn babies diagnosed with CF each year
- Mean survival of women with cystic fibrosis now into their thirties due to better disease management and treatment advances
- As CF is a recessive disorder, a child must inherit a defective gene from each parent. Each time 2 carriers conceive, there is a 25 % chance that the newborn will have CF, a 50 % chance that the newborn will be a carrier, and a 25 % chance of the newborn being a non-carrier

Introduction

- Progressive chronic bronchopulmonary disease is the major cause of morbidity and mortality in Cystic fibrosis (CF)
- Major manifestations of cystic fibrosis include:
  - Chronic obstructive pulmonary disease
  - Pancreatic enzyme deficiency
  - CF related diabetes
  - CF related liver disease
  - Small intestinal obstruction (Gillet et al. 2002)
  - Sinus disease
- Women with cystic fibrosis may also have:
  - Decreased fertility
  - Decreased body mass index
  - Unfavourable cervical mucus
- Pre-pregnancy body weight and spirometry (especially forced expiratory volume in 1 second [FEV_1] are useful predictors of maternal and neonatal outcomes (Jankelson et al. 1998)
- Recurrent severe infection is a poor prognostic factor due to increased maternal mortality
- Women with mild disease (FEV_1 > 80 % predicted) have been reported to tolerate pregnancy well, whilst those with advanced pulmonary disease (FEV_1 < 60 % predicted) may have poorer outcomes with potential deterioration in spirometry, and possible preterm infants (Jankelson et al. 1998; Edenborough et al.2008)
- Women with CF with pancreatic sufficiency generally maintain better spirometry and nutritional status than women with CF with pancreatic insufficiency

Pre-pregnancy counselling

- Usually carried out by the CF Consultant and CF Multidisciplinary Team at the Royal Adelaide Hospital. Fertility clinics (Repromed and SA Fertility) and the South

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Australian Clinical Genetics Service at the Women's and Children's Hospital can also be involved in the counselling process

- It is advisable for partners to be tested for carrier status and the risk of affected offspring calculated before pregnancy
  - If the partner is not a carrier then the risk of the offspring having CF is low (less than 0.5 %)
  - If the partner is a carrier, then the risk of the offspring having CF is 50 %. In this situation referral to the South Australian Clinical Genetics Service for counselling regarding reproductive options should be offered

Reproductive options if the partner is a carrier include:

- An acceptance of the 50 % risk to offspring, with testing of the baby for CF after birth to allow treatment if affected
- Prenatal testing by CVS at 11 weeks of pregnancy with the option of termination of pregnancy if the fetus is shown to be affected
- Preimplantation Genetic Diagnosis, in which embryos conceived by IVF are tested and only those shown to be unaffected by CF chosen for transfer to try to establish a pregnancy
- Utilisation of a sperm or oocyte donor who is not a carrier for CF to reduce the risk of an affected child
- Choosing not to have biological children

- Women with CF will be reviewed and monitored regularly by all members of the CF Multidisciplinary Team before and during pregnancy to optimise all aspects of health management. This may include assessments from the ;
  - Dietitian
  - Physiotherapist
  - Social Worker
  - Clinical Psychologist
  - Clinical Nurse
  - Consultant
  - Gastroenterologist
  - Endocrinologist
- Maternal mortality is not significantly greater than that of age-matched, non-pregnant women with CF

Counselling:

- Explain the need to continue treatments, including treatment for infective exacerbations. Attending required outpatient clinic appointments should also be emphasised. The Royal Adelaide Hospital and Women's and Children's Hospital pharmacies have collaborated on drug information for women with Cystic Fibrosis in pregnancy

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- Discuss with the woman and her partner:
  - The likely effect of pregnancy on the clinical course of CF (depending on the stage in her disease progression)
  - Impact of CF and it's treatment on pregnancy outcomes (related to potential deterioration in spirometry during pregnancy), including risk of hospitalisation and preterm birth secondary to decline in respiratory function
  - Issues around the burden of child rearing for someone with respiratory disease and the implication of premature death
- Women with severe pulmonary disease (FEV_1 < 60 %) should be advised about the risks of pregnancy and coping with their disease post delivery
- In the absence of reversible causes, delivery is the preferred treatment for respiratory failure

Factors associated with an increased maternal risk include:

- Pulmonary hypertension
- Cyanosis
- Arterial hypoxemia (O_2 saturation < 90 %)
- Moderate to severe lung disease (FEV_1 < 60 % predicted)
- Pre pregnancy evidence of poor nutritional status

Risks to the fetus

- Preterm birth
- Intrauterine growth restriction (uteroplacental insufficiency)
- Cystic fibrosis

Antenatal care

- Referral to a tertiary centre with Level VI facilities. Collaboration between this centre and the CF Team is vital
- Joint initial assessment by a respiratory physician and an obstetrician experienced in dealing with problems of CF in pregnancy
- If prenatal diagnosis of fetal CF is requested, consider chorionic villus sampling for early diagnosis and where requested, termination of an affected fetus

Particular attention to:

Dietary management

- Assessed by the CF Dietitian
- Maintenance of adequate nutrition – many women have pancreatic insufficiency and require enzyme supplements and a high caloric intake
- Screen for Vitamin D deficiency and treat as required
- Measure Vitamin A and E levels and supplement as required

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Diabetes

- Management of CF related diabetes – occurs in 20-30 % adults with CF and 15 % have impaired glucose tolerance
- Oral Glucose Tolerance Test (OGTT) is recommended at booking visit and repeated at, 20 to 24 weeks and at 30 to 34 weeks

Iron deficiency anaemia (IDA)

- IDA is common in CF and oral supplementation is often indicated. Screen for anaemia at booking visit and again at 28 weeks
- Encourage the woman to:
  - Increase her dietary intake of iron
  - Optimise absorption of iron by increasing intake of vitamin C and reducing foods that reduce bioavailability e.g. tannins (for further information, refer to the PPG 'anaemia in pregnancy)

Respiratory management assessed by the CF physiotherapist

- Baseline pulmonary function tests, such as FVC, FEV_1, lung volumes, pulse oximetry, and arterial blood gases as indicated. These values should not change appreciably in the early stage of pregnancy
- Serial monitoring of values during gestation and address deterioration in pulmonary function
- Early and adequate treatment of respiratory tract infections
- Regular fetal growth monitoring (measure fundal height and serial ultrasound evaluations of fetal growth and amniotic fluid volume)
- Anaesthetic referral and antenatal review

Anaesthetic review

- Arrange early anaesthetic review to assess
  - SpO2
  - Lung function
  - Weight
  - Diabetes
  - If pulmonary hypertension is present

Other concerns include the presence of:

  - Severe respiratory disease and infection
  - Gastro-oesophageal reflux

- In advanced lung disease the requirement for assisted ventilation should be considered
- Adequate early analgesia in labour and flexible post-partum analgesia to permit physiotherapy and early mobilisation is advantageous

Intrapartum care

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- Management in consultation with obstetric physician
- Aim for vaginal birth and reserve Caesarean section for obstetric indications
- Epidural is preferred over general anaesthesia should operative delivery be necessary
- Consider continuous external fetal monitoring as indicated
- Continuous monitoring of maternal oxygen saturation using pulse oximetry and administer O_2 therapy as required. Non-invasive ventilation (NIV) may also be considered
- Consider assisted birth if prolonged 2nd stage (predisposition to pneumothoraces)

Postpartum care

- Recommend extra help and support with care of baby to prevent deterioration in maternal health
- Encourage breastfeeding as long as adequate nutrition can be maintained to meet the increased energy demands
- The commonly indicated CF drugs are safe in breastfeeding with the exception of cotrimoxazole, which should not be used in the first week after birth or where the newborn baby is jaundiced because of the risk of kernicterus

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Safety of Cystic Fibrosis Medications in Pregnancy

NOTE: It is important to remember that UNDERTREATMENT may also be hazardous to a pregnant woman and her fetus

Agents which CAN BE USED in Pregnancy

Oral Medication
Calcitriol (Monitor neonates for hypocalcaemia)
Calcium
Cholecalciferol
Ergocalciferol
Pancreatic Enzymes (Creon®, Creon Forte®)
Multivitamins
Sodium Chloride
Ursodeoxycholic acid (limited data)
Vitamin E (high doses need review)
Vitamin K1 (phytomenadione)
Vitamin A. Retinol is safe up to a dose of 8000IU/day. Betacarotene is safe in pregnancy.
VitABDECK® capsules contain retinol 2500IU and betacarotene 3mg.

Inhaled Medication
Beclomethasone
Budesonide or Budesonide/Eformoterol
Colistin **
Dornase Alfa
Fluticasone or Fluticasone/salmeterol
Salbutamol nebuliser & puffer
Salmeterol
Sodium Chloride
Terbutaline
Tobramycin Inhalation **

Antibiotics **
Amoxycillin or Amoxycillin/clavulanate
Azithromycin
Aztreonam
Cephalosporins – cefaclor, ceftazidime, cephalothin or cephalexin
Ciprofloxacin (limited data)
Co-Trimoxazole (**NOTE:** Sulphamethoxazole is CONTRAINDICATED in LATE pregnancy; risk of kernicterus, jaundice and haemolytic anaemia in the neonate)
Dicloxacillin
Flucloxacillin
Meropenem (limited data)
Piperacillin
Ticarcillin & potassium clavulanate (Timentin®)
Tobramycin (Use IV only if inhalation therapy has failed (Inhalation dose 250mg bd. This has minimal systemic absorption)

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Royal Adelaide Hospital Medicines Information Centre
Women's & Children's Hospital Medicines & Drug Information Centre
Dr Mark Morton, Dr Bill Hague, & Dr Erin Clarke, Obstetric Physicians,
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Abbreviations

CF	Cystic fibrosis
CFTR	Cystic fibrosis transmembrane conductance regulator protein
et al.	And others
FEV_1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
CVS	Chorionic villus sampling
IVF	In vitro fertilisation
SA	South Australia
Hb	Haemoglobin
HbA1c	Glycoslated haemoglobin
%	Percent
e.g.	For example
mg	Milligram(s)
g	Gram(s)
RDS	Respiratory distress syndrome
WHO	World Health Organisation
ADIPS	Australasian Diabetes in Pregnancy Society
OGCT	Oral glucose challenge test
OGTT	Oral glucose tolerance test
GDM	Gestational diabetes mellitis
BGL	Blood glucose level
NIV	Non invasive ventilation

Version control and change history

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Version	Date from	Date to	Amendment
1.0	30 April 07	18 Jan 11	Original version
2.0	18 Jan 11	current	

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