

## 2. CONTRACEPTION, PRE-CONCEPTION COUNSELING, AND PREGNANCY

### Principles

- To facilitate effective, safe contraception for individuals with SCD who are aiming to prevent conception.
- To provide appropriate pre-conception hemoglobinopathy screening and genetic counseling for individuals with SCD and their partners.
- To educate women with SCD about the maternal and fetal risks associated with pregnancy, and to optimize timing of pregnancy with disease stability.
- To provide comprehensive, multidisciplinary medical care for women with SCD during pregnancy, labour, and the post-partum period.

### Recommendations

#### Contraception

- For women with SCD who wish to prevent pregnancy, contraception — including barrier methods, intra-uterine device, and progesterone-only hormonal contraception — may be considered. Progesterone-only contraception is effective, and may be associated with reduced sickle pain.

#### Pre-conception Counseling

- Men and women with SCD should be counseled about the genetic inheritance of SCD, and the availability of partner genetic screening and counseling prior to planning conception.
- Women planning or considering pregnancy should receive counseling about the known fetal and maternal risks. Pre-conception medical status should be optimized, including immunization and folic acid supplementation. Hydroxyurea and chelation therapy should be discontinued prior to conception.

#### Pregnancy

- During pregnancy, women should be followed by a multi-disciplinary obstetrical team knowledgeable in the care of SCD, with input from maternal-fetal-medicine, hematology, neonatology, and anesthesia.
- NSAIDs should be avoided in the first and third trimesters, but can be used judiciously between 12 and 28 weeks gestational age.
- Opiate use should be optimized to effectively control pain. Neonates with chronic in utero opioid exposure should be monitored and managed for opioid withdrawal.

#### Labour and Delivery

- Delivery should take place in an expert centre, with availability of fetal and maternal monitoring, and attention to maternal hydration, warmth, and adequate analgesia.

#### Post-partum

- Post-partum VTE prophylaxis should be offered for women with any additional risk factors (e.g., history of prior VTE, Caesarean section, or reduced post-partum mobility).

### Contraception

For women with sickle cell disease (SCD) who wish to prevent pregnancy, contraception — including barrier methods, an intra-uterine device (IUD), and progesterone-only hormonal contraception — may be considered. Progesterone-only contraception is effective, and may be associated with reduced sickle pain.<sup>1-3</sup> There is no clear evidence of harm with combined oral contraception.<sup>4</sup> An IUD is an effective method of long-term contraception. There is no evidence of harm with an IUD, and no theoretical concerns with IUD use.<sup>4</sup> Progesterone-based IUD is being used increasingly in some centres, but has not been investigated in SCD.<sup>5</sup>

## **Elements of Pre-conception Consultation**

### **a) Genetic Counseling**

Patients with SCD who are planning a pregnancy should be aware of the inheritability of SCD. Partners should undergo hemoglobinopathy testing, prior to pregnancy when possible, to determine fetal risk of clinical disease; any positive partner testing must be followed by detailed genetic counseling for the couple as to the potential risk and probability of conceiving an affected fetus. Pre-implantation genetic diagnosis may be considered in relevant circumstances.<sup>6</sup>

### **b) Maternal and Fetal Risk Assessment**

Women with sickle cell disease who are considering pregnancy should receive careful counseling about the maternal and fetal risks associated with pregnancy. Thorough sickle cell and obstetric history should be obtained. Regular medications must be reviewed. A detailed physical examination should be performed, with recording of pre-pregnancy weight and height, as well as splenic size.

Pregnancy is associated with increased incidence of pain episodes, infection, pulmonary complications, venous thromboembolism (VTE), antepartum bleeding, and hospitalization in women with SCD.<sup>7-10,17</sup> Women with SCD are also at an increased risk of pre-eclampsia.<sup>7,10,11</sup> Because of this, pregnancy should be timed during a time of relative disease stability.

Fetal risks include intrauterine growth restriction, fetal anemia due to maternal alloantibodies, premature labour and delivery, and stillbirth.<sup>7-9,11,12</sup> There is an increased rate of cesarean section for pregnant women with SCD.<sup>10</sup> As a result of higher rates of maternal and fetal complications, women with SCD should be followed closely in a high-risk obstetric unit knowledgeable in the care of SCD.

### **c) Hydroxyurea discontinuation**

Discontinuation of hydroxyurea prior to conception is advised, due to evidence of teratogenicity in animals. Although retrospective observational data of women who received hydroxyurea during pregnancy suggests no specific adverse outcomes in fetal life, infancy, or childhood,<sup>13,16</sup> more robust prospective and long-term data are still needed to confidently recommend continuation of hydroxyurea in pregnant SCD patients.

### **d) Chelation Therapy Discontinuation**

Chelation therapy should be discontinued during pregnancy. In cases of critical iron overload, deferoxamine can be used safely in the second and third trimesters, and while breastfeeding.

### **e) Analgesia**

Analgesics should be reviewed. Non-steroidal anti-inflammatory drugs (NSAIDs) are best avoided during the first and third trimesters, as they have been linked with an increased risk of miscarriage in the former and premature closure of the fetal ductus arteriosus in the later. Judicious use of NSAIDs between 12 and 28 weeks of gestation, however, can be a useful adjunct in attaining pain control. Women requiring analgesia for sickle pain should be prescribed opioids in doses sufficient to manage pain. Following delivery, a pediatric consultation should be obtained for infants with *in utero* opioid exposure to observe for and manage neonatal opioid dependency and withdrawal.

### **f) Folic Acid**

Supplementation with folic acid 5 mg daily is recommended prior to conception and throughout pregnancy, in view of the ongoing background hemolysis, which increases the risk of folate deficiency.<sup>14</sup> From the fetal perspective, folic-acid supplementation is particularly essential during the time of neural-tube closure, which corresponds to the first four weeks of gestation.

### **g) Laboratory and Screening Evaluations**

Initial comprehensive laboratory testing must be obtained, and should include complete blood count with reticulocyte count, hemoglobin electrophoresis to determine baseline sickle hemoglobin percentage (HbS%), serum ferritin levels, liver and kidney function, blood group, and antibody screen, red blood cell phenotype (if not obtained in the past), and serology for human immunodeficiency virus (HIV), hepatitis B and hepatitis C.

Screening for end-organ complications should include a retinal exam, echocardiography to rule out pulmonary hypertension and ventricular dysfunction, and pulmonary function testing in patients with respiratory symptoms.

#### **h) Immunizations and Chronic Infection**

Many women with SCD undergo auto-splenectomy, and are therefore at risk of infection with encapsulated organisms. As such, immunizations against haemophilus influenza type B, pneumococcus, and meningococcus should be up to date. Additionally, patients should be immunized against hepatitis B virus. Yearly influenza vaccines should be encouraged.

### **Management in Pregnancy**

#### **a) Principles of Care**

Pregnant women with SCD should be followed closely in a high-risk obstetric unit knowledgeable in the care of SCD. **Any relevant counseling, clinical assessment or testing that was not completed prior to conception should be performed early in pregnancy** (e.g., baseline hemoglobin and hemolytic screen; blood group and screening for RBC alloantibodies; testing for iron overload; assessment of renal and liver function; echocardiography; and retinal exam) (*see section above entitled “Elements of Pre-Conception Consultation”*)

#### **b) Maternal Laboratory Monitoring**

Regular monitoring of hemoglobin levels should be initiated.

Asymptomatic urinary-tract infections (UTIs) are common in pregnancy, and may precipitate sickle cell crisis. A UTI can also evolve into pyelonephritis, which is associated with an increased risk of pre-term labour. Because of this, consideration should be given to collection of monthly mid-stream urine samples for analysis and treatment as appropriate.

#### **c) Fetal Monitoring**

If exposure to teratogenic medication has taken place early in gestation, an early anatomy ultrasound around 15 weeks, and a level II anatomy ultrasound between 18 and 20 weeks gestational age are recommended.

In view of the higher risk of adverse fetal outcomes, a number of which may be placentally mediated, placental assessment in the form of placental biochemistry as well as ultrasound evaluation of the placenta, including uterine artery Doppler, may be considered. In the late second and third trimesters, serial ultrasounds for fetal growth and well being, including assessment of fetal Doppler, amniotic fluid volume, and biophysical profile, are strongly recommended.

#### **d) Role of Red Cell Transfusions**

Routine use of prophylactic red blood cell transfusion in pregnancy is not advised. A randomized controlled trial of prophylactic transfusion versus on-demand transfusion in pregnant women with sickle cell anemia (HbSS) was associated with reduced painful episodes, but there was no significant difference in fetal outcome, at the expense of a four-fold increase in the number of red cell units transfused.<sup>15</sup> Indications for transfusion in pregnancy may include: acute chest syndrome, recurrent pain episodes, symptomatic anemia, or placentally mediated intrauterine growth restriction. Exchange transfusion may be considered in place of simple transfusion. (*For more information of transfusions, see Part I, section 2 on Transfusion*)

### **Labour and Delivery**

Delivery should take place in an expert centre, with availability of relevant maternal and fetal monitoring. Spontaneous labour can be awaited, with an aim for vaginal delivery. Caesarean sections should be reserved for the usual obstetric indications. Maternal hydration should be emphasized, either via the oral or intravenous route, as should maintenance of maternal warmth and comfort, including adequate pain relief and supplemental oxygen, as required.

## Postpartum Care

Following delivery, a pediatric assessment should be available for infants with *in utero* opioid exposure, to observe for and manage neonatal opioid dependency and withdrawal. This can be facilitated through an antenatal Pediatric consultation in the third trimester, or via consultation of the Pediatric service at the time of delivery, depending on local practice.

Post-partum venous thromboembolism (VTE) prophylaxis may be considered for all women with SCD, and should be offered to patients with additional risk factors (e.g., history of VTE, Caesarean section, or reduced post-partum mobility).

Contraception and plans for future pregnancies should be discussed. Resumption of pre-pregnancy medication must be re-evaluated.

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