

SICKLE CELL DISEASE and PREGNANCY

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PLAN

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- Introduction and definition
- Epidemiology and pathophysiology
- Effects of pregnancy on sickle cell disease
- Effects of sickle cell disease on pregnancy
- Management
- Conclusion

OBJECTIVES

- Improve the management of sickle cell patients during pregnancy
- Prevent the mortality and morbidity associated to the pathology

INTRODUCTION (1)

HISTORY

- Description: 1900 James HERRICK, Chicago
- Identification: 1949 Linus Carl PAULING and associates
- 1st prenatal diagnosis: 1978 KAN and DOZY

INTRODUCTION (2)

- Medical teams for many years have discouraged the occurrence of pregnancy in homozygote sickle cell patients.
- With a longer life span and improved quality of life, these patients are becoming more and more pregnant.
- These pregnancies are high risk pregnancies for mother and fetus.

INTRODUCTION (3)

- In fact pregnancy is source of acute decompensation of the sickle cell disorder.
- Sickle cell disease influences the evolution of pregnancy with fetal and maternal consequences.

EPIDEMIOLOGY

		Homozygous HbSS %	Heterozygous HbAS %	Double heterozygous %
USA	Black Americans	3-9	8-16	
	White Americans	1-8	8-10	8-14
EUROPE	UK (Pakistanis - blacks)	3-7	6-15	10-12
	Others Europeans	2-8	3-8	
Caribbeans		1-5	3-8	
Africa		1-10	10-25	<1
Cameroun		2-5	10-15.5	Rare

Table 1: Geographical repartition of sickle cell disease

Pathophysiology

- Sickle cell disease is a hemoglobinopathy, a monosomic gene disorder which transmission is autosomal recessive.
- HbS is formed as the result of a single gene defect causing substitution of Valine for glutamic acid in position 6 of the β chain of adult hemoglobin (HbSS).

Effects of sickle cell disease on pregnancy (1)

Transmission risk: autosomal recessive hemoglobinopathy associated or not to thalassemia (SC/Sb Thal)

Antenatal screening:

- Biopsy of trophoblastic tissues (11th week)
- Amniocentesis (15th week)

Also: - preimplantation diagnosis

- screening of fetal cells in maternal blood

Effects of sickle cell disease on pregnancy (2)

- Infertility
- Increased risk of abortion
- Infectious risk
- Risk of preterm deliveries(1-30%)
- Risk of high blood pressure and pre-eclampsia (1-30%)
- Risk of IUGR (1-25%)
- Risk of stillbirth (1-6%)
- Risk of maternal mortality
- High level of C section

Effects of pregnancy on sickle cell disease (1)

- Cardiac output: well adapted, no alteration
- Ventricular systolic function: no alteration
- Ventricular diastolic function: ventricular filling defects
- Acute pulmonary edema: increased risk during immediate pre and post-partum
- Anemia by dilution associated with normal pregnancy: aggravation of pre-existing anemia

Effects of pregnancy on sickle cell disease (2)

- Supplementary blood transfusion: aggravates iron overload in this patients
- Vaso-occlusive crisis: increased

NB: These situations are favored by physiological modifications during pregnancy, stopping hydroxyurea treatment and the presence of obstetrical complications (pyelonephritis, pre-eclampsia)

Management (1)

MONITORING OF PREGNANCY

- Monthly obstetrical consultations +/- 28-30 weeks of gestation and then every 15 days
- Early diagnosis of vascular disorders
- Monthly biometric measurements with Manning's score and umbilical fetal Doppler
- Global management by obstetrician and hematologist

Management (2)

- Aspirin 100mg/day
- Supplement with folic acid 5mg/day (FOldine® Acfol®)
- Don't give iron (risk of hemochromatosis) except in case of documented iron deficiency
- Monthly urine cultures
- Adequate rest

MANAGEMENT (3)

VASO-OCCLUSIVE CRISIS (1):

- Alert the obstetrician and the anesthetist
- In intensive care unit (potential severity+++) especially thoracic syndrome: 20% mortality
- Reduce pain: Perfalgan®, ketoprofene, if >32 gestational age: morphinic (avoid anti-inflammatory drugs which can cause hemolysis)

MANAGEMENT (4)

VASO OCCLUSIVES CRISIS (2):

- Hydrate: RL, to be adapted with renal function and blood electrolytes. Blood Na can be useful to correct acidosis
- Warm+++ or warming blankets if possible
- Oxygenate: 4 to 6 liters per min
- Bed rest
- In case of failure of the above measures: transfuse slowly 2 pints of blood (phenotyped)

Management (5)

DURING LABOR (1):

- Give peridural analgesia as much as possible: pain is risk factor for vaso-occlusive crisis
- Continuous warming+++
- Give oxygen 4-6 liters/min
- Hydrate as much as possible (sufficient fluid and electrolytes)
- Avoid drugs which can cause hemolysis
- Bone deformation rendering intubation difficult

Management (6)

DURING LABOR (2)

- Systematic antibioprophyllaxis (amoxicillin 2g IV)
- Avoid blood loss as much as possible: GATPA (active management of the 3rd stage of delivery), rapid repair of episiotomies
- Blood transfusion: systematic?
Case by case?

Management (7)

Post partum:

- Increased risk+++
- If possible, follow up at intensive care unit
- Analgesia to be continued
- Antibiotics: 7 to 10 days
- Neonatal screening (6th month) unless the DNA based Dg was done
- Discuss contraception
- Follow up (mother and child) if possible out of hospital

Management (8)

What to do with long term treatments (hydroxyurea, deferoxamin)?

- Deferoxamin is an iron chelator
- Hydroxyurea (Hydrea®) is an antimetabolic drug used in SCD for repeated and invalidating crisis. It inhibits DNA synthesis
- Contra-indicated in case of pregnancy
- Ideally: to be stopped before pregnancy

Management (9)

HIV infection and sickle cell patient:

- HIV screening should be systematically done in these patients because of multiple transfusions
- Remember: In this patients there is total hyperlymphocytosis (due to hypersplenism)
- The indication of ART should depend on lymphocytes count $<15\%$ or \downarrow CD4/CD8 ratio
- Avoid zidovudine (AZT®), Retrovir®)
- HYdroxyurea + Stavudine, didanosine: increasing risk of neurologic toxicity

CONCLUSION

Sickle cell disease is a major complication and an important risk factor for perinatal morbidity and mortality.

Management should be multidisciplinary. It should also have major actions with the offer of genetic counselling and prenatal diagnosis for couples at risk.