



## EISENMENGER SYNDROME

### Background

Eisenmenger syndrome is defined as the development of pulmonary hypertension in response to a left-to-right cardiac shunt with consequent bidirectional or reversal (right-to-left) of shunt flow.

Initially, left-to-right intracardiac shunting is associated with increased flow (and sometimes transmitted pressure) through the pulmonary vasculature. This results in pulmonary vascular remodeling and leads to pulmonary vascular disease. The pulmonary arterial hypertension and associated elevation in right heart pressures result in reversal of the shunt with either right-to-left or bidirectional flow, which is called Eisenmenger syndrome.

Congenital heart defects that can lead to Eisenmenger syndrome include: atrial septal defects, ventricular septal defects, persistent arterial ducts, as well as more complex defects such as atrioventricular septal defects, truncus arteriosus, aortopulmonary window, complex pulmonary atresia, and the univentricular heart.

As a result of the right-to-left shunt, patients are chronically hypoxemic, hence cyanotic. Eisenmenger syndrome is associated with complications in many systems and is considered a multi-system disorder.

Cardiac complications include:

- a) supraventricular arrhythmias
- b) ventricular arrhythmias
- c) congestive heart failure
- d) progressive valvular disease
- e) sudden death

Non-cardiac complications include:

- a) bleeding (pulmonary hemorrhage, gastrointestinal, cerebral)
- b) ischemic complications (thromboembolic events, paradoxical emboli, air embolism)
- c) renal dysfunction
- d) symptoms related to hyperviscosity (headache, dizziness, visual disturbances, altered mentation, tinnitus, fatigue)
- e) iron deficiency (due to inappropriate phlebotomy for secondary erythrocytosis)
- f) pulmonary arterial dilation
- g) infections (endocarditis, cerebral abscess, pneumonia)
- h) gout
- i) hypertrophic pulmonary osteoarthropathy

### Effects of pregnancy-related hemodynamic changes

The hemodynamic changes of pregnancy are usually poorly tolerated in women with Eisenmenger syndrome. (see Cardiovascular Changes During Pregnancy) Most women with Eisenmenger syndrome are in a precariously balanced state and an important principle of care is to not disrupt this balance. In women with Eisenmenger syndrome and a low cardiac output state, the compromised right

ventricle may not meet the demands of increasing blood volume and cardiac output associated with pregnancy. In addition, a fixed pulmonary vascular resistance with a resulting inability to increase pulmonary blood flow may not accommodate an increase in cardiac output. Similarly, large fluctuations in blood volume both pre and post partum may not be tolerated by an already compromised cardiovascular system. The fall in peripheral vascular resistance that occurs during pregnancy can augment right-to-left shunting, worsening maternal hypoxemia and cyanosis (1). During pregnancy, the blood becomes more hypercoagulable and in the cyanotic patient the risk of deep venous thrombosis, pulmonary infarction, and/or paradoxical embolus and stroke increases.

### **Maternal cardiac complications**

Pregnancy is a cause of significant mortality in most published series of women with Eisenmenger syndrome. A systematic review of published studies from 1978-1996 examined maternal mortality rates in women with Eisenmenger syndrome and demonstrated mortality rates of 56% (2). A more recent review suggested that mortality remains high. (3) Most complications occur near term and early (1<sup>st</sup> week) post-partum, and therefore extended post-partum hospital observation is suggested. Mortality is typically from heart failure, sudden death presumably due to arrhythmias, or thromboembolic events.

During pregnancy, it is important to watch for cardiac symptoms including increasing fatigue, worsening peripheral edema, palpitations, chest pain that could reflect right ventricular ischemia, and/or volume overload and presyncope/syncope with exertion reflecting a decrease in cardiac output. However, other complications as described can also occur, particularly thromboembolism.

### **Fetal complications**

Miscarriage is common in cyanotic women. Intrauterine growth restriction is seen in 30% of pregnancies as a result of maternal hypoxemia. Premature labour is found in 50-60% of instances and the high perinatal mortality rate (28%) is due mostly to prematurity. In one study of women with Eisenmenger syndrome, 47% delivered at term, 33% between 32 and 36 weeks, and 20% before 31 weeks of gestation (2).

### **Management strategies**

#### **Preconception counseling/Contraceptive methods**

Based on the high mortality risk both during pregnancy and peripartum, women with Eisenmenger syndrome should be strongly advised against pregnancy (2,3,4). Some women who are fully informed and understand the maternal and fetal risk and complications may still become pregnant, and unfortunately women may present pregnant without having received appropriate preconceptual counseling

In the current era, many women with Eisenmenger syndrome are treated with pulmonary vasodilators. Preconception discussion with a pulmonary hypertension specialist regarding pulmonary vasodilator therapy during pregnancy is important if women are actively trying, against advice, to conceive, as some vasodilators are teratogenic.

A discussion about contraceptive methods is imperative (4). (see Contraception) Progesterone-only formulations as depot injections and subdermal implants (Implanon®) are a reasonable option. Progesterone-only pills are not optimal because of unacceptably low efficacy rates. Contraceptive pills containing estrogen (combined contraceptive pills) are contraindicated due to an increased risk of thromboembolism.

The insertion of intra-uterine contraceptive devices can be associated with vasovagal reactions, which can be devastating in women with pulmonary hypertension. Some women will consider sterilization due to the high-risk nature of a pregnancy. However, such a decision may have a major psychological impact and needs to be fully discussed with the appropriate caregivers. Moreover, the laparoscopic procedure carries risk in this population, as it requires insufflation of the abdomen with carbon dioxide, intermittent head down tilt and positive pressure ventilation, all of which reduce cardiac output and may be poorly tolerated. There is also a risk of air embolism, which may pass through the shunt to the brain (paradoxical embolism) in face of a right to left shunt. If sterilization is chosen, it is strongly recommend that it be performed at a centre with experience in the care of patients with pulmonary hypertension/Eisenmenger syndrome. Essure® is a new sterilization technique, involving the insertion of stents hysteroscopically into the Fallopian tubes using sedation and local anesthesia. Early studies suggest it may be safe and has a low failure rate.

Transmission of congenital heart disease to offspring should be discussed. The risk of the fetus having structural cardiac defects varies between 3% and 50%, compared with the background risk of 1% for the general population. This risk will depend on the underlying cardiac lesion of the mother.

As certain anticoagulants and cardiac medications are contraindicated in pregnancy, medication use should be reviewed if a woman is seriously contemplating pregnancy or is pregnant. The MOTHERISK website is an excellent resource. (<http://www.motherisk.org>)

### **Ante-partum care**

If a woman with Eisenmenger syndrome becomes pregnant, coordinated care should be established early, involving a congenital heart disease specialist, pulmonary hypertension specialist, high-risk obstetrician, and an obstetrical anesthetist. Close cardiovascular monitoring, with specific attention to volume status, is essential throughout pregnancy and the peripartum period. Serial echocardiograms are important to assess the size and function of the right ventricle. Some experts follow serial b-type natriuretic peptide levels.

Management of volume status is imperative. Hypovolemia can lead to increased right to left shunting, reduced cardiac output and refractory hypoxemia. Similarly, volume overload should also be avoided as it cannot be accommodated by the compromised pulmonary vascular bed and/or right ventricle and can result in heart failure and increasing right to left shunt. Very frequent follow-up is necessary during the later stages of pregnancy as cardiac output rises, and as pulmonary vascular disease may progress.

Treatment with pulmonary vasodilator therapy should be discussed with a pulmonary hypertension expert. While no pulmonary vasodilators are considered completely safe during pregnancy, there are case reports/case series in the literature describing the use of pulmonary vasodilators during pregnancy. (5,6,7) However, use of bosentan is not advised in pregnancy owing to the teratogenic effects seen in animal studies (8).

When needed, admission to a hospital equipped with a multidisciplinary team experienced in the management of cardiac disease in pregnancy and pulmonary hypertension is important. Depending on the individual, bed rest may be considered to reduce cardiac demands. Treatment for heart failure may be necessary.

These women are also vulnerable to thromboembolism. Underlying pulmonary thromboembolic disease is common, even in non-pregnant women. Thromboprophylaxis is essential at any time that the woman is relatively immobile. An appropriate anticoagulation plan should be devised with a hematologist/thrombosis expert when required.

Fetal echocardiography can be offered to the expectant mother to screen for congenital heart defects. A fetal echocardiogram is done at approximately 20 weeks gestation.

## **Labour and delivery**

Labour and delivery must be planned carefully with a multidisciplinary team well in advance. The plan should be communicated to the patient and tertiary and local healthcare teams.

Successful vaginal and cesarean deliveries have been reported. The decision regarding mode of delivery should be based on the individual patient and the local obstetrical experience. If vaginal delivery is chosen, good pain management is very important.

Epidural anesthesia should be initiated early and local anaesthetic drugs should be given in small and incremental doses. In general less local anaesthetic and more narcotic is preferred to decrease the likelihood of further decrease in peripheral vascular resistance. During labour Valsalva maneuver should be avoided. To decrease maternal expulsive efforts during the second stage of labour, forceps or vacuum delivery is often utilized. To decrease potential harmful complications from difficult mid-cavity assisted delivery, uterine contractions are often utilized to facilitate the initial descent of the presenting part.

Fall in blood pressure in response to anesthetic can be dangerous for women with Eisenmenger syndrome and therefore blood pressure needs to be monitored closely. Oxytocic drugs such as oxytocin, which induces vasodilation and arterial hypotension, should be avoided if possible.

Immediately post partum hemorrhage (a complication of cyanotic heart disease) should be watched for and aggressively treat

Maternal monitoring will often include telemetry, pulse oximetry, and invasive blood pressure monitoring. Invasive pulmonary artery pressure monitoring is not routinely indicated and can be dangerous.

Air/particulate filters for all intravenous lines are essential for women with Eisenmenger syndrome. Compression stockings or thromboguards are very important around the time of delivery, along with early ambulation.

## **Post-partum care**

The mortality risk remains particularly high postpartum and many experts advise an extended postpartum period of monitoring in hospital. Attention to volume status is important.

After discharge, close postpartum monitoring is necessary. Care should focus in particular on managing volume status. The risk of pregnancy related complications exists until 6 months post-partum at which time pregnancy related hemodynamic changes will have fully returned to baseline. Follow-up at a frequency thought to be appropriate by the physician should take place until 6 months post-partum.

## **References**

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