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Eisenmenger Syndrome: Why Contraception in these Women?

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Abstract

Introduction: Einsenmenger syndrome (ES) appears when chronic pulmonary hypertension arising from a left-to-right intra-cardiac shunt leads to a reversal of this shunt and, inevitably, cyanosis. Currently, treatment is aimed at improving patient survival and functional capacity. After ES develops, transplantation is the final therapeutic option. Pregnancy is absolutely contraindicated, with a reported rate of mortality ranging from 30-50%; therefore, a safe and appropriate method of contraception should be imperative for these patients.

Hysteroscopic sterilization is the ideal method, however, for a patient who declines nonreversible methods, other options are progestin-only contraception with depot medroxyprogesterone acetate injections, etonogestrel implant or an intrauterine device (IUD). A copper-containing IUD is not recommended but a Levonogestrel IUD is an option for mildly cyanotic women who are at low risk of acquiring a sexually transmitted disease and is the preferred method because it reduces menstrual flow by 40-50% and may induce amenorrhoea. Menorrhagia is a common problem in women with cyanotic heart disease and its suppression is often helpful.

Objectives: The authors intend to review the literature and report a case of a 47 year-old woman with ES, with severe menorrhagia and consequent haemodynamic repercussion.

Conclusions: In these women, contraception should be used not only to prevent an unintended pregnancy but also to control menorrhagia in order to avoid anaemia and a further imbalance in cardiovascular status.

Keywords: Eisenmenger syndrome; Cyanotic heart disease; Menorrhagia; Contraception

Introduction

In 2005 there were an estimated 1 million adults living with congenital heart disease, with an expected increase in prevalence of 5% per year [1]. About 90% of children born with cyanotic heart disease nowadays are expected to reach adult age, many of them with a good functional status [2].

Eisenmenger syndrome is the extreme manifestation of pulmonary arterial hypertension associated with congenital heart disease [3]. Roughly 5-10% of patients with congenital heart disease develop pulmonary arterial hypertension of variable severity that impacts on quality of life, morbidity and mortality. Approximately 4% of these patients, undergoing tertiary care in Europe and North America, have Eisenmenger syndrome and a greater proportion of patients may be found in developing countries [4].

Objective

The authors intend to review the literature and report a case of a 47 year-old woman with ES, with severe menorrhagia and consequent haemodynamic repercussion.

Methods

The methodology used was the systematic review of scientific literature by PubMed, Ovid and Medline. Fourteen articles were selected for review, published between 1979 and 2015, in English, including only studies in humans.

Physiopathology of Einsenmenger Syndrome

Einsenmenger syndrome (ES) happens when chronic pulmonary hypertension due to a left-to-right intra-cardiac shunt (caused by ventricular septal defects, atrial septal defects or, less commonly, patent ductus arteriosus) leads to a reversal of this shunt and, inevitably, cyanosis. Diagnosis requires the exclusion of other causes of pulmonary hypertension and, in some cases, it is not established until adulthood [5]. ES sufferers progressively develop cyanosis and intolerance to physical exertion, with or without symptoms of pulmonary hypertension such as syncope and arrhythmias, and, occasionally, myocardial infarction, pulmonary haemorrhage or cerebral vascular accidents [6].

Currently treatment is aimed at improving patient survival and functional capacity. Pulmonary vasodilator therapy may improve haemodynamic status and quality of life in some patients. Other important aspects of management include avoidance of high-risk situations such as pregnancy, isometric exercise or high altitude, non-cardiac surgery, and specific attention to haematologic problems [7]. The mean survival of patients with ES has been reported to be 37 years, although the individual course is quite variable [8].

Patients with chronic pulmonary hypertension physiologically develop secondary polycythaemia (with increased haemoglobin and haematocrit levels), since the desaturated blood stimulates medullary production of red blood cells in order to improve tissue oxygenation. Any cause of dehydration or hypovolaemia can cause hypotension, hypoxia and, if severe, haemoconcentration with an increase in the risk of thromboembolic phenomena. On the other hand, bleeding disorders arise from platelet dysfunction, which, associated with a decrease in coagulation factors, lead to a predisposition to either spontaneous haemorrhage (gengivorrhagia, haemoptysis or menorrhagia) or bleeding during invasive procedures.

Einsenmenger Syndrome in Gynecology

Menstrual abnormalities are common in patients with congenital heart defects. There is an increase in mean menarche age, and primary amenorrhea is more prevalent [9]. It is hypothesized that chronic hypoxia has repercussions in ovarian function, with consequent inadequate menstrual cycles [9]. Women who become cyanotic after menarche, especially in advanced stages of the disease, demonstrate an increase in incidence of menstrual irregularities (such as oligomenorrhea, menorrhagia or metrorrhagia) when compared to the normal population or mildly cyanotic patients10. It is still unclear why these abnormal (and sometimes alternating) patterns occur, and many factors are thought to play a role: chronic anovulatory cycles, dysfunction of the hypothalamic-pituitary-gonadal axis and abnormal haemostasis secondary to chronic hypoxia and hyper viscosity [10].

Regardless of aetiology, these findings have important repercussions especially in cyanotic women. The anovulatory cycles lead to an increase in risk of endometrial carcinoma due to continuous endometrial proliferation resulting from non-oestrogenic opposition [10]. Furthermore, women with constant blood losses may become iron depleted and anaemic, however, iron reposition must be monitored in order to balance the consequences of hyper viscosity these women are already subjected to [5]. Menorrhagia is a contra-indication to anticoagulation and, as such, its suppression is vital.

As more women with cyanotic heart disease survive into childbearing age, a larger number of them has the potential to become pregnant1. Amongst the cardiac pathologies that contraindicate pregnancy are: ES, Marfan syndrome with aortic root dilatation, moderate-to-severe left ventricular outflow obstruction and left ventricular ejection fraction of <35%. The highest maternal risk is attributed to ES, with a maternal mortality of up to 50%, and the mortality risk cannot be predicted individually [2]. The majority of maternal deaths occur during the first week after delivery but can occur during gestation, labour, or more than week after delivery. Physiologic changes in pregnancy increase demands on the heart. Pulmonary hypertension is associated with a high morbidity and mortality during pregnancy: increases in cardiac output, blood volume, contractility, and heart rate can cause significant circulatory burden, which can lead to cardiac compromise, especially in a pregnant women with cyanotic heart disease.8 During labour and delivery, uterine contraction can cause a temporary increase in circulating blood volume of up to 500 ml, increase in stroke volume, and increased cardiac output of up to 30-50% higher than at the onset of labor [2]. The fixed pulmonary arterial resistance cannot accommodate the haemodynamic fluctuations of labour, delivery and the puerperium. Most deaths are due to thromboembolism, volume depletion (which can augment the right-to-left shunt and precipitate intense cyanosis) and preeclampsia. In addition, a sudden increase in systemic vascular resistance may fatally reduce cerebral blood flow [2]. Due to all these reasons, the women and their partners should be educated regarding a safe and appropriate method of contraception. Incidence of unintended pregnancy in this population is reported in up to 54% of women and European studies identified 56-79% of these patients using barrier methods or no contraceptive methods at all [11]. The selection of a contraceptive method for the woman with cyanotic heart disease must be individualized, taking into account the primary cardiac defect, related surgical interventions, and post-operative residua and sequelae. Hysteroscopic sterilization is the ideal method, since it is irreversible and minimally invasive [12]. Combined oral contraceptives (estrogen-progestin) are contraindicated because of the increased risk of thromboembolism, thus making them unacceptable for women with right-to-left shunts, pulmonary vascular disease, prosthetic devices or other materials susceptible to thrombus formation. Thromboembolic effects are primarily attributed to the estrogenic component of the formulation, but studies report a minimal increase in platelet activation and coagulability [11]. In patients that decline irreversible methods, other options are:

- Progestin-only contraception with desogestrel pill, depot medroxyprogesterone acetate injections or etonogestrel subcutaneous implant. They inhibit ovulation, thicken cervical mucus and suppress growth and development of the endometrium thus producing an unfavourable endometrial lining, with no measurable impact on clot formation or platelet behaviour. Unwanted side effects include breakthrough vaginal bleeding and amenorrhoea-the latter being an advantage in these women. Low-dose progestin implants provide contraceptive protection for up to 3 years.
- Intrauterine device (IUD) is an option for acyanotic or mildly cyanotic women who are at low risk of acquiring sexually transmitted infections. The levonogestrel-realising IUD is preferred because it reduces menstrual blood loss by 40-50% and may induce amenorrhoea in a significant amount of women. This IUD releases 20 micrograms/day of levonorgestrel and is effective for 5 years. They also can initially cause abnormal bleeding or spotting, but after 3-6 months hypomenorrhoea or amenorrhoea is expected. A copper-containing IUD, however, is not recommended in cyanotic women with haematocrit levels above 55% because intrinsic haemostatic defects increase the risk of

excessive menstrual bleeding, which is already common with the cooper-containing IUD [13].

Case Report

We present the case of a 47 year-old nulliparous woman with Eisenmenger syndrome due to an atrioventricular septal defect, with severe menorrhagia and consequent haemodynamic repercussion. Relevant past medical history also included ischaemic heart disease with consequent heart failure (class III/IV), an ischaemic cerebrovascular accident with subsequent left sided hemiparesis, atrial fibrillation and hypothyroidism. She was referred to our hospital's Gynaecology specialist clinic due to menorrhagia with haemodynamic repercussion (haemoglobin of 14 g/dL - usual for the patient 18 g/dL), which was refractory to desogestrel use. Oral anticoagulation was contraindicated due to the severe blood loss. Gynaecologic examination and pelvic ultrasound were both normal. We attempted use of a levonogestrel-realising intrauterine device. There were no complications during insertion due to the softer tissues of cyanotic women even though the patient was a virgin, however, because of the persistent and significant bleeding, the device was expelled after one week. Subsequently, an etonogestrel implant was applied, which was effective in the control of menorrhagia and consequent recovery to normal haemoglobin levels.

Conclusions

Eisenmenger syndrome is amongst the pathologies in which contraception is used not only to avoid pregnancy (which is contra-indicated), but also as a means of medical treatment for menorrhagia.

If only contraception is intended, tubal ligation can also be considered, however, anaesthetic risks are considerable. In our case, contraception wasn't the primary goal. The main issue was to control the menorrhagia in order to avoid volume depletion and institute anticoagulation.

The levonogestrel-realising intrauterine device reduces menstrual flow in around 80-96% of women during at least 12 months, with a low incidence of side effects and a similar efficacy to endometrial ablation [13]. This endometrial effect seems to persist for 5 years in women in reproductive age, and therefore has a long therapeutic effect [13]. This form of contraception, as evidenced by the literature, should be considered first line treatment for idiopathic menorrhagia: its insertion is simple, it has sustained effect, it is well tolerated, and it has a good cost-benefit relationship, thus reducing the need for surgery. IUD-related infections have been thought to be due to transient microbiologic contamination of the endometrium at the time of insertion, however, the infection rate from 1 month after insertion through the full lifespan of the device has been reported to be 1.4 cases per 100 years and virtually no cases have been reported in women with no risk factors for STDs. Furthermore, infective endocarditis associated with IUDs is rare. The administration of prophylactic antibiotics solely to prevent endocarditis in high-risk patients is not recommended for those who undergo genitourinary tract procedures and, therefore, should not be used when inserting IUDs [14].

Regarding the etonogestrel subcutaneous implant, this device can itself cause metrorrhagia, and, in these patients, introducing combined oral contraceptives even if temporary to control the abnormal bleeding is not possible. Additionally, progesterone and medroxiprogesterone can cause fluid retention, and should not be prescribed to patients with heart failure. These methods should, therefore, be used with caution and decision of use decided on an individual basis.

As a final note, hysterectomy might by indicated if any of the contraceptive methods fail, with a view to haemodinamically stabilize the patient.

Regardless, the use of long-acting reversible contraceptives, including intrauterine devices and subdermal implants, which are safe for most women with congenital heart disease, is still low [11].

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