SULPROSTONE AND MYOCARDIAL ISCHEMIA : A CASE REPORT

SULPROSTONE ET ISCHEMIE MYOCARDIQUE : A PROPOS D'UN CAS

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Abstract

Sulprostone is the prostaglandin recommended for the treatment of severe postpartum bleeding due to uterine atonia which resists to the treatment with oxytocin. Sulprostone has many benign side effects. Serious complications such as myocardial ischemia may exceptionally occur.
We report the case of myocardial ischemia in a parturient after the administration of sulprostone . In our case report, myocardial ischemia has occurred following the administration of sulprostone in a pre-eclamptic patient with hemodynamic instability and severe anemia.

Key-words: Sulprostone; Myocardial ischemia; Haemorrhage.

Résumé

Sulprostone est la prostaglandine recommandée pour le traitement des hémorragies sévères du postpartum par atonie utérine résistantes à l'ocytocine. Sulprostone a plusieurs effets secondaires bénins. Des complications sérieuses telles que l'ischémie myocardique surviennent exceptionnellement.
On rapporte le cas d'une ischémie myocardique chez une parturiente après l'administration de sulprostone. Dans ce cas, l'ischémie myocardique est survenue chez une patiente pré-éclamptique avec instabilité hémodynamique et anémie sévère.

Mots - clés : Sulprostone ; Ischémie myocardique ; Hémorragie.

ملخص

السولبروستون هو البروستاجلاندين الموصى به لعلاج نزيف ما بعد الولادة الحاد نتيجة ضعف الرحم المقاوم للأوسيتوسين.
للسلبروستون العديد من الآثار الجانبية و يمكن حدوث مضاعفات خطيرة مثل نقص تروية عضلة القلب بصفة استثنائية. قمنا بالإبلاغ عن حالة نقص تروية عضلة القلب في حالة ولادة بعد تلقي السولبروستون. في هذه الحالة، حدث نقص تروية عضلة القلب عند مريضة مصابة بمرض تسمم الحمل مع عدم استقرار الضغط وفقر الدم الحاد.

الكلمات المفاتيح: السولبروستون ; نقص تروية القلب ; نزيف

INTRODUCTION

Obstetrical haemorrhage is the first cause of maternal mortality. It accounts for approximately 25% of all deaths of pregnant women worldwide [1]. It complicates approximately 6% of pregnancies [1].

Sulprostone (Nalador), an analogue of prostaglandin E2, is an injectable prostaglandin recommended for the treatment of severe postpartum bleeding due to uterine atonia which resists to the treatment with oxytocin [2]. It has been marketed since 1986.

Sulprostone has many benign side effects that may appear during its use (nausea, vomiting, and hyperthermia). Serious complications such as myocardial necrosis, cardiac arrest, arrhythmia, and deterioration of renal function may exceptionally occur [3]. They must be diagnosed in time to ensure good management.

In this context, we report the case of myocardial ischemia in a parturient after the administration of sulprostone.

CASE REPORT

Mrs. EA, 38 years- old-woman, with unknown medical history, 3G3P with 2 living children, pregnant at 31 weeks of amenorrhea with a badly followed pregnancy, consulted at the regional hospital for bleeding and abdominal pain.

The patient had 160 /90 mmHg blood pressure and tenderness in the abdomen. She presented an eclamptic convulsion during the transport to our hospital. The diagnosis of retroplacental haematoma was done. The baby died in utero.

Sent directly to the surgical unit, the patient was in hemorrhagic shock with low blood pressure (80 mm Hg of systolic pressure and tachycardia at 135 bpm). Cardiopulmonary auscultation was without abnormalities. Quickly, two venous lines and bladder catheterization were done. A blood group with a triple biological check-up was done.

A cesarean section was done under general anesthesia in emergency (orotracheal intubation under propofol - succinylcholine and maintained by propofol). It has allowed the extraction of a stillborn weighing 1.8 kg and the confirmation of the retroplacental haematoma weighing about 500g. Meanwhile, the patient received 1 g of Tranexamic acid, 1g of fibrinogen, and was filled by 1.5 l of physiological serum, 1 l of Lactated Ringer's solution and 0.5 l of hydroxyethyl starch solution. A stable hemodynamic status was restored without resorting to catecholamines. Antibiotic prophylaxis based on cefazolin was administered.

Three slow intravenous bolus of oxytocin (Syntocinon) (5 IU) associated to the infusion of 10 IU diluted in 500 ml of Lactated Ringer's solution were administered. Nevertheless, a good uterine contraction wasn't obtained. The use of sulprostone was decided by the obstetrician and the anesthesist because of uterine atonia. A dose of 500µg was administered by an infusion pump for one hour.

Initial tests showed anemia with 7 g / dl of hemoglobin, high creatinine 256 µmol / l. Heamostasis tests and liver-function tests were normal. She was transfused in the operating room with 2 units of packed red blood cells. Magnesium sulfate was administered. She was extubated without incident and then transferred to the resuscitation unit. The patient maintained hemodynamic stability (blood pressure about 120/60 mm Hg) with a good neurological status. The clinical examination didn't show abnormalities. The uterine retraction was satisfactory. The hemoglobin concentration decreased to 6.8 g / dl requiring transfusion of two other units of packed red blood cells with 4 units of fresh frozen plasma. The coagulation tests were normal. There has also been a worsening of renal function with creatinine at 560 umol / l. The patient was anuric. High doses of Furosemide were prescribed. An abdominal ultrasound was done. It was normal.

The biological check-up also revealed elevated troponin Ic levels with downward deflection of ST in the electrocardiogram in the anterior- inferior territory. The troponin kinetics (every 6 hours) was to ascend until 41 µg/l (threshold of positivity is 0.01 µg/l). The patient did not show clinical symptoms. The evolution was good with regression of electrical and biological signs in the second postoperative day. The diagnosis of myocardial ischemia was made. The patient was just supervised.

The patient was kept in the resuscitation unit for 4 days. The diuresis has taken back. Then, she was transferred to the renal unit where the diagnosis of acute tubular necrosis was made. In collaboration with cardiologists, an exploration of the coronary state was decided after this episode.

It was also normal.

DISCUSSION

The uterine inertia is the most frequent cause of postpartum haemorrhage (80 %)[1]. The treatment is based on agents stimulating the uterine contraction : intravenous oxytocin, methylergometrine (Methergin) no more used because of its vasoconstrictor effects, or synthetic prostaglandin as sulprostone used in case of failure or limited response to oxytocin[4]. The success of these agents is dependent on the time of beginning of their administration. The time is a major prognostic factor. The risk of therapeutic ineffectiveness is 8 times higher if the administration began more than 30 minutes after the diagnosis of postpartum hemorrhage [4].

The failure of medical treatment indicates interventional procedures: selective arterial embolization, surgical clipping of the arteries or sometimes hysterectomy in case of failure of conservative methods or in life-threatening situations[5].

Sulprostone is an analogue of prostaglandin E2, a synthetic derived product of dinoprostone. It is an injectable prostaglandin recommended for the treatment of severe postpartum hemorrhage due to uterine atony resistant to the treatment with oxytocin[1].

It acts selectively on the gravid uterus, in the uterine cervix and mainly in the myometrium (increased basal tone of the uterine muscle and the appearance of rhythmic contraction)[4].However, the concept of selectivity is relative. Thus, sulprostone has other effects, particularly on other smooth muscle fibers of the body.

It has other effects: mild systemic vasodilating action adjusted by the increase of heart rate and cardiac output[4]. This hypotensive effect can make the hemodynamic state worse if hemorrhage and hypovolemia are insufficiently compensated. It is also coronarodilator [4]. However, in some cases, it has paradoxical effect. It becomes a vasoconstrictor and hypertensive drug (increases pulmonary pressures and causes pulmonary edema) and very rarely coronaroconstrictor [2]. Prostaglandin E2 may also increase the level of transaminase. It causes vasodilatation in the kidneys with increase in renal blood flow, glomerular filtration, renin secretion and decreases tubular reabsorption of sodium.

Minor side effects are frequent when using therapeutic doses of sulprostone. Nausea, vomiting and diarrhea can be reported by contraction of smooth muscle fibers [5]. Headache, skin flushing and shiver are sometimes noticed because of its skin vasodilator effect. Hyperthermia around 38.5° C is also frequent by the action of prostaglandins on the centers of thermoregulation, making difficult the differential diagnosis of infectious complications [2]. Besides, it may induce platelet aggregation with high doses. It can cause bronchial constriction in some patients although its effect as a dilatator of bronchial smooth muscle [2].

Cardiovascular events have been reported but are very rare. Several clinical cases of cardiovascular events were published type of cardiac arrest, myocardial ischemia, myocardial infarction, or ventricular arrhythmia(7–10) (je n'ai pas compris)

The incidence of cardiovascular accidents with sulprostone is unknown and very low, but their existence must be known.

The mechanism of these accidents, sometimes without exploration is most often the coronary spasm in healthy or diseased coronary [8]. There is a contradiction between the action of sulprostone like a coronarodilator and the hypothesis of spasm.

Sulprostone is spasmogenic under certain conditions and on some backgrounds, such as age > 35 years, smoking > 10 cigarettes per day and pre-eclampsia [10]. Some routes of administration (such as intramuscular and intra- myometrial administration [2]). and some associations (with methylergometrine or norepinephrine [11]). expose to these accidents. These accidents may occur in healthy or diseased coronary arteries. However, the hemodynamic (hypotension), sympathetic and metabolic effects (tachycardia, severe anemia) associated to significant bleeding may also increase coronary resistance. Despite the theoric risk of increasing cardiovascular risk, the use of adrenaline or noradrenaline isn't prohibited in cases of cardiac arrest when sulprostone is administered [12]. The administration of sulprostone alone is not a risk factor for myocardial infarction during a severe postpartum hemorrhage.

In our case report, myocardial ischemia has occurred following the administration of sulprostone in a pre-eclamptic patient with hemodynamic instability and severe anemia. The blood loss led to a sympathetic response in the coronary arterial system.

The contraindications of sulprostone are cardiovascular antecedent (angina pectoris, Raynaud's syndrome, arrhythmia, heart failure , hypertension) , factors contributing to coronary artery disease (age > 35 years , active smoking (> 10 cigarettes per day) or smoking stopped < 2 .

years) , history of severe asthma or asthma-like bronchitis, thromboembolic history, epileptic antecedent, severe disturbance of liver or kidney function or disequilibrium of the diabetes. When the postpartum hemorrhage is life-threatening, these contraindications become relatives [9] .

For coronary events, it was often difficult to distinguish spasm and myocardial infarction: the electrocardiogram is often normal and the other tests (troponin, coronary angiography and ultrasound) were not always reported. These accidents were often very severe and were life-threatening in 48 % of cases.

The electrocardiogram is normal in more than 50% of patients having a myocardial infarction. So it can't claim the absence of ischemic damage especially in healthy patients. The most observed abnormality is the downward deflection of ST. Maternal tachycardia is often associated. Cardiac ultrasound, performed when these variations are observed, usually doesn't find abnormalities[13].

The dosage of troponin Ic is interesting. Because of its cardiac specificity, the increase of its rate is the marker of myocardial infarction . In pregnancy and childbirth circumstances, troponin is the marker of choice for many reasons. In fact, the troponin level never exceeds the normal threshold in young healthy patients after childbirth. It is not modified by the type of anesthesia, the duration of labor or the type of the delivery [13,14]. Besides, uterine contractions during labor and childbirth increase the concentration of non-specific cardiac markers (CK, CPKmb, myoglobin) but not the concentration of troponin [14]. Also, the increase of the level of troponin Ic is observed only during myocardial ischemia [13]. That's why troponin remains the only specific marker of myocardial ischemia during the pregnancy, the labor and the postpartum.

CONCLUSION

Sulprostone is the most powerful utero -tonic. It should be used early in obstetric hemorrhage due to uterine atony. The maximum dose of 500µg / h must be administred without exceeding a total dose of 1.5 mg per 24 hours. It induces mild effects. Its complications and particularly cardiac ischemia must be known. They are exceptional but can be serious. These severe complications should not, however, forbid the use of this drug whose efficiency has been demonstrated in postpartum hemorrhage. In our observation, the pre-eclampsia, blood loss, hypotension and tachycardia are factors that aggravate the spasm caused by sulprostone.

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