

Emergency Obstetric Anesthesia in Patients Receiving Ritodrine Therapy for Preterm Labor

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Preterm labor and delivery constitute major problems in obstetrics. Despite appropriate use of tocolytic therapy, some preterm deliveries are unavoidable and cesarean section is often the mode of delivery. The interactions of beta sympathomimetic tocolytics with anesthetic agents have potential problems for anesthetic management. In this study, our aim was to evaluate the experience of the anesthetic management of cesarean section in patients who received intravenous ritodrine to inhibit preterm labor. Twenty patients, in two groups, between the age of 18 and 35 who had undergone a cesarean section following failure to inhibit preterm labor with intravenous ritodrine therapy as study or control group were studied. Maternal heart rate, blood pressure, serum potassium and glucose levels were evaluated. Mean maternal heart rate in the operating room in ritodrine group was 119±4 bpm, in control group was 84±4 bpm. At the operating theater, mean systolic and diastolic blood pressures of the ritodrine and control groups were 103±7 mmHg, 64±6 mmHg and 118±7 mmHg, 78±4 mmHg, respectively. Serum potassium levels showed a moderate decrease during ritodrine infusion. We consider that central venous pressure (CVP) detection reduces the risk of pulmonary edema and cardiac failure in the course of general anesthesia and recommend that anesthesia be deferred at least 45 minutes following discontinuation of ritodrine in order to minimize the drug interactions with anesthetics.

Key Words: Obstetric anesthesia, ritodrine therapy, preterm labor, tocolysis

Erken travay için ritodrin tedavisi alan hastalarda acil obstetrik anestezi

Erken travay ve doğum önemli problemler oluşturmaktadır. Tokolitik tedavi yapılmasına rağmen, bazen erken doğum önlenemez ve sezaryen uygulamak gerekebilir. Anestezik ilaçlarla beta sempatikomimetik ilaçların etkileşimleri anestezinin uygulanması sırasında bazı problemlerin çıkmasına sebep olabilir. Yaşları 18 ile 35 arasında olan, erken travay nedeni ile ritodrin kullanılan, araştırma ve kontrol grubundan oluşan ve Sezaryen yapılan toplam 20 hasta çalışmaya alındı. Anne kalp hızı, sistolik ve diastolik kan basıncı, serum potasyumu ve glikozu değerlendirildi. Ortalama anne kalp hızı ritodrin grubunda 119±4/dakika, kontrol grubunda 84±4/dakika bulundu. Ameliyathanede sistolik ve diastolik kan basınçları ritodrin grubunda 103±7 mmHg, 64±6 mmHg ve kontrol grubunda ise 118±7 mmHg, 78±4 mmHg idi. Serum potasyum değeri ritodrin grubunda orta derecede düşüş gösterdi. Anestezi esnasında akciğer ödemi ve kalp yetmezliği riskini azaltmak için santral venöz basınç tespitinin uygun olacağını ve anestezik ilaçlarla etkileşimin ritodrinin kesilmesinden 45 dakika geçtikten sonra en aza indiği sonucuna vardık.

Anahtar Kelimeler: Obstetrik anestezi, ritodrin tedavisi, erken doğum, tokoliz

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INTRODUCTION

Preterm labor and delivery constitute major problems in obstetrics. The first choice tocolytic agents are often beta 2 sympathomimetic drugs(1). Beta sympathomimetic drugs are widely used in the management of premature labor(2,3). They act on uterine receptors, causing a reduction in uterine contractions (tocolysis). Even relatively selective beta 2 sympathomimetics, given in the recommended dose, may cause dysrhythmias, pulmonary edema and myocardial ischemia(3). In addition, beta sympathomimetic agents in high doses may cause severe maternal hypotension that could aggravate the existing fetal distress(4).

Despite appropriate use of tocolytic therapy, some preterm deliveries are unavoidable and cesarean section is often the mode of delivery. The interactions of beta sympathomimetic tocolytics with anesthetic agents pose potential problems for anesthetic management(1).

Our aim in this study was to evaluate the experience of the anesthetic management of cesarean section in patients who received intravenous ritodrine to inhibit preterm labor.

MATERIALS AND METHODS

This study was approved by the human ethic committee of Atatürk University Research Hospital. Twenty patients, in two groups, between the age of 18 and 35 who had undergone a cesarean section following failure to inhibit preterm labor with intravenous ritodrine therapy as study or control group was studied. We excluded women with chronic hypertension, pregnancy-induced hypertension, diabetes mellitus, cardiac disease, liver or renal disease, or central nervous system disorders. Women who

were treated with other sympathomimetic agents, methylxantines, narcotics, parasympholytics, or potassium depleting drugs were also excluded. Prior to the study, each patient underwent a complete physical examination, and an electrocardiogram was obtained. Each patient had blood withdrawn for the determination of a complete blood count (CBC), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubine, blood urea nitrogen (BUN) and creatinine. We inserted to all patients a central venous catheter (Cava Fix, 75 cm) via antecubital vein to detect central venous pressure (CVP) in order to reduce the risk of pulmonary edema and cardiac failure. The infusion rate of ritodrine was initiated at 100 micro g/min and increased until the frequency of contractions are reduced to every 10 minute, until labor is inhibited, side effects occur, or a maximal rate of 350 microg/min is reached. Maternal heart rate, blood pressure, serum potassium and glucose levels were evaluated as an index of beta sympathomimetic effect of ritodrine infusion. In the operating theater, the patient was turned to the left side 15 degree to prevent the supine hypotensive syndrome and oxygen was administered. Transverse skin incision was made using the standard technique(1). The incision-delivery time was 3 min 30 seconds. Anesthesia for cesarean section was induced with thiopentone 4 mg/kg iv and atracurium 0.8 mg/kg iv after endotracheal intubation general anesthesia maintenance was achieved with isoflurane 1% and oxygen 40% until delivery of infant. After clamping the umbilical cord, we gave patients 2 µg/kg fentanyl iv for intraoperative analgesia. Comparisons between the placebo and ritodrine data were made using student's-t test and chi-square analysis. The probability values were taken from two-tailed tables and only values <0.05 were considered statistically significant.

FINDINGS

All the patients given general anesthesia were comparable in age and weight. Before tocolysis, there was no statistically difference in heart rates between the ritodrine and control group. There was no statistically significant difference in CBC, AST, ALT, ALP, bilirubine, BUN and creatinin between the ritodrine and control group. In ritodrine group, mean maternal heart rate on discontinuation of the drug was 119 ± 4 bpm. In control group, mean maternal heart rate in the operating room was 84 ± 4 bpm. This difference was statistically significant and continued during the operation. (Figure 1) Before tocolysis, there was no statistically difference in systolic and diastolic blood pressures between the two groups. At the operating theater, mean systolic and diastolic blood pressures of the ritodrine and control groups were 103 ± 7 mmHg, 64 ± 6 mmHg and 118 ± 7 mmHg, 78 ± 4 mmHg, respectively. These differences in systolic and diastolic blood pressures of the two groups were statistically significant and continued 45 minutes after induction. (Figure 2 and 3) Serum potassium levels showed a moderate decrease during ritodrine infusion (from 4.19 to 3.81 mEq/L) and

returned to preinfusion level after the operation. In control group, there was no statistically significant changes in serum potassium levels during the operation. No differences in serum glucose levels of the two groups were statistically significant. Blood loss was estimated at 300 ml. The maternal postoperative status was uneventful. One ventricular arrhythmia and three severe hypotensive episodes were observed during the general anesthesia. Statistically significant changes in heart rate occurred during the general anesthesia. A statistically significant decrease in mean arterial blood pressure was noted during the general anesthesia. The CVP values were in normal ranges during the operations in two groups and the differences in CVP of the ritodrine and control groups were statistically insignificant.

DISCUSSION

Beta sympathomimetic agents (e.g. ritodrine, terbutaline) are often given for tocolysis. Ritodrine and terbutaline are relatively selective for the beta 2 receptor. Beta 1 receptor stimulation occurs resulting in increased maternal heart rate and

Figure 1. Heart rate changes during anesthesia

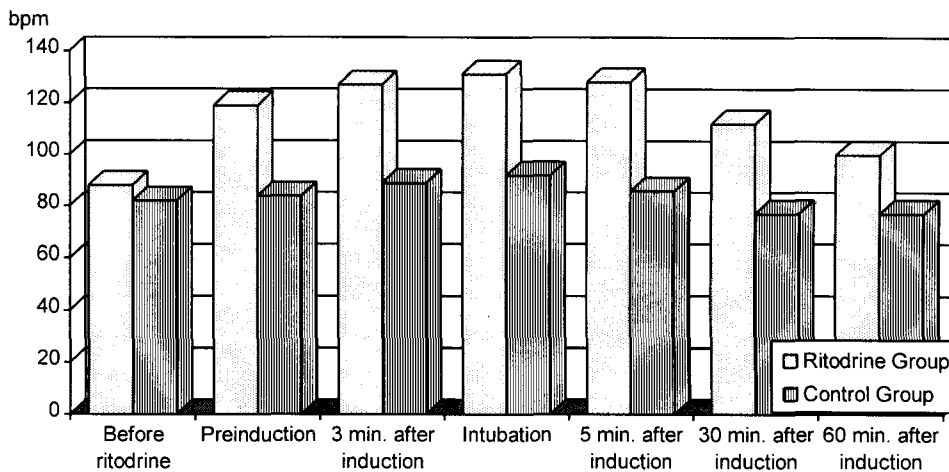
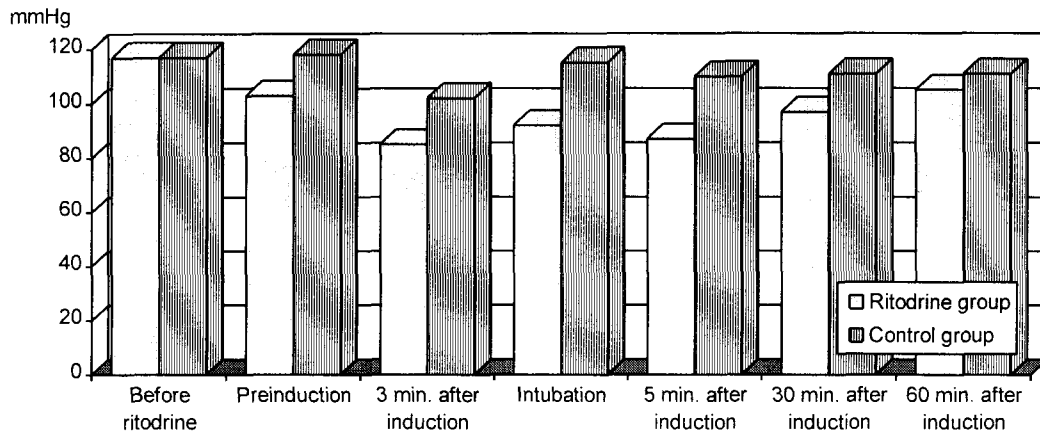


Figure 2. Systolic blood pressure changes during anesthesia

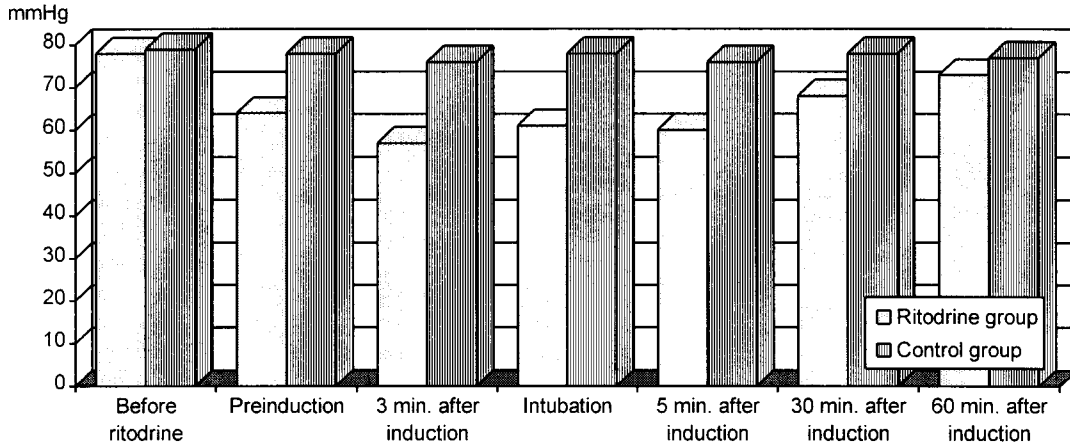
systolic arterial pressure, decreased diastolic arterial pressure, and unchanged or decreased MAP. Unfortunately, the half-lives of the beta sympathomimetic tocolytic agents in pregnant women are prolonged. Distribution phase and equilibrium phase half-lives for ritodrine in pregnant women are 32 ± 21 minutes and 17 ± 10 hour, respectively(5).

Fetal distress in labor can be attributed to compression of the umbilical cord, intrauterine growth retardation, abnormal uterine activity, and maternal arterial hypotension. There is a linear relationship between fetal heart rate and ventricular output, while vagal stimulation reduces fetal heart rate with a linear decrease in ventricular output. Therefore by reversing fetal bradycardia by means of beta sympathomimetic drugs, the fetal cardiac output should improve because of the increase in the fetal heart rate. Stimulation of alpha receptors in the uterus increase activity, while beta receptor stimulation inhibits activity. The effective dose is 150-350 microg with an initial dose of 50 micro g/min. Tachycardia as a result of sympathetic stimulation during an iv infusion is a specific problem during cesarean section. This effect may be reversed by the administration of a beta blocker such as

proctolol. However, these drugs have side-effects such as showing the fetal and neonatal bradycardia and neonatal hypoglycemia, and increased uterine activity in early labor. Beta blocker should not be given until the cord has been clamped, in order to avoid neonatal complications(6).

Persistent tachycardia causing hemodynamic disturbance requires treatment and other published cases have shown a response to discontinuation of therapy, although cardioversion may be required(7,8). Fluid balance in the preoperative period must be carefully controlled, the drug induced tachycardia may be clinically misinterpreted as a sign of hypovolemia(3,9). It has been reported that ritodrine induced tachycardia associated with fluid overload in late pregnancy, precipitated cardiac failure.

Another important factor is fluid overload. This resulted from the drug itself and from prolonged intravenous infusion, and is exacerbated by pregnancy. It has been demonstrated that restricting fluid intake, and using dextrose rather than saline to infuse the drug, reduces the incidence of pulmonary edema. Even in normal pregnancy, there are increases in blood volume,

Figure 3. Diastolic blood pressure changes during anesthesia

total body water, stroke volume and cardiac output, which are increased during labor. Beta sympathomimetics also produce a rise in cardiac work, and can precipitate pulmonary edema in previously normal patients. We used the dextrose 5% solution to infuse the ritodrine. In our study, significant residual beta sympathomimetic effects of ritodrine, maternal tachycardia, hypotension and hypokalemia, persisted longer than 30 minutes after discontinuation of the drug.

In conclusion, we consider that CVP detection reduces the risk of pulmonary edema and cardiac failure in the course of general anesthesia and recommend that anesthesia be deferred at least 45 minutes following discontinuation of ritodrine in order to minimize the drug interactions with anesthetics.

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