

## **Epidural anesthesia for cesarean section in triplet pregnant women with toxemia and complications of ritodrine therapy: five case reports**

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### **Introduction**

With the recent increase in the incidence of multiple pregnancy as a result of ovulation induction, the demand for appropriate anesthetic management in multiple pregnancy has also increased. Multiple pregnancy is accompanied by several problems and is associated with substantially increased risk of maternal, fetal, and neonatal mortality and morbidity.<sup>1</sup> Among these complications, prematurity is the most serious [1]. For the prevention of premature labor and prolongation of gestation, ritodrine, a tocolytic agent, is widely used despite its serious maternal side effects [2]. Perioperative maternal and fetal complications may be reduced by the selection of appropriate anesthetic technique and a clear understanding of the potential interactions between tocolytic agents and the anesthetic drugs.

We report the anesthetic management of five patients with triplet pregnancy with toxemia of pregnancy and complications due to ritodrine therapy. Epidural anesthesia was indicated for cesarean section and was performed without any intraoperative complications.

### **Case report**

Five women with triplet pregnancy ranging in age from 27 to 35 years were admitted to our hospital for prevention of premature labor during their early pregnancy.

All of them also had mild to severe toxemia of pregnancy. They had all conceived after being treated for infertility. The gestational age was  $33.8 \pm 3.1$  weeks (mean  $\pm$  SD), and the weight gain was  $8.6 \pm 2.6$  kg. The profile of each patient is shown in Table 1. All patients were treated with tocolytic agents to prevent premature labor, and three of them also received cervical cerclage under caudal epidural anesthesia. The total dose of ritodrine administered and the associated complications encountered are summarized in Table 2. Ritodrine was administered intravenously from 13 to 34 weeks of gestation until delivery at initial dose rates ranging from 50 to 100  $\mu\text{g}/\text{min}$  and maximum dose rate ranging from 180 to 320  $\mu\text{g}/\text{min}$ . Chest radiography demonstrated pulmonary congestion in cases 1 and 3 before cesarean section, as well as anemia in case 1, and dyspnea and hypoxia before anesthesia in case 2. Examination in case 2 revealed a pH of 7.457,  $\text{Paco}_2$  of 23.7 mmHg, and  $\text{Pao}_2$  of 61.3 mmHg. Oxygen (3 l/min) was administered through a face mask, and  $\text{Pao}_2$  was improved markedly, to 100.4 mmHg.

Emergency cesarean section was indicated in three of the women, and an elective cesarean section in two. In each woman, epidural anesthesia consisting of a single injection of 10–12 ml of 2% mepivacaine was performed at the L1-2 level in the left lateral position with concurrent epidural catheter insertion. Subsequently, all patients received an additional perineal analgesia. Caudal epidural anesthesia with 10 ml of 1% mepivacaine was performed in all women except one whose sacral hiatus was difficult to locate because of obesity; the latter patient received spinal anesthesia with 0.75 ml of 0.5% tetracaine. The level of block, assessed by the pinprick method, extended from T6 to S5.

During operation, 500–1000 ml of lactated Ringer's solution was administered. In case 2, approximately 800 ml of lactated Ringer's solution and 500 ml of colloid solution were administered. The estimated

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**Table 1.** Profiles of patients, pregnancy, and cesarean sections

Case			Pregnancy			Neonates/Babies		
No.	Age	BW (kg)	Wk.	Weight gained (kg)	Complications	Anesthesia	Apgar score	Birth weight (g)
1	30	57	29	7	Mild toxemia, anemia	Lumbar and caudal epidural	7, 3, 7	1310, 1080, 1220
2	36	60	33	7	Severe toxemia	Lumbar epidural, spinal	9, 7, 3	1895, 1728, 1770
3	35	75	34	13	Mild toxemia	Lumbar and caudal epidural	9, 8, 10	1652, 1814, 1596
4	26	85	37	7	Mild toxemia	Lumbar and caudal epidural	9, 9, 9	1722, 2280, 1940
5	27	76	36	9	Mild toxemia	Lumbar and caudal epidural	9, 8, 9	2268, 2332, 2338

BW, body weight; wk., weeks of gestation.

**Table 2.** Ritodrine and complications

Case no.	Started wk. ( $\mu\text{g}/\text{min}$ )	Initial dose ( $\mu\text{g}/\text{min}$ )	Maximum dose (mg)	Total dose (days)	Duration	Complications
1	25	50	200	1745	27	Pulmonary congestion, tachycardia
2	24	50	300	14050	59	Pulmonary edema, tachycardia
3	13	100	320	57900	148	Pulmonary congestion, tachycardia
4	34	67	180	3670	19	Tachycardia
5	19	100	280	18000	93	None

wk., week.

blood loss including the amniotic fluid ranged from 800 to 1500 ml. The mean operation time was  $51 \pm 12.9$  min, and the range was 30–65 min. Anesthesia and operation proceeded uneventfully without any intra-operative complications.

The mean birth weight of the neonates was  $1796 \pm 389$  g and the mean Apgar score was  $7.7 \pm 2.1$  at 5 min. Although there were no stillbirths, one neonate (case 1) with an Apgar score of 7 died due to intracerebral hemorrhage 3 days after birth.

## Discussion

Multiple pregnancy is accompanied by conditions unfavorable to the well-being of both the mother and the fetuses. The maternal mortality rate is increased two- to threefold compared with that in single pregnancies [1]. Among fetal complications, prematurity is the most important one, occurring six to ten times more frequently than in single births. The neonatal mortality rate among triplets is almost 20 times higher than that among single births [3]. Birth weight is a vital factor affecting the survival of fetuses and for this reason beta-mimetic agents are frequently applied to prevent premature labor and hence prolong gestation.

There is at present no method of anesthesia for cesarean section that does not carry some risk of complications in patients with multiple pregnancy, and any anesthetic management requires consideration of both the maternal and fetal risks. Since gravid uterus leads to aorto-caval compression, causing maternal hypotension

and adverse effects on uterine perfusion, care should be taken to administer sufficient fluids intravenously and to avoid supine hypotension due to uterine displacement when regional anesthesia is applied. In general, epidural anesthesia induces less severe hypotension than does spinal anesthesia and is less hazardous than general anesthesia. Thus, epidural anesthesia may be the preferred method of anesthesia in multiple pregnancy. In contrast to regional anesthesia, when general anesthesia is selected numerous immediate disadvantages should be considered. The fetuses are usually premature and vulnerable, and may therefore have increased susceptibility to the depressant effects of general anesthetics. Moreover, patients with multiple pregnancy are without exception at increased risk of aspiration of the gastric contents because the gross enlargement of the uterus causes a delay in gastric emptying and because the increase of progesterone level decreases gastric motility [4].

Among several beta-mimetic agents, ritodrine is most commonly used for the treatment of preterm labor [2]. A number of serious maternal complications such as pulmonary edema, myocardial ischemia, cardiac arrhythmia, cerebral vasospasm, hypotension, hyperglycemia, and fluid overload with dilutional anemia have all been reported in patients treated with ritodrine [5]. There is an apparent relationship between early side effects, such as chest pain, tachycardia, shortness of breath, and vomiting, and the infusion rate, plasma concentration, and rate of change of each [6,7]. However, the relationship between ritodrine and late effects, such as fluid retention, decrease of hematocrit, and pul-

monary edema, has not yet been well studied. Caritis has suggested that these effects may be related to the duration of therapy, total fluid intake, and perhaps the total dose of the drug administered [8]. To our knowledge, there have been no prospective clinical studies of anesthetic management after the administration of beta-adrenergic agents. The common complications of ritodrine and potential pathophysiological changes should always be taken into consideration before a patient is anesthetized. Patients treated with beta-adrenergic agents for tocolysis, especially ritodrine, have an increased risk of arrhythmias at the time of induction, and anesthetic agents with sympathomimetic effects should be avoided or used with great caution [9]. It has been recommended that induction of general anesthesia should be delayed until at least 10 min after discontinuation of beta-adrenergic infusion [10]. It has also been reported that a delay of 15 min is sufficient to allow slowing of the maternal heart rate before slow induction of epidural anesthesia [2].

The perioperative courses of our patients provide excellent case studies of the problems of the parturient with multiple pregnancy and tocolytic therapy with ritodrine. We observed no complication during anesthetic management with regional anesthesia in the five triplet patients. Given the adverse effect of regional anesthesia and the risk of hypotension in multiple pregnancy, epidural anesthesia is relatively safer and preferable. All except one of the preterm infants, delivered under epidural anesthesia, had Apgar scores of at least 7 at 5 min. We selected and administered ritodrine from the early stage of pregnancy until delivery in all cases. Among the numerous side effects of ritodrine, tachycardia, pulmonary congestion, and pulmonary edema were encountered in four, two, and one of the patients, respectively. Despite the risk of overhydration, lactated Ringer's solution was administered because regional anesthesia causes sympathetic block which may lead to hypotension. In case 2, before anesthesia the patient showed pulmonary edema which led to dyspnea and hypoxia; these were corrected with oxygen therapy. Colloid solution (500 ml) was administered in this case and effectively decreased pulmonary edema. In our patients, we noted no obvious relation between

the total dose of ritodrine and the complications that developed.

In the anesthetic management of multiple pregnancy, it is important to understand the specific physiological changes of multiple pregnancy and minimize the complications not only of the multiple pregnancy itself but also of the beta-adrenergic agents for tocolysis and their interaction with the agents administered for anesthetic management.

In summary, we report five patients with triplet pregnancy who underwent cesarean section, in whom lumbar epidural anesthesia was selected. All of the patients showed mild to severe toxemia of pregnancy and premature labor, and all received ritodrine for tocolysis. Tachycardia, pulmonary congestion, and pulmonary edema were encountered, but the anesthetic management and operation nevertheless proceeded uneventfully without any intraoperative complications.

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