—Original—

Effects of Intravenous Infusion Rate of Oxytocin on Thoracic Epidural Pressure in Parturients Undregoing Elective Cesarean Section

Takehiko Kikutani, Masayuki Oshima, Kikuzo Sugimoto and Yoichi Shimada

Department of Anesthesiology, Nippon Medical School Second Hospital

Abstract

The effects of intravenous oxytocin on thoracic epidural pressure during cesarean section were studied in 90 parturients (American Society of Anesthesiologists physical atatus class I or II) after obtaining informed consent. The subjects were randomized to either a control (control group; n = 30), bolus (bolus group; n = 30) or drip treatment group (drip group; n = 30). The subjects were anesthetized with 11～12 mg of intrathecal isobaric bupivacaine (0.5%). An epidural catheter placed at Th 11/12 was connected to a pressure transducer to continuously monitor thoracic epidural pressure. Ten units of oxytocin were administered over 30 seconds in the bolus group and over 5 minutes in the drip group after fetus delivery. We analyzed epidural pressure, mean blood pressure, and heart rate, until 5 minutes after fetus delivery. Epidural pressures in both bolus and drip groups increased after fetus delivery compared with control group ($P < 0.0001$). Epidural pressure immediately after placental delivery in the bolus group was higher than in the control group ($p < 0.0001$) and epidural pressure at 5 minutes after fetus delivery in the drip group was higher than in the control group ($p = 0.0452$). There were no significant differences in changes in blood pressure and heart rate among the three groups. We concluded that the increase in epidural pressure with intravenous administration of oxytocin 10 units over 5 minutes was lower than with intravenous administration of oxytocin 10 units over 30 seconds after fetus delivery. (J Nippon Med Sch 2003; 70: 475–479)

Key words: epidural pressure, obstetrical anesthesia, cesarean section, oxytocin

Introduction

Oxytocics have been used to facilitate uterine contraction, and to prevent postpartum hemorrhage during cesarean section[1,2]. Oxytocin, one of the oxytocics that are available for intravenous administration, is a powerful stimulator of contraction in the uterus[1,3], but bolus infusion of oxytocin induces an increase in venous compliance that causes hypotension and tachycardia[4,5]. Because of its short half-life[6], intravenous administration rates and doses of oxytocin for induction and augmentation of labor or prevention of postpartum hemorrhage were empirical and variable[2,7]. We reported the effects of bolus infusion of methylergometrine and oxytocin on thoracic epidural pressure during cesarean section, and concluded the increase in epidural pressure after oxytocics administration was associated with uterine contraction[8]. In our report, the epidural pressure

Correspondence to Takehiko Kikutani, MD, Department of Anesthesiology, Nippon Medical School Second Hospital, 1–396 Kosugi-cho, Nakahara-ku, Kawasaki City, Kanagawa 211–8533, Japan
E-mail: take.145@viola.ocn.ne.jp
Journal Website (http://www.nms.ac.jp/jnms/)

increased immediately after bolus infusion of oxytocin but decreased at 5 minutes after the administration. In this study, we examined the effects of the intravenous infusion rate of oxytocin on thoracic epidural pressure in parturients undergoing cesarean section under spinal anesthesia.

Materials and Methods

This study was approved by the Nippon Medical School Second Hospital Ethics Committee. After obtaining informed consent, we studied 90 parturients (ASA; American Society of Anesthesiologists physical status, class I or II) who were free of any significant cardiac disorder and pre-eclampsia or had not received tocolytic agents. The subjects were scheduled for elective cesarean section under spinal anesthesia and were not administered intravenous ephedrine to treat hypotension after the induction of spinal anesthesia until fetus delivery. We randomly assigned the subjects into three groups; a control group (n=30), a bolus group (n=30) and a drip group (n=30).

The subjects received 0.5 mg of intramuscular atropine as a premedication upon arrival in the operating room. An intravenous line was placed in their forearm. The subjects received intravenous fluid (Solita-T No. 1: Na 90 mEq/L, Cl 70 mEq/L, L-Lactate 20 mEq/L, Glucose 2.6 g/dl, Shimizu-Takeda Chemical Industries, Osaka, Japan) at a rate of 10 ml/kg/hr. The subjects were placed in the right decubitus position. The epidural space was identified at the Th 11/12 intervertebral space using the "loss of resistance to saline" technique. An epidural catheter for 18G needles (Hakko, Tokyo, Japan) was placed through a 17G Tuohy needle (Super Dull, Hakko, Tokyo, Japan) and was threaded 5 cm cephalad. After the catheter was filled with 0.3 ml of normal saline, it was connected to a pressure transducer (DTX™Plus, Becton Dickinson, Franklin Lakes, U.S.A.). For spinal anesthesia, we administered 11～12 mg of isobaric bupivacaine (Marcain® Injection spinal 0.5% Isobaric, AstraZeneca, London, U.K.) intrathecally at the L 3/4 intervertebral space using a 25G Quincke needle (Spinocan®, B. Brown, Tuttlingen, Germany). After placing the subject in a supine position, we started the continuous measurement of epidural pressure (Bioview 4000, NEC, Tokyo, Japan) using the external auditory canal as the zero reference point. Supine hypotension syndrome was treated by manual left uterine displacement. The intravenous fluid was administered at a steady rate until 5 minutes after fetal delivery.

A skin incision was made 15 minutes after spinal anesthesia was administered, when sensory block level was confirmed above Th6. After double ligation of the umbilical cord, we administered 10 IU of oxytocin (Atonin®-O, Teikoku Hormone, Tokyo, Japan) diluted in 10 ml of normal saline as an intravenous injection over 30 seconds in the bolus group, and 10 IU of oxytocin diluted in 20 ml of normal saline as an intravenous infusion over 5 minutes using an infusion pump system (TE-311, Terumo, Tokyo, Japan) in the drip group. In the control group, we administered intravenous bolus infusion of methylergometrine 0.2 mg at 5 minutes after fetus delivery. Uterine manipulation after placental delivery was performed while the uterus was displaced outside the abdominal cavity.

We analyzed epidural pressure, non-invasive blood pressure and heart rate in the three groups 5 minutes after spinal anesthesia, immediately before skin incision, immediately after placental delivery, and 5 minutes after fetal delivery.

The subjects were sedated with intravenous midazolam 10 mg and received lactate ringer or/and hydroxyethylstarch infusions to maintain bleeding and hypotension 5 minutes after fetus delivery. Intravenous ephedrine was also used to treat hypotension. At the end of the surgery, the epidural catheter was connected to a portable infusor filled with local anesthetics and opioids for postoperative analgesia.

Data are expressed as mean±SD except for patient demographics, which are expressed as median and range, or proportion of subjects. The Kruskal-Wallis test was used to analyze demographic data, and a repeated measures analysis of variance (ANOVA) or factorial ANOVA with Scheffe test for post hoc comparisons were used to analyze the epidural pressure, mean blood pressure, and heart rate data. Statistical significance was taken as $P<0.05$.

Table 1 Patient Demographics and Spinal Anesthesia Data

Variable *	Control Group (n=30)	Bolus Group (n=30)	Drip Group (n=30)
Age (year)	31.5 (22—38)	31.5 (24—40)	31.5 (25—40)
Height (cm)	157 (145—170)	158 (147—171)	158 (145—172)
Weight (kg)	62.5 (52—89)	63.5 (52—86)	62 (46—89)
Gestation (week)	38 (31.7—41.7)	38.2 (33—41.8)	38.1 (33.8—41.4)
ASA class Ⅰ/Ⅱ	23/7	23/7	23/7
Analgesia (Th)	4 (2—5)	4 (2—5)	4 (2—5)

Values are median (range) or proportion of subjects. Statistical analysis was performed with Kruskal-Wallis test. * There were no statistical significant differences among the three groups. ASA: American Society of Anesthesiologists physical status.

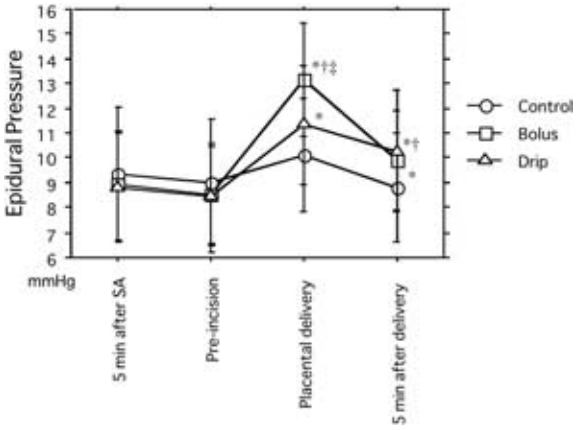

Fig. 1 Epidural pressures in the bolus and drip groups increased after fetus delivery compared to the values obtained before skin incisions ($p<0.0001$: both groups). The increases in epidural pressures in the bolus and drip groups were higher than in the control group ($P<0.0001$: both groups). Data are expressed as mean±SD. Statistic analysis was performed with repeated measure analysis of variance and factorial analysis of variance with Scheffe test for post hoc comparisons. *$P<0.05$ compared with 5 min after SA or Pre-incision; †$P<0.05$ compared with control group; ‡$P<0.05$ compared with drip group. SA: Spinal Anesthesia, Control: Control group, Bolus: Bolus group, Drip: Drip group.

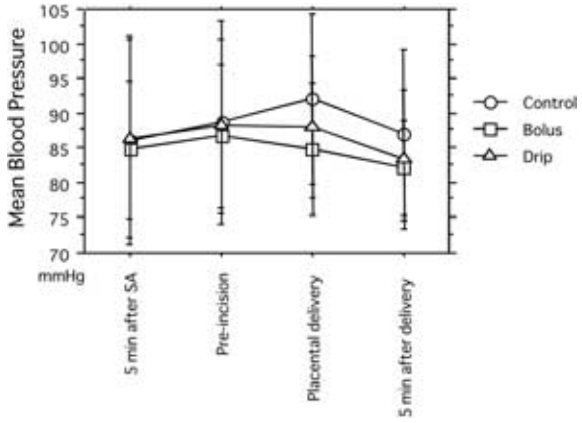

Fig. 2 Mean blood pressure changes. There were no statistical significant differences in mean blood pressures among the three groups. Data are expressed as mean±SD. Statistic analysis was performed with repeated measure analysis of variance. SA: Spinal Anesthesia, Control: Control group, Bolus: Bolus group, Drip: Drip group.

Results

There was no significant difference in patient demographics or the level of sensory block among the three groups (**Table 1**).

Epidural pressures (**Fig. 1**) in the both bolus and drip groups significantly increased after fetus delivery compared to the values obtained before the skin incisions were made ($p<0.0001$: both groups), and there were significant differences in epidural pressures among the three groups ($p<0.0001$). Epidural pressure in the bolus group significantly increased after fetus delivery compared to the drip ($p<0.0001$) and control ($p<0.0001$) groups, and epidural pressure in the drip group significantly increased after fetus delivery compared to the control group ($p<0.0001$). Epidural pressures at placental delivery in the bolus group were higher than in the control ($p<0.0001$) and drip ($p=0.0135$) groups. Epidural pressure at placntal delivery in the drip group was higher than in the control group ($p=0.452$).

Mean blood pressures (**Fig. 2**) in both the bolus

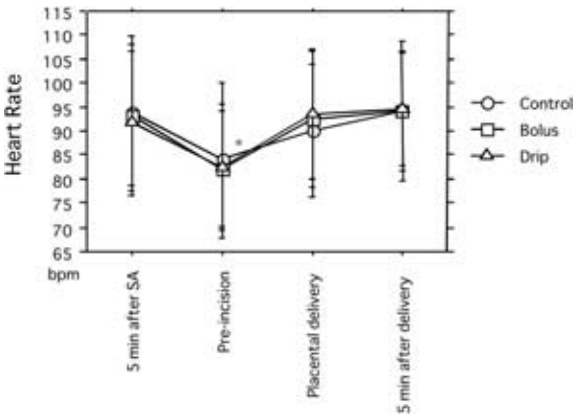

Fig. 3 Heart rates decreased at pre-incision in all groups ($p < 0.0001$). There were no statistical significant differences in the changes in heart rates among the three groups. Data are expressed as mean ± SD. Statistic analysis was performed with repeated measure analysis of variance with Scheffe test for post hoc comparisons. *$P < 0.05$ compared with 5 min after SA and placental delivery and/or 5 min after delivery in all groups. SA: Spinal Anesthesia, Control: Control group, Bolus: Bolus group, Drip: Drip group.

and drip groups decreased after fetus delivery ($p = 0.026$: bolus group, $p = 0.0089$: drip group). There were no significant differences in mean blood pressures among the three groups ($P = 0.1439$).

Heart rates (**Fig. 3**) were significantly lower immediately before skin incision in all groups ($P < 0.0001$). There were no significant differences in the changes in heart rates among the three groups ($P = 0.7109$).

Discussion

It is well known that uterine contraction displaces the blood inside the uterus towards the venous system and causes "auto-transfusion" that results in an increase of 300 to 500 m*l* in central venous blood as well as an increase in cardiac output of 10～25%[9]. The "auto-transfusion" is observed even when a parturient receives paracervical and pudendal nerve block, or caudal analgesia[10]. The increased blood flow through the inferior vena cava during uterine contraction also causes a blood flow increase in the epidural venous plexus, resulting in an increase in lumbar epidural pressure[11], and the increases in central venous pressure and epidural pressure are simultaneous with an increase in intrauterine pressure[12].

In our study, oxytocin used to facilitate uterine contraction during cesarean section increased thoracic epidural pressure compared to the control group. The differences in thoracic epidural pressures among the groups may reflect the differences in the degree of uterine contraction. Oxytocin has a shorter onset time and its half-life is only a few minutes[6]. Although oxytocin can increase central venous pressure by augmenting uterine contraction, the effect on central venous pressure after intravenous administration of oxytocin is short and slight[13,14]. The effects of oxytocin on uterine contraction depend on the numbers of oxytocin receptors on the uterus rather than plasma concentration of oxytocin[3], and the oxytocin receptors on the pregnant uterus increase at term under the effects of estrogen[15]. These might explain why bolus infusion of oxytocin caused a higher increase in epidural pressure compared to drip infusion of oxytocin immediately after placental delivery. Intravenous oxytocin over 5 IU administered at a rate of 1.0 IU/min had no beneficial effects on uterine tone or blood loss during elective cesarean section[4]. The results of our study suggest that intravenous oxytocin at a rate from 1.0 to 2.0 IU/min would decrease the degree of elevation in epidural pressure with uterine contraction induced by intravenous bolus administration of oxytocin over 5 IU after fetus delivery.

The volume effects of the epidural space could theoretically influence the spread of sensory blockade during regional anesthesia and result in decreased initial doses of local anesthetics[16,17] or "top-ups"[18,19]. On the other hand, it has been reported that uterine contraction dose not affect the spread of sensory blockade with lumbar epidural anesthesia during cesarean section[20]. In the report, epidural catheters were placed in the lower lumbar region and clinically smaller doses of local anesthetics were administered during uterine contraction. In our study, epidural catheters were placed in the thoracic region and thoracic epidural pressure increased after fetus delivery. While the possibility of volume effect in the epidural space remains to be explored,

our data suggest that it would be prudent to avoid epidural injection in the thoracic region to prevent high spread of sensory or motor blockade in parturients undergoing cesarean section.

In conclusion, additional epidural injections can be safely administered in parturients treated with intravenous drip infusion of oxytocin after fetus delivery during cesarean section under thoracic epidural or combined spinal and thoracic epidural anesthesia. In contrast, thoracic epidural injection should be avoided immediately after intravenous bolus infusion of oxytocin, but is acceptable after 5 minutes of the bolus administration if hypotension and tachycardia have not occurred.

References

1. Zingg HH: Oxytocin and uterine activity. Front Horm Res 2001; 27: 57–65.
2. Chou MM, Mackenzie IZ: A prospective, double-blind, randomized comparison of prophylactic intramyometrial 15-methyl prostaglandin F 2 alfa, 125 micrograms, and intravenous oxytocin, 20 units, for the control of blood loss at elective cesarean section. Am J Obstet Gynecol 1994; 171: 1356–1360.
3. Wray S: Uterine contraction and physiological mechanisms of modulation. Am J Phsiol 1993; 264: C 1–18.
4. Hendricks CH, Brenner WE: Cardiovascular effects of oxytocic drugs used post partum. Am J Obstet Gynecol 1970; 108: 751–760.
5. Secher NJ, Arnsbo P, Wallin L: Haemodynamic effects of Oxytocin (Syntocinon®) and methyl ergometrine (Methergin®) on the systemic and pulmonary circulations of pregnant anesthetized women. Acta Obstet Gynecol Scand 1978; 57: 97–103.
6. Saameli K: An indirect method for the estimation of oxytocin blood concentration and half-life in pregnant women in near term. Am J Obstet Gynecol 1963; 85: 186–192.
7. Sarna MC, Soni AK, Gomez M, Oriol NE: Intravenous oxytocin in patients undergoing elective cesarean section. Anesth Analg 1997; 84: 753–756.
8. Kikutani T, Shimada Y: Effects of methylergometrine and oxytocin on thoracic epidural pressure during cesarean section. J Obstet Gynaecol Res 2003; 29: 180–185.
9. Ueland K, Hansen JM: Cardiovascular dynamics. 2. Posture and uterine contractions. Am J Obstet Gynecol 1969; 103: 1–7.
10. Ueland K, Hansen JM: Cardiovascular dynamics. 3. Labor and delivery under local and caudal analgesia. Am J Obstet Gynecol 1969; 103: 8–18.
11. Bromage PR: Continuous lumbar epidural analgesia for obstetrics. Can Med Assoc J 1961; 85: 1136–1140.
12. Bonica JJ: Obstetric anesthesia and analgesia, 1980; pp 7, World federation of society of anaesthesiologists, Amsterdam.
13. Anderson TW, De Pauda CB, Stenger V, Prystowsky H: Cardiovascular effects of rapid intravenous injection of synthetic oxytocin during elective cesarean section. Clin Pharmcol Ther 1965; 6 : 345–349.
14. Vaughan Williams C, Johnson A, Ledward R: A comparison of central venous presssure changes in the third stage of labour following oxytocic drugs and diazepam. J Obstet Gynaecol Br Commonw 1974; 81: 596–599.
15. Fuchs AR, Fuchs F, Husslein P, Soloff MS: Oxytocin receptors in the human uterus during pregnancy and parturition. Am J Obstet Gynecol 1984; 150: 734–741.
16. Bonica JJ: Maternal anatomic and physiological alternations during pregnancy and parturition. Principles and practice of obstetric analgesia and anesthesia 2nd ed (Bonica JJ, McDonald JS, eds) , 1995; pp 45–82, Williams and Wilkins, Malvern.
17. Bromage PR: Mechanism of action of extradural analgesia. Br J Anaesth 1975; 47: 199–211.
18. Blumgart CH, Ryall D, Dennision B, Thompson-Hill LM: Mechanism of extension of spinal anaesthesia by extradural injection of local anaesthetic. Br J Anaesth 1992; 69: 457–460.
19. Stienstrd R, Dahan A, Alhadi BZ, van Kleef JW, Burm AG: Mechanism of action of an epidural top-up in combined spinal epidural anesthesia. Anesth Analg 1996; 83: 382–386.
20. Sivakumaran C, Ramanathan S, Chalon J, Turndorf H: Uterine contractions and spread of local anesthetics in the epidural space. Anesth Analg 1982; 61: 127–129.

(Received, June 11, 2003)
(Accepted, June 30, 2003)