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ORIGINAL

Analgesic Effect of Bupivacaine –Dexmedetomidine versus Bupivacaine– Sufentanil in Spinal Anesthesia during Cesarean Section

Efecto analgésico de la bupivacaína-dexmedetomidina frente a la bupivacaína-sufentanilo en la anestesia raquídea durante la cesárea

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Abstract

The aim of this study is evaluating the analgesic effect of bupivacaine- dexmedetomidine versus bupivacaine- sufentanil in spinal anesthesia during cesarean section. In this double blinded randomized clinical trial study, 60 parturients of ASA class I and II undergoing elective cesarean section were randomly allocated into one of the two groups: group 1 received 12.5 mg bupivacaine (0.5%) + 5µg sufentanil and group 2 received 12.5 mg bupivacaine (0.5%) + 2.5 µg dexmedetomidine by 25 Quincke needle, in midline approach and in levels of L3-L4 and L2-L3 in a sitting position. Routine monitoring included ECG, SPO2, HR, and BP was done for each patient. Maternal heart rate and blood pressure were registered before spinal anesthesia. Sensory tests were done assessing the loss of pinprick sensation by a 23G slowed needle every two minutes. The time for sensory blockade to reach T4 level as well as the time for its returning to two lower level (T6) were recorded and the surgery begun when block reached T4 level. Then, the level of anesthesia was checked every ten minutes until the two pinprick block level regressed. The umbilical cord blood samples were taken after delivery to determine the PH and newborn's Apgar scores were recoreded and assessed at minutes of 1 and 5. At the end of surgery, the patient's pain score were determined using visual analog scale (VAS). Common complications of spinal anesthesia including hypotension (SBP <20% initial blood pressure or less than 90 mmHg, bradycardia (HR <20% initial heart rate), nausea, vomiting, pruritus, and respiratory depression (RR <10) were also checked and recorded. Time for sensory block to reach T4, regression to T6 sensorry level and duration of analgesic time and block motor regression time in dexmedetomidine group was longer than sufentanil group and use of ephedrine was more in dexmedetomidine group than sufentanil. Considering pH of umbilical cord blood, two group were not signisicantly different. Two groups were not significantly different in terms of other adverse effects incidence (nausea, vomiting, headache, and pruritus) and Apgar score at minutes of 1 and 5. Based on results, addition of dexmedetomidine to bupivacaine in spinal anesthesia, during cesarean section can be associated with greater success and fewer complications. Sensory and motor block duration is significantly longer in dexmedetomidine group and provide intraoperative and postoperative longer and better analgesia and doesn't have any significant complication for mother and infant.

Key words: Analgesic, Bupivacaine,Dexmedetomidine, Bupivacaine, Sufentanil, Spinal Anesthesia, Cesarean.

Resumen

El objetivo de este estudio es evaluar el efecto analgésico de la bupivacaína-dexmedetomidina frente a la bupivacaína-sufentanilo en la raquianestesia durante la cesárea. En este estudio de ensayo clínico aleatorizado doble ciego, 60 parturientas de clase I y II de ASA sometidas a cesárea electiva se asignaron aleatoriamente a uno de los dos grupos: el grupo 1 recibió 12,5 mg de bupivacaína (0,5 %) + 5 µg de sufentanilo y el grupo 2 recibió 12,5 mg bupivacaína (0,5%) + 2,5 µg dexmedetomidina mediante aguja de Quincke 25, en abordaje de línea media y en niveles de L3-L4 y L2-L3 en sedestación. El monitoreo de rutina incluyó ECG, SPO2, HR y BP se realizó para cada paciente. La frecuencia cardíaca materna y la presión arterial se registraron antes de la anestesia espinal. Se realizaron pruebas sensoriales evaluando la pérdida de la sensación de pinchazo con una aguja ralentizada de 23G cada dos minutos. Se registró el tiempo para que el bloqueo sensorial alcanzara el nivel T4 así como el tiempo para que volviera a los dos niveles inferiores (T6) y la cirugía comenzó cuando el bloqueo alcanzó el nivel T4. Luego, el nivel de anestesia se verificó cada diez minutos hasta que el nivel de bloqueo de dos pinchazos retrocedió. Se tomaron muestras de sangre del cordón umbilical después del parto para determinar el PH y se registraron y evaluaron los puntajes de Apgar del recién nacido en los minutos 1 y 5. Al final de la cirugía, se determinó el puntaje de dolor del paciente mediante escala analógica visual (VAS). Complicaciones comunes de la anestesia espinal que incluyen hipotensión (PAS <20% presión arterial inicial o menos de 90 mmHg, bradicardia (FC <20% frecuencia cardíaca inicial), náuseas, vómitos, prurito y depresión respiratoria (RR <10) también fueron revisadas y El tiempo para que el bloqueo sensorial alcance T4, la regresión al nivel sensorial T6 y la duración del tiempo analgésico y el tiempo de regresión motora del bloqueo en el grupo de dexmedetomidina fue mayor que en el grupo de sufentanilo y el uso de efedrina fue mayor en el grupo de dexmedetomidina que en el de sufentanilo. sangre, dos grupos no fueron significativamente diferentes Dos grupos no fueron significativamente diferentes en cuanto a la incidencia de otros efectos adversos (náuseas, vómitos, dolor de cabeza y prurito) y la puntuación de Apgar en los minutos 1 y 5. Según los resultados, la adición de dexmedetomidina a bupivacaína en anestesia espinal, durante la cesárea se puede asociar con mayor éxito y menos complicaciones. La duración del bloqueo sensorial y motor es significativamente larga er en el grupo de dexmedetomidina y proporciona una analgesia intraoperatoria y postoperatoria más larga y mejor y no tiene ninguna complicación significativa para la madre y el bebé.

Palabras clave: analgésico, bupivacaína, dexmedetomidina, bupivacaína, sufentanilo, anestesia espinal, cesárea.

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Introduction

Cesarean section is performed under general anesthesia, spinal, epidural or spinal-epidural technique[1]. However, neuraxial techniques are more popular among anesthesiologists due to high morbidity and mortality incidence caused by complications during airway management in pregnant patients who undergo general anesthesia and high level of aspiration risk in these patients[2,3]. Neuraxial anesthesia has been proposed as elective anesthesia for caesarean section in most countries[4]. One of the most common contraindication to neuraxial anesthesia includes a decrease in blood pressure[5]. Compared to spinal anesthesia, this complication occurs more frequently in epidural analgesia[6]. Nevertheless, regional anesthesia has become the preferred technique over epidural analgesia for caesarean delivery throughout the world due to its availability and higher success rates, and fast block onset and technique implementation. Because of its limited duration, other techniques are taken into consideration instead of spinal anesthesia in order to control postoperative pain such as intravenous patient-controlled analgesia method (PCA); however, this method is not without any problem due to restricted and expensive PCA pumps and possible loss of its function. Therefore, use of adjuvant drugs to increase the duration of analgesia after surgery by single shot spinal is taken into consideration. Opioids including fentanyl, sufentanil, and morphine are addictive drugs which are used for analgesic purposes[7-9]. However, opioid use is associated with increased adverse effects such as nausea, vomiting, constipation, urinary retention, and early or unpredictable respiratory depression[10]. Alpha2-adrenergic agonists like clonidine and more recently dexmedetomidine have been considered because they able to speed up the effects of local anesthetics without opioids side effects and to increase the duration of postoperative analgesia[11-13]. Other additive drugs are magnesium sulfate and vasoconstrictors like epinephrine and neostigmine[14,15]. In the current study, the analgesic effect of dexmedetomidine addition to bupivacaine was compared with the analgesic effect of sufentanil addition to bupivacaine in spinal anesthesia during cesarean surgery.

Material and methods

This double blinded randomized clinical trial was conducted in Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Sixty parturient of ASA class I and II undergoing elective cesarean section included in this study. This study was approved by the ethics committee and the written informed consent was obtained from all patients. Patients with multiple pregnancies, hypertension, placenta previa, placental detachment or any other organic problems were excluded from the study. Patients were randomly allocated into one of the two groups using random number table. group 1 received 12.5 mg bupivacaine (0.5%) + 5µg sufentanil and group 2 received 12.5 mg bupivacaine (0.5%) + 2.5 µg dexmedetomidine by 25 Quincke needle, in midline approach and in levels of L3-L4 and L2-L3 in a sitting position. Routine monitoring included ECG, SPO2, HR, and BP was done for each patient. Maternal heart rate and blood pressure were registered before spinal anesthesia. Performing spinal anesthesia in a sitting position, the patients then immediately were made to lie supine. The hypotension episodes were treated with an intravenous bolus of ephedrine 5 mg, with a maximum bolus dose of 10 mg. In the event of bradycardia (HR <20) 0.5 mg atropine was administered. The time of drug injection into the intrathecal space was considered as onset time. Sensory tests were done assessing the loss of pinprick sensation by a 23G slowed needle every two minutes. The time for sensory blockade to reach T4 level (appropriate level of anesthesia in caesarean section) as well as the time for its returning to two lower level (T6) were recorded and the surgery begun when block reached T4 level. Then, the level of anesthesia was checked every ten minutes until the two pinprick block level regressed. The umbilical cord blood samples were taken after delivery to determine the PH and newborn's Apgar scores were reviewed and assessed at minutes of 1 and 5. At the end of surgery, the patient's pain score were determined using visual analog scale (VAS) ranged from 0 to 10 (zero: no pain and ten: worst possible pain). Duration of analgesia (VAS <4) and complete motor block regression time were assessed and recorded based on Modified Bromage Scale Assessment (no motor block = 0, hip block 1 =, hip and knee block = 2, hip, knee, and ankle block = 3). Complete regression of motor block to Bromage Scale is considered as zero. At the time of vas> 4, meperidine (50 mg) was administered through intramuscular injection. Common complications of spinal anesthesia including hypotension (SBP <20% initial blood pressure or less than 90 mmHg, bradycardia (HR <20% initial heart rate), nausea, vomiting, pruritus, and respiratory depression (RR <10) were also checked and recorded.

Results

This clinical trial was conducted on 60 parturients undergoing elective cesarean section. Mean age of participants in sufentanil group was 29.67 and 29.86 in dexmedetomidine group (p.value=0.494). Two groups were significantly different regarding, mean time of sensory block for reaching to T4 and regression to T6 level, duration of analgesia (based on VAS score), time for removal of motor block (according to Bromage Scale), and amount of ephedrine dose adminstered during surgery for compensating the hypotension. Time for sensory block to reach T4, regression to T6 sensorry level and duration of analgesic time and block motor regression time in dexmedetomidine group was longer than sufentanil group and use of ephedrine was more in dexmedetomidine group than sufentanil. Considering pH of umbilical cord blood, two group were not signisicantly different. Two

groups were not significantly different in terms of other adverse effects incidence (nausea, vomiting, headache, and pruritus) and Apgar score at minutes of 1 and 5.

Discussion

This study has compared the analgesic effect of dexmedetomidine addition to bupivacaine with sufentanil addition to bupivacaine regarding spinal anesthesia during cesarean section. Among the examined variables, two groups were statistically different in terms of mean time to T4 and regress to T6 sensory level, duration of analgesia (VAS<4), motor block regression time (Bromage Scale), and the amount of administered dose of ephedrine. The onset time of sensory block to T4 ,regression to T6 sensorry level and duration of analgesic time and block motor regression time was longer in dexmedetomidine group but occurrence of hypotention and use of ephedrine was more in dexmedetomidine group more than sufentanil group. Umbilical cord blood pH values in the two groups were not significant either. However, two groups were not significantly different regarding the incidence of side effects (nausea, vomiting, headache, and pruritus) and Apgar score at minutes of 1 and 5. Kurhekar et al. done a double blind study in patients undergoing gynaecological surgeries under spinal anaesthesia involving 25 patients in each group. Group M received 15 mg of 0.5% hyperbaric bupivacaine with 250 µg of morphine while Group D received 15 mg of 0.5% hyperbaric bupivacaine with 2.5 µg of dexmedetomidine . Time for first rescue analgesic and total analgesic demand were similar in both groups. Duration of sensory and motor block was significantly higher in dexmedetomidine group. Itching was noticed in 36% and nausea in 52% of patients in the morphine group, either of which was not seen in dexmedetomidine group[16].

Yong-Hong Bi et al. evaluated the effect of low dose of dexmedetomidine as an adjuvant to bupivacaine in cesarean surgery on sixty parturients with the American Society of Anesthesiologists (ASA) physical status I or II anesthetized with intrathecal bupivacaine(10mg) alone or in combination with dexmedetomidine (3 µg and 5 µg). This group showed that the use of dexmedetomidine especially at the dose of 3µg as an adjuvant to bupivacaine in cesarean surgery provides better intraoperative somato-visceral sensory block characteristcs and postoperative analgesia, which produced no influence on Apgar scores, side effects and stress response[17].

Xiao et al. compared the intrathecal administration of different doses of bupivacaine and sufentanil during cesarean delivery of parturients with severe preeclampsia. This study was performed on 200 parturients who were under spinal epidural anesthesia during cesarean section. They divided into four groups and received 4-6-8-10 mg of hyperbaric intrathecal bupivacaine mixed with 2.5 µg of sufentanil. Spinal anesthesia at T6 sensory level was achieved within 10 minutes and no added medication was required during the surgery. It was observed that a reduced dose of intrathecal bupivacaine can decrease the incidence of maternal hypotension. The incidence of hypotension was higher in groups received 8 and 10 mg in comparison with other groups received 4 and 6 mg. Meanwhile, in the 4-mg- group, satisfaction of muscle relaxation was lower than the other groups[18].

Bang et al. compared the clinical efficacy of addition of various doses of sufentanil to hyperbaric bupivacaine 0.5% for parturients undergoing cesarean section under spinal anesthesia. The effects of adding 2.5 and 5 µg of sufentanil were explored on 105 parturients divided into 3 groups. Subjects were divided into group 1(control), group 2 (sufentanil 2.5 µg), and group 3 (sufentanil 5 µg), each combined with hyperbaric bupivacaine 0.5%. Variables like maximum sensory block and motor block, quality of anesthesia and analgesia during surgery, duration of anesthesia, and side effects were evaluated considering doses. No significant difference was noted in 3 groups, in terms of maximum level of sensory block and motor block. The recovery of sensory block in group 3 was considerably slower in comparison with group 1. The quality of intraoperative anesthesia and its effective duration, in term of muscle relaxation, improved with the addition of sufentanil dose. Nausea and vomiting occurred in sufentanil group. Moreover, incidence of pruritus and hypotension was directly related to the dose of intrathecal sufentanil. It was decided that addition of 2.5 µg sufentanil can bring about adequate and appropriate intraoperative anesthesia, as well as minimum postoperative complications for the mother[19].

Another study by Sun et al. compared the effect of intrathecal bupivacaine alone, with bupivacaine + Fentanyl and bupivacaine + dexmedetomidine in c-section. Ninety full term parturients with ASA class I and were divided into 3 groups: group B, group F+B, and group D+B. It was found that the regression to T10 level was significantly longer in group D+B. The sensory block was also longer in group D+B. However, no significant difference was observed in sensory block duration. Postoperative pain was considerately delayed in group D+B, and no significant difference was recognized in infants' Apgar scores. Thus, it was concluded that, in cesarean section, administering dexmedetomidine as an adjuvant with bupivacaine can provide a more appropriate intraoperative and postoperative anesthesia, without any side effect or negative effect on infant's Apgar score[20].
Hanoura et al. showed the effect of dexmedetomidine combined with bupivacaine and fentanyl on postoperative anesthesia and analgesia, in c-section under spinal epidural anesthesia. Fifty full term parturients with ASA class I and II were divided into two groups: group FB and group DBF. There was no significant difference in the onset of block to T4 sensory level. Postoperative pain was considerately delayed in group DBF, and no difference was recognized

in infants' Apgar scores. It was then inferred that addition of dexmedetomidine can improve the intraoperative and postoperative conditions and doesn't have any significant complication for mother and infant[21].

In a research by Halder et al. in India, the effects of various doses of dexmedetomidine as adjuvant in bupivacaine in subarachnoid block for traumatized lower limb orthopedic surgery, under spinal anesthesia were examined. It was performed on 80 patients (20- 60 yrs). Patients were divided into two equal groups of D5 and D10. Group D5 received 3 mg of hyperbaric bupivacaine 0.5% + 5 µg dexmedetomidine in 0.5 cc of normal saline, intrathectally. Likewise, group D10 received 3 mg of hyperbaric bupivacaine 0.5% + 10 µg dexmedetomidine in 0.5 cc of normal saline, intrathectally. Sensory and motor block in group D 10 was faster. Furthermore, sensory and motor block duration and time to first analgesic use were longer in D10[22].

Numerous reports were published regarding the safe use of dexmedetomidine in infants and children. In two studies performed on 140 children of 1-7 yrs, dexmedetomidine was administered as sedation for CT and MRI compared to propofol and midzolam. The results were desirable and no complications were recognized. In one report, 1-3 micro/kg of dexmedetomidine was proposed as the only administered anesthetic for pediatric anesthesia under direct laryngoscopy and bronchoscopy to maintain spontaneous breathing through providing suitable surgery and hemodynamic conditions. Dexmedetomidine was administered as premedication before surgery, sedation and analgesic agent during painful and stressful procedures such as CT and MRI intravenously, intramuscularly, intranasally, and caudally. The use of dexmedetomidine had positive effects and no side effects had been observed[23,24].

In a study by Karaman et al., dexmedetomidine (in dose of 200mcg/kg) was administered to pregnant rats subcutaneously, and no teratogenic effect was observed. In another study, it was administered intravenously in dose of 96mcg/kg to pregnant rabbits. There was no teratogenic effect in this study either. The administered dose for rats was twice as much as the maximum dose recommended for human intravenously. Unlike, the administered dose for rabbits was as much as the maximum dose recommended for human intravenously[25].

Research on the effects of dexmedetomidine on physiology of uteroplacental and embryo indicates dexmedetomidine increases uterine contractions in rats and isolated human myometrium, at simulated clinical concentration Dexmedetomidine is a dose-dependent uterotonic agent; therefore, it can be used as an adjunct to oxytocin. In a study comparing the use of clonidine and epidural dexmedetomidine, less amount of dexmedetomidine was found in the maternal circulation, and a smaller amount was transferred to the fetal blood circulation and no side effect was observed[26,27].

Conclusion

The addition of dexmedetomidine to bupivacaine in spinal anesthesia, during cesarean section can be associated with greater success and fewer complications. Sensory and motor block duration is significantly longer in dexmedetomidine group and provide intraoperative and postoperative longer and better analgesia and doesn't have any significant complication for mother and infant.

Conclict of interest

No

Table I: Investigated variables in two groups.

Variables	Group 1 (sufentanil)	Group 2 (dexmedetomidine)	p. value
T4 (minutes)	4.4333	6.8000	0.0001
T6 (minutes)	82.0000	167.6667	0.0001
Analgesia time (minutes)	179.5000	311.8333	0.0001
Motor block (minutes)	103.1667	272.0000	0.0001
Ephedrine dose (mg)	4.0000	12.6667	0.0001
Umbilical cord	3377	3377	0.114

Table II: Frequency of side effects incidence in two groups.

Variable	Group 1(sufentanil)	Group 2 (dexmedetomidine)	P .value
Nausea /vomiting	7	7	0.999
Headache	0	0	1.000
Pruritus	2	0	0.492

Table III: Comparison of Apgar score mean at minutes of 1 and 5 in two groups.

Apgar	Group 1(sufentanil)	Group 2 (dexmedetomidine)	P .value
A1	8.9667	8.9667	73000
A5	9.9667	9.9667	73000

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