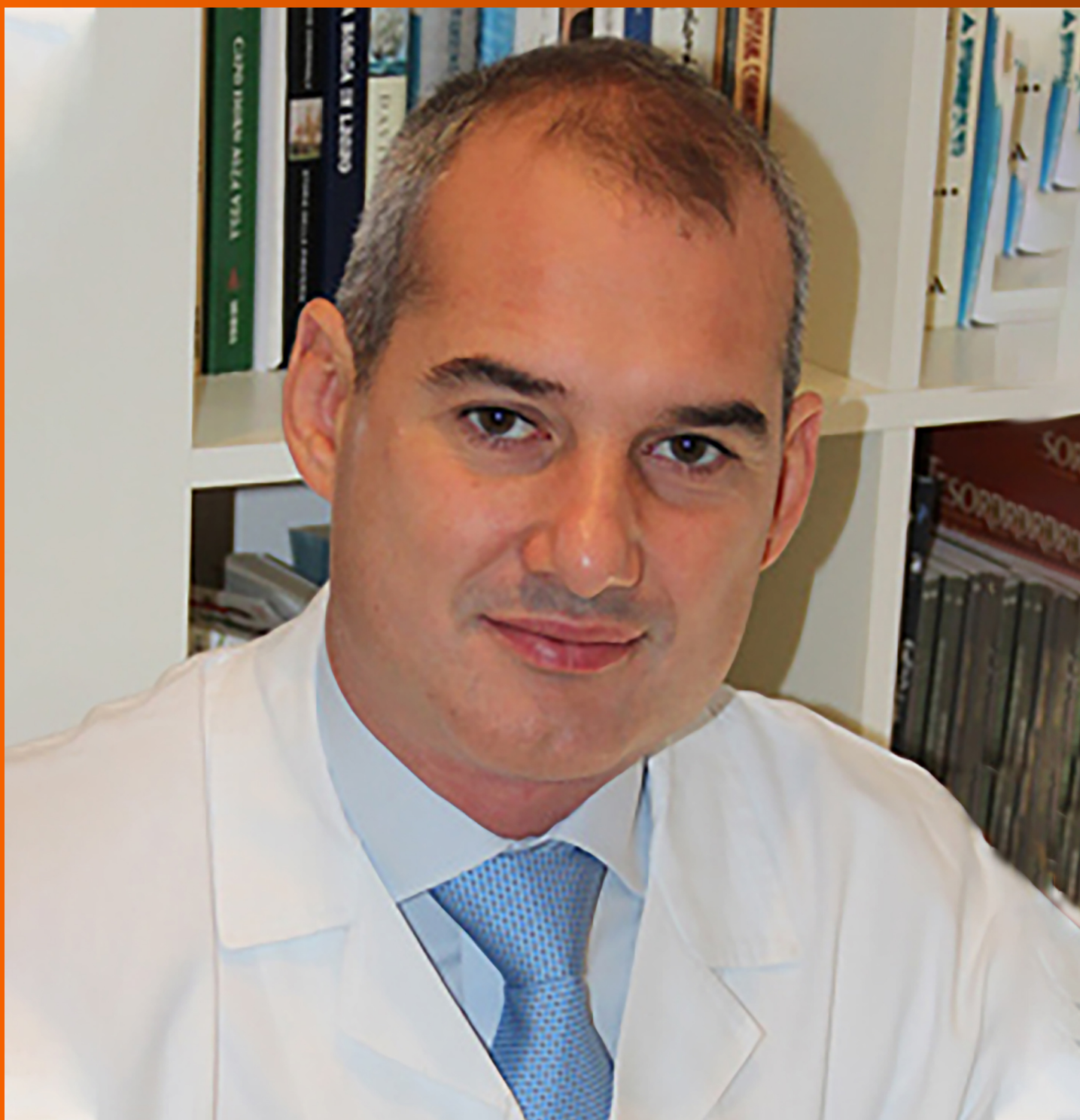


World Journal of *Clinical Cases*

World J Clin Cases 2021 August 16; 9(23): 6582-6963



Contents

Thrice Monthly Volume 9 Number 23 August 16, 2021

OPINION REVIEW

- 6582 COVID-19 pandemic, as experienced in the surgical service of a district hospital in Spain

Pérez Lara FJ, Jimenez Martinez MB, Pozo Muñoz F, Fontalba Navas A, Garcia Cisneros R, Garcia Larrosa MJ, Garcia Delgado I, Callejon Gil MDM

REVIEW

- 6591 Beta-carotene and its protective effect on gastric cancer

Chen QH, Wu BK, Pan D, Sang LX, Chang B

- 6608 Liver transplantation during global COVID-19 pandemic

Alfishawy M, Nso N, Nassar M, Ariyaratnam J, Bhuiyan S, Siddiqui RS, Li M, Chung H, Al Balakosy A, Alqassieh A, Fülöp T, Rizzo V, Daoud A, Soliman KM

- 6624 Nonalcoholic fatty pancreas disease: An emerging clinical challenge

Zhang CL, Wang JJ, Li JN, Yang Y

MINIREVIEWS

- 6639 Novel mechanism of hepatobiliary system damage and immunoglobulin G4 elevation caused by *Clonorchis sinensis* infection

Zhang XH, Huang D, Li YL, Chang B

- 6654 Intestinal microbiota participates in nonalcoholic fatty liver disease progression by affecting intestinal homeostasis

Zhang Y, Li JX, Zhang Y, Wang YL

- 6663 Theory and reality of antivirals against SARS-CoV-2

Zhao B, Yang TF, Zheng R

- 6674 Acute acalculous cholecystitis due to infectious causes

Markaki I, Konsoula A, Markaki L, Spornovasilis N, Papadakis M

ORIGINAL ARTICLE

Case Control Study

- 6686 Innate immunity – the hallmark of *Helicobacter pylori* infection in pediatric chronic gastritis

Meliş LE, Mărginean CO, Săsară MO, Mocan S, Ghiga DV, Bogliş A, Duicu C

Retrospective Study

- 6698 Effects on newborns of applying bupivacaine combined with different doses of fentanyl for cesarean section

Wang Y, Liu WX, Zhou XH, Yang M, Liu X, Zhang Y, Hai KR, Ye QS

- 6705** Awake fiberoptic intubation and use of bronchial blockers in ankylosing spondylitis patients
Yang SZ, Huang SS, Yi WB, Lv WW, Li L, Qi F
- 6717** Efficacy of different antibiotics in treatment of children with respiratory mycoplasma infection
Zhang MY, Zhao Y, Liu JF, Liu GP, Zhang RY, Wang LM
- 6725** Expression of caspase-3 and hypoxia inducible factor 1 α in hepatocellular carcinoma complicated by hemorrhage and necrosis
Liang H, Wu JG, Wang F, Chen BX, Zou ST, Wang C, Luo SW
- 6734** Increased morbidity and mortality of hepatocellular carcinoma patients in lower cost of living areas
Sempokuya T, Patel KP, Azawi M, Ma J, Wong LL

SYSTEMATIC REVIEWS

- 6747** Safety of pancreatic surgery with special reference to antithrombotic therapy: A systematic review of the literature
Fujikawa T, Naito S
- 6759** What paradigm shifts occurred in the management of acute diverticulitis during the COVID-19 pandemic? A scoping review
Gallo G, Ortenzi M, Grossi U, Di Tanna GL, Pata F, Guerrieri M, Sammarco G, Di Saverio S

CASE REPORT

- 6768** Pylephlebitis — a rare complication of a fish bone migration mimicking metastatic pancreatic cancer: A case report
Bezerra S, França NJ, Mineiro F, Capela G, Duarte C, Mendes AR
- 6775** Solitary seminal vesicle metastasis from ileal adenocarcinoma presenting with hematospermia: A case report
Cheng XB, Lu ZQ, Lam W, Yiu MK, Li JS
- 6781** Hepatic abscess caused by esophageal foreign body misdiagnosed as cystadenocarcinoma by magnetic resonance imaging: A case report
Pan W, Lin LJ, Meng ZW, Cai XR, Chen YL
- 6789** 2+0 CYP21A2 deletion carrier — a limitation of the genetic testing and counseling: A case report
Xi N, Song X, Wang XY, Qin SF, He GN, Sun LL, Chen XM
- 6798** Psoriasis treatment using minimally manipulated umbilical cord-derived mesenchymal stem cells: A case report
Ahn H, Lee SY, Jung WJ, Pi J, Lee KH
- 6804** Double intussusception in a teenage child with Peutz-Jeghers syndrome: A case report
Chiew J, Sambanthan ST, Mahendran HA

- 6810** Nedaplatin-induced syndrome of inappropriate secretion of antidiuretic hormone: A case report and review of the literature
Tian L, He LY, Zhang HZ
- 6816** Nasal metastases from neuroblastoma-a rare entity: Two case reports
Zhang Y, Guan WB, Wang RF, Yu WW, Jiang RQ, Liu Y, Wang LF, Wang J
- 6824** Nocardiosis with diffuse involvement of the pleura: A case report
Wang P, Yi ML, Zhang CZ
- 6832** Prenatal diagnosis of triphalangeal thumb-polysyndactyly syndrome by ultrasonography combined with genetic testing: A case report
Zhang SJ, Lin HB, Jiang QX, He SZ, Lyu GR
- 6839** Blue LED as a new treatment to vaginal stenosis due pelvic radiotherapy: Two case reports
Barros D, Alvares C, Alencar T, Baqueiro P, Marianno A, Alves R, Lenzi J, Rezende LF, Lordelo P
- 6846** Diverse microbiota in palatal radicular groove analyzed by Illumina sequencing: Four case reports
Tan XL, Chen X, Fu YJ, Ye L, Zhang L, Huang DM
- 6858** Autism with dysphasia accompanied by mental retardation caused by *FOXP1* exon deletion: A case report
Lin SZ, Zhou XY, Wang WQ, Jiang K
- 6867** *FGFR2-TSC22D1*, a novel *FGFR2* fusion gene identified in a patient with colorectal cancer: A case report
Kao XM, Zhu X, Zhang JL, Chen SQ, Fan CG
- 6872** Trismus originating from rare fungal myositis in pterygoid muscles: A case report
Bi L, Wei D, Wang B, He JF, Zhu HY, Wang HM
- 6879** Retroperitoneal laparoscopic partial nephrectomy for unilateral synchronous multifocal renal carcinoma with different pathological types: A case report
Xiao YM, Yang SK, Wang Y, Mao D, Duan FL, Zhou SK
- 6886** Diffuse large B cell lymphoma originating from the maxillary sinus with skin metastases: A case report and review of literature
Usuda D, Izumida T, Terada N, Sangen R, Higashikawa T, Sekiguchi S, Tanaka R, Suzuki M, Hotchi Y, Shimoizawa S, Tokunaga S, Osugi I, Katou R, Ito S, Asako S, Takagi Y, Mishima K, Kondo A, Mizuno K, Takami H, Komatsu T, Oba J, Nomura T, Sugita M, Kasamaki Y
- 6900** Manifestation of acute peritonitis and pneumonedema in scrub typhus without eschar: A case report
Zhou XL, Ye QL, Chen JQ, Li W, Dong HJ
- 6907** Uterine tumor resembling an ovarian sex cord tumor: A case report and review of literature
Zhou FF, He YT, Li Y, Zhang M, Chen FH
- 6916** Dopamine agonist responsive burning mouth syndrome: Report of eight cases
Du QC, Ge YY, Xiao WL, Wang WF

- 6922** Complete withdrawal of glucocorticoids after dupilumab therapy in allergic bronchopulmonary aspergillosis: A case report
Nishimura T, Okano T, Naito M, Tsuji C, Iwanaka S, Sakakura Y, Yasuma T, Fujimoto H, D'Alessandro-Gabazza CN, Oomoto Y, Kobayashi T, Gabazza EC, Ibata H
- 6929** Sirolimus treatment for neonate with blue rubber bleb nevus syndrome: A case report
Yang SS, Yang M, Yue XJ, Tou JF
- 6935** Combined thoracoscopic and laparoscopic approach to remove a large retroperitoneal compound paraganglioma: A case report
Liu C, Wen J, Li HZ, Ji ZG
- 6943** Menetrier's disease and differential diagnosis: A case report
Wang HH, Zhao CC, Wang XL, Cheng ZN, Xie ZY
- 6950** Post-salpingectomy interstitial heterotopic pregnancy after *in vitro* fertilization and embryo transfer: A case report
Wang Q, Pan XL, Qi XR
- 6956** Ulnar nerve injury associated with displaced distal radius fracture: Two case reports
Yang JJ, Qu W, Wu YX, Jiang HJ

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Retrospective Study

Effects on newborns of applying bupivacaine combined with different doses of fentanyl for cesarean section

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Abstract

BACKGROUND

The choice of anesthesia for cesarean section is very important.

AIM

To compare the effects of applying bupivacaine combined with different doses of fentanyl on newborns after cesarean section.

METHODS

We randomly divided one hundred and twenty patients undergoing cesarean section into the following 4 groups: group B (bupivacaine group), group BF10 (bupivacaine combined with 10 µg fentanyl), group BF30 (bupivacaine combined with 30 µg fentanyl) and group BF50 (bupivacaine combined with 50 µg fentanyl). The heart rate, mean arterial pressure, block plane fixation time and sensory block time were recorded. Umbilical artery blood was then collected immediately after fetal delivery for blood gas analysis and qualitative detection of fentanyl. Additionally, data on the neonatal 1-min and 5-min Apgar scores, results of umbilical artery blood gas analysis and qualitative detection of fentanyl in umbilical artery blood were recorded.

RESULTS

Although the mean arterial pressure decreased in all four groups at 3 min after anesthesia, the percentage of the decrease was less than 20% of the baseline. In addition, there were no significant differences in the 1-min or 5-min Apgar scores or the umbilical artery blood gas analysis among the four groups ($P > 0.05$).

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Moreover, the concentration of fentanyl in umbilical artery blood was qualitatively detected using an ELISA kit, and the results in the four groups were negative.

CONCLUSION

Bupivacaine combined with fentanyl spinal anesthesia is effective in cesarean section.

Key Words: Bupivacaine; Fentanyl; Spinal anesthesia; Cesarean section; Newborn

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Core Tip: We examined the effects of bupivacaine combined with different doses of fentanyl on newborns delivered by cesarean section.

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INTRODUCTION

In older parturients, parturients with difficulties and other parturients who cannot give birth vaginally, the demand for cesarean section[1,2] has increased, and the vaginal delivery rate has decreased in recent years. However, the choice of anesthesia for cesarean section is very important. It is necessary for anesthesiologists to carefully consider this in order to select reasonable anesthetic methods and appropriate anesthetic drugs.

Spinal anesthesia[3,4] is a common method of anesthesia for cesarean section. In fact, many studies have shown that opioids plus local anesthetics can have many benefits, such as prolonging the time of intraoperative and postoperative analgesia[5], effectively inhibiting the traction reaction caused by surgery[6] and allowing more stable hemodynamics[7]. Fentanyl[8] is a commonly used opioid drug and is administered by intrathecal injection. However, reports on whether fentanyl enters the blood and affects the safety of newborns are rare.

Thus, this study aimed to qualitatively detect the concentration of fentanyl in umbilical artery blood using an ELISA kit[9] to examine the effects of bupivacaine combined with different doses of fentanyl on newborns delivered by cesarean section.

MATERIALS AND METHODS

Materials

This study was approved by the Medical Ethics Committee of our hospital (Ethical approval Number: 063) and all patients signed an informed consent form.

One hundred and twenty cases of singleton full-term cesarean section were selected, whose characteristics were as follows: ASA grade: II, age: 25-35 years old, weight: 70-90 kg, no obstetrical-related complications (such as hypertensive disorder complicating pregnancy, pregnancy complicated with diabetes, maternal congenital heart disease, placental abruption, fetal distress, placenta previa, etc.), no known fetal developmental abnormalities and malformations, no infectious diseases such as syphilis, hepatitis B and HIV, and no contraindications to lumbar anesthesia.

Methods

Grouping: The patients were randomly divided into 4 groups: bupivacaine (B) group (0.75% bupivacaine 2 mL + cerebrospinal fluid total 3 mL); BF10 group: (0.75% bupivacaine 2 mL + fentanyl 10 µg + cerebrospinal fluid total 3 mL); BF30 group: bupivacaine combined with fentanyl 30 µg group (0.75% bupivacaine 2 mL + fentanyl

30 µg + cerebrospinal fluid total 3 mL); Group BF30: bupivacaine combined with fentanyl 30 µg group (0.75% bupivacaine 2 mL + fentanyl 30 µg + cerebrospinal fluid total 3 mL). BF50 group: bupivacaine combined with fentanyl 50 µg group (0.75% bupivacaine 2 mL + fentanyl 50 µg total 3 mL).

Anesthesia procedure: Electrocardiograph (ECG), heart rate, blood pressure and pulse oxygen saturation were monitored regularly in all parturients. Venous access on one side of the upper limb was achieved and 500 mL of warm compound sodium chloride was infused at a speed of 30 mL/min. The routine preparation of first aid drugs phenylephrine (40 µg/mL) and atropine 0.5 mg was conducted. All patients were placed in the left recumbent position, the L3-4 intervertebral space was punctured using a 25G lumbar anesthesia needle, and local anesthesia with lidocaine 2 mL was administered. When two breakthroughs were felt, colorless transparent cerebrospinal fluid which flowed smoothly was seen after the core of the needle was removed, and the drug solution was injected at the speed of 0.2 mL/s. Finally, patients were asked to turn over and lie flat after anesthesia, the operating bed was tilted 15 degrees to the left, and the patient inhaled oxygen by mask. ECG, heart rate, blood pressure and pulse oxygen saturation were continuously monitored.

Main observation indices

The heart rate and mean arterial pressure were recorded every 3 min.

The fixed time of block plane and the maintenance time of sensory block were recorded.

Apgar scores in 1 min and 5 min in newborns were recorded.

The surgical assistant collected 1 mL umbilical artery blood using a blood gas needle for analysis and the results were recorded immediately after delivery of the fetus.

Umbilical artery blood (3 mL) was collected using a heparinized aseptic syringe and injected into vacuum collection vessels. The upper serum was collected and stored in a -80°C refrigerator and the concentration of fentanyl was determined after high-speed centrifugation.

Statistical analysis

The data from each group were analyzed using SPSS19.0 statistical software. The measurement data were expressed as mean ± SD. The *t* test was used for comparisons between groups, the χ^2 test for comparisons of counting data and Fisher's exact probability method was used to compare rates. *P* values < 0.05 were considered statistically significant.

RESULTS

There were no significant differences in age, height, weight, gestational age, ASA grade and basal mean arterial pressure (MAP) between the groups (Table 1).

The results of related indices of anesthesia and surgery in the four groups were as follows: Although MAP decreased 3 min after anesthesia, the percentage of decrease in the basic value was less than 20%. In addition, there were no significant differences in the time from the completion of anesthesia to fetal delivery and the duration of surgery in each group (*P* > 0.05). Furthermore, there was a significant difference in the recovery time of sensory block among the four groups (*P* < 0.05) (Table 2).

Neonatal Apgar scores and umbilical artery blood gas analysis among the four groups were not significantly different (*P* > 0.05) (Table 3).

The qualitative test results for fentanyl in umbilical artery blood in the four groups were negative according to the standard analysis of the test results of the Fentanyl Group ELISA Kit (NEOGEN, United States) (Table 4).

Fentanyl group ELISA Kit criteria

Positive results: the absorbance was less than or equal to the standard specified by the laboratory, and positive results were quantitatively detected by gas chromatography or mass spectrometry.

Negative results: the absorbance was greater than the standard specified by the laboratory.

Table 1 Comparison of general data in the four groups of patients ($n = 30$, mean $\pm$ SD)

	B	BF ₁₀	BF ₃₀	BF ₅₀
Age	28.9 $\pm$ 4.3	29.1 $\pm$ 3.0	28.0 $\pm$ 2.8	28.3 $\pm$ 2.4
Weight (kg)	75.1 $\pm$ 3.9	74.1 $\pm$ 6.6	73.6 $\pm$ 3.8	74.1 $\pm$ 4.4
Height (cm)	163.7 $\pm$ 4.2	162.2 $\pm$ 3.7	163.3 $\pm$ 2.7	162.8 $\pm$ 2.5
Gestational age (wk)	38.4 $\pm$ 1.3	38.4 $\pm$ 1.3	38.6 $\pm$ 0.8	38.7 $\pm$ 0.9
ASA grade (I/II)	22/8	23/7	22/8	23/7
MAP (mmHg)	91.6 $\pm$ 7.3	90.0 $\pm$ 7.1	93.0 $\pm$ 9.6	89.7 $\pm$ 7.1
Heart rate	89.0 $\pm$ 15.2	89.8 $\pm$ 14.1	92.8 $\pm$ 20.3	93.5 $\pm$ 10.4

Group B (bupivacaine group), BF10 group (bupivacaine combined with 10 μ g fentanyl), BF30 group (bupivacaine combined with 30 μ g fentanyl), BF50 group (bupivacaine combined with 50 μ g fentanyl). MAP: Mean arterial pressure.

Table 2 Comparison of the results of related indices of anesthesia and surgery in the four groups of patients ($n = 30$, mean $\pm$ SD)

	B	BF ₁₀	BF ₃₀	BF ₅₀
3 min MAP decreased after anesthesia (as a percentage of the basal value) %	11.5	10.9	7.6	8.6
The time of sensory block reaching T6 (min)	4.13 $\pm$ 0.74	3.23 $\pm$ 0.48	3.24 $\pm$ 0.40	3.22 $\pm$ 0.56
The time when movement was completely blocked (min)	9.85 $\pm$ 1.34	8.10 $\pm$ 1.15	7.70 $\pm$ 0.92	7.80 $\pm$ 1.24
Time from completion of anesthesia to cesarean section (min)	13.75 $\pm$ 1.20	13.60 $\pm$ 1.44	13.96 $\pm$ 1.48	13.72 $\pm$ 1.31
Duration of operation (min)	59.40 $\pm$ 7.33	60.75 $\pm$ 4.56	59.28 $\pm$ 4.22	61.30 $\pm$ 6.36
Sensory block recovery time (min)	254.95 $\pm$ 23.32	301.10 $\pm$ 18.75	322.75 $\pm$ 22.21	373.15 $\pm$ 20.74

Group B (bupivacaine group), BF10 group (bupivacaine combined with 10 μ g fentanyl), BF30 group (bupivacaine combined with 30 μ g fentanyl), BF50 group (bupivacaine combined with 50 μ g fentanyl). MAP: Mean arterial pressure.

Table 3 Neonatal umbilical artery blood gas analysis and Apgar score ($n = 30$, mean $\pm$ SD)

	B	BF ₁₀	BF ₃₀	BF ₅₀
pH	7.34 $\pm$ 0.04	7.32 $\pm$ 0.07	7.33 $\pm$ 0.06	7.34 $\pm$ 0.04
PO ₂ (mmHg)	42.3 $\pm$ 3.8	43.4 $\pm$ 6.0	42.6 $\pm$ 3.6	42.8 $\pm$ 5.6
PCO ₂ (mmHg)	31.1 $\pm$ 1.7	30.8 $\pm$ 2.0	30.9 $\pm$ 1.9	30.2 $\pm$ 1.8
BE (mEq/L)	-3.1 $\pm$ 0.5	-3.2 $\pm$ 0.8	-3.3 $\pm$ 0.5	-3.1 $\pm$ 0.9
Lac (mmol/L)	1.68 $\pm$ 0.33	1.68 $\pm$ 0.2	1.67 $\pm$ 0.25	1.68 $\pm$ 0.19
1 min Apgar score $\leq$ 7(N)	0	0	0	0
5 min Apgar score $\leq$ 7(N)	0	0	0	0

Group B (bupivacaine group), BF10 group (bupivacaine combined with 10 μ g fentanyl), BF30 group (bupivacaine combined with 30 μ g fentanyl), BF50 group (bupivacaine combined with 50 μ g fentanyl).

DISCUSSION

As an opioid analgesic, fentanyl is suitable for sedation and labor pain before, during and after anesthesia[10]. Although animal reproduction studies have suggested that fentanyl has toxic side effects on the fetus, no corresponding human experiments have been carried out[11]. In fact, fentanyl can pass through the placenta and may affect the fetal heart rate during delivery, but it has little effect on respiratory and nervous system function in perinatal newborns[12]. In addition, many studies have shown that

Table 4 Qualitative detection of fentanyl concentration in umbilical artery blood (OD value) ($n = 30$, mean $\pm$ SD)

OD										
BF ₁₀	0.139	0.143	0.129	0.136	0.125	0.147	0.141	0.141	0.147	0.132
	0.137	0.138	0.139	0.157	0.150	0.136	0.140	0.146	0.136	0.141
	0.145	0.139	0.139	0.158	0.150	0.136	0.141	0.144	0.161	0.158
BF ₃₀	0.132	0.143	0.138	0.160	0.154	0.161	0.143	0.141	0.141	0.137
	0.140	0.152	0.161	0.142	0.142	0.137	0.153	0.152	0.151	0.142
	0.139	0.136	0.138	0.141	0.154	0.148	0.136	0.153	0.139	0.139
BF ₅₀	0.138	0.153	0.152	0.151	0.142	0.139	0.136	0.139	0.151	0.154
	0.152	0.152	0.142	0.143	0.141	0.153	0.147	0.155	0.151	0.152
	0.150	0.150	0.152	0.147	0.152	0.150	0.152	0.143	0.151	0.152
Control	0.112									

opioids combined with local anesthetics can prolong the time of analgesia and maintain the stability of vital signs, which is of extraordinary importance for ensuring a normal cesarean section in pregnant women and for reducing postoperative complications. Consequently, the benefits of spinal anesthesia combined with fentanyl may outweigh the potential hazards.

The results of this study showed that bupivacaine combined with fentanyl spinal anesthesia provided a good anesthetic effect during cesarean section and that the duration of sensory block was prolonged with increasing fentanyl concentration. In addition, blood pressure in the four groups decreased 3 min after anesthesia, but the decrease was 20% lower than the baseline. Consistent with the research results of many scholars[13-17], the hemodynamics were stable, and no neonatal adverse events were observed.

The application of opioids in the spinal canal can enhance the degree of sensory block but cannot enhance the sympathetic block[18]. It has been found that fentanyl can act directly on opioid receptors in the spinal cord and on the thalamus, hypothalamus, reticular system and neurons by directly acting on opioid receptors in the spinal cord and absorbing blood through the paraspinal venous plexus[19]. In theory, fentanyl is slowly absorbed into the blood through the subarachnoid venous plexus following subarachnoid injection. In addition, the dosage of fentanyl in the subarachnoid space is lower, the circulation of cerebrospinal fluid is slow, and the blood concentration of the drug can be ignored. Moreover, coupled with hemodilution after absorption and the decomposition of fentanyl by the maternal liver and placental barrier, the amount of fentanyl entering the fetus is small and thus has little effect on newborns. To some extent, umbilical artery blood gas and lactic acid are the best indices of neonatal oxygenation and acid-base status[20]. In our study, the concentration of fentanyl in umbilical artery blood was qualitatively detected by ELISA, and the results of the four groups were all negative. The Apgar scores of the newborns at 1 min and 5 min were all above 7, and there was no difference in the results of umbilical artery blood gas analysis between the four groups. The fact that the time from completion of spinal anesthesia to delivery in this study was within 15 min may account for this difference. Consequently, we believe that we will have a more comprehensive understanding of the mechanism of fentanyl between the mother and fetus by including different times from spinal anesthesia administration to delivery and a larger sample size. However, this requires further study. Future multi-center studies are needed to confirm these findings.

CONCLUSION

In general, the anesthetic effect of bupivacaine combined with different doses of fentanyl in cesarean section was satisfactory. In addition, the qualitative detection of fentanyl concentration in umbilical artery blood following the administration of 10 μ g, 30 μ g and 50 μ g fentanyl, were negative, which suggested the safety of fentanyl in newborns.

ARTICLE HIGHLIGHTS

Research background

The choice of anesthesia for cesarean section is very important. It is necessary for anesthesiologists to carefully consider this in order to select reasonable anesthetic methods and appropriate anesthetic drugs.

Research motivation

Reports on whether fentanyl enters the blood and affects the safety of newborns are rare.

Research objectives

Examine the effects of bupivacaine combined with different doses of fentanyl on newborns delivered by cesarean section.

Research methods

One hundred and twenty patients undergoing cesarean section were randomly divided into the following 4 groups: group B (bupivacaine group), group BF10 (bupivacaine combined with 10 µg fentanyl), group BF30 (bupivacaine combined with 30 µg fentanyl) and group BF50 (bupivacaine combined with 50 µg fentanyl).

Research results

There were no significant differences in the 1-min or 5-min Apgar scores or the umbilical artery blood gas analysis among the four groups ($P > 0.05$).

Research conclusions

Bupivacaine combined with fentanyl spinal anesthesia is effective in cesarean section.

Research perspectives

Different anesthetics will have different effects on newborns during cesarean section. Safer intravenous anesthetics should be investigated.

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