The Efficacy of Postoperative Wound Infusion with Bupivacaine for Pain Control after Cesarean Delivery: Randomized Double Blind Clinical Trial

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Abstract

Objective: This study investigated the efficacy of bupivacaine wound infusion for pain control and opioid sparing effect after cesarean delivery.

Materials and methods: We conducted a randomized double blind, placebo controlled clinical trial on 60 parturients undergoing cesarean section at a university hospital in Tehran. Patients were randomized to receive a pump infusion system that was filled with either 0.25% bupivacaine or equal volume of distilled water. A catheter was placed above the fascia and connected to electronic pump for 24 hours. Postoperative analog pain scores and morphine consumption were assessed at 6, 12 and 24 hours. Also time interval to first ambulation, length of hospitalization, complications and patient satisfaction were recorded. Data were analyzed using the SPSS software and $P < 0.05$ was considered statistically significant. Mann-Whitney u-test, student t-test and chi-square were used.

Results: There were no differences in patient demographics and length of hospitalization and patient-generated resting pain scores between the two groups. Pain scores after coughing and leg raise during the first 6 postoperative hours were significantly less in the Bupivacaine group ($P<0.001$). The total dose of morphine consumption during the 24 hours study period was 2.5 ± 2.5 mg vs. 7.3 ± 2.7 mg for the bupivacaine and control groups, respectively ($P<0.001$). Compared with the control group, time to first ambulation was shorter in the bupivacaine group (11± 5h vs. 16 ± 4h) ($P< 0.01$).

Conclusion: Bupivacaine wound infusion was a simple and safe technique that provides effective analgesia and reduces morphine requirements after cesarean delivery.

Keywords: Postoperative pain, Cesarean delivery, Bupivacaine

Introduction

Postoperative pain management is one of the important issues in surgery which has significant effects on the health care system. Postoperative pain leads to delayed patient ambulation, prolongation of hospitalization, increased atelectasis, vascular thrombosis, and ultimately patient dissatisfaction. Administration of analgesic drugs postoperatively results in pulmonary function improvement by relieving patient's pain, and is accompanied by decreased constipation, reduction in the side effects of vascular thromboembolism, and shortening of the convalescence period (1, 2).

As a result of their predictable analgesic and anesthetic sparing properties, opioid analgesic drugs are often administered during the postoperative period;

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however, they are associated with a sundry of side effects such as dizziness, respiratory depression, ileus, nausea, vomiting, pruritus, and urinary retention. To control and treat pain, these drugs need to be frequently injected either intravenously or intramuscularly, which is required for stabilizing the drug at a level being constantly higher than the minimum effective analgesic concentration (MEAC). However, inadequate and unpredictable blood concentrations during the injection intervals make it difficult to determine a proper dosage and to bring the drug to a stable concentration state. As a result, it requires precise nursing care to prevent an overdosed intravenous injection which is accompanied by a great weakening of the central nervous and respiratory systems. In most cases where pain control is affected by the administration of opioid analgesics and based on patient requirement and demand, sufficient analgesia does not usually develop. Certainly, analgesic drugs devoiding the above side effects and providing better and longer lasting postoperative analgesic effect are sought (1,2).

Because of analgesic properties and lack of opioid-induced adverse effects, local anesthetic drugs are increasingly used in the treatment of surgical pain. After local anesthetic infiltration into the surgical wound, these drugs provide good postoperative analgesic effect by modulating peripheral pain transduction. However, their short duration of action requires repeated drug administration and constitutes a major limitation to their widespread use.

To overcome this limitation, an electronic infusion pump has been used to facilitate patient-controlled administration of the analgesic drug. This device constitutes an analgesic technique which shortens the delay between the start of pain and analgesic administration, and more than any other procedure, helps patients to have a better and longer lasting analgesic condition and reduces opioid requirements and related unwanted side effects. (3)

Numerous research studies have been conducted in this area; however, there are no sufficient data to support the efficacy of this device in the treatment of postoperative pain. Therefore, due to the differences in the results of previous studies, the purpose of this study was to investigate the efficacy of bupivacaine wound irrigation via an electronic infusion pump in controlling pain after cesarean delivery and reducing opioid requirements.

Materials and methods

This randomized double-blind, placebo-controlled clinical trial was approved in the ethical committee of Reproductive Health Center of Shahid Beheshti University and was conducted as that center`s research proposal. Sixty parturients undergoing cesarean delivery for various indications from November 2003 to December 2004, were enrolled into this study after giving their written consent to this participation. Patients underwent lower segment (kerr) cesarean section through a Pfannenstiel incision. In all cases, a standard spinal anesthesia was administered such that a sensory block up to the T_6 level was built and no opioid drug was used during anesthesia. When an inadequate sensory block occurred, general anesthesia was performed and the patient was excluded from the study.

Patients with a history of clinically significant cardiovascular, pulmonary, hepatic, renal, neurologic, metabolic, infectious, psychological diseases, coagulopathy, HELLP syndrome, and history of narcotic abuse were excluded from the study. Participating patients were randomly assigned to the bupivacaine group (n=30) and the control or distilled water (n=30) group, based on random numbers table. The technique of data collection was observation, interview and use of completed data forms for the study and control groups.

The pain control system was an adjustable electronic infusion pump connected to a catheter and a feeding tube, which was selected owing to its availability and low cost. The terminal 2.5 cm of the catheter had a number of holes to allow the release of the infusion solution. The microset connected to the pump was filled with an equal volume of 100 ml of bupivacaine 0.25% or distilled water.

During the surgery, after the closure of the fascia, first, the subcutaneous tissue was infused with 20 ml of the solution concerned. Then, the catheter was inserted by the surgeon in the subcutaneous space and above the fascia with the proximal catheter tip sited at the point that demarcated 50% of the length of the surgical wound, and the distal tip was fixed to the skin from the end of the surgical wound using a separate suture. By using an aseptic technique, the catheter was connected to the infusion pump. The infusion pump had an automatic clamp and was adjusted that when analgesia was required, it allowed only 10 ml of the solution to be infused in a six-minute interval only one time each hour.

To decrease pain following uterine contractions, all patients received an Indomethacin suppository in the postanesthesia care unit. Then, all patients were

Table 1: Demographic and clinical conditions in the two groups

	Bupivacaine (n=30)	Control (n=30)	P value
Age (yr)	25±8	28±10	NS
Weight (kg)	71±20	74±18	NS
Height (cm)	160±8	160±5	NS
Gravidity	3±2	3.5±2.5	NS
Parity	2±1	3±2	NS
Gestational Age (wk)	38±3	37±7	NS
Anesthetic time (min)	70±20	67±23	NS
Surgery time (min)	30±10	32±8	NS
Incision length (cm)	15±3	15±3	NS
Ambulation time (hour)	11±5	16±4	< 0.01
Hospitalization time (day)	2±1	2±1	NS

* Values are mean ± SD

transferred to the inpatient ward for using an infusion pump and determining the pain score. Postoperative pain was assessed every hour by means of a visual analog scale (VAS) that consisted of a 100-mm horizontal baseline (0 = minimal and 100 = maximal) with vertical anchors at each end.Pain score of 40 mm or more, 20 minutes after initiating the infusion constituted the trigger for morphine administration. The dose of morphine was 0.1 mg/kg IV with a ceiling of 10 mg in 24 hours after the surgery, which was initiated with an initial bolus of 2 mg, and repeated with a 1 mg dose in 10-min intervals until a pain score of 30 was recorded.

All perioperative and postoperative data were collected by the staff who was blinded to the patient randomization and nature of the infusion solution, and then results were recorded in the data sheets. Meanwhile, the participating patients were blinded to the nature of the administered drugs.

The main criteria for patient assessment were VAS for pain and the amount of morphine administered. The amount of morphine used at 6, 12 and 24 hours after the surgery was recorded. Also, pain score during the first 6 postoperative hours was recorded at rest, on coughing and after leg raise. Patient satisfaction with the analgesia within the first 24 postoperative hours was recorded using a verbal scale of poor, satisfactory, good and excellent. Postope-rative hospitalization period, patient ambulation time, and likely postoperative complications arising from pain or morphine administration were recorded in the data sheets. Out of bed time or patient ambulation time was measured hourly from completion of surgery till time of the first ambulation.

On completion of the study, the catheter was removed by using an aseptic technique. WBC count was checked before and 48 hours after the surgery. All patients were recommended to come to the hospital one week after the surgery to have the incision site checked for wound infection and removing the stitches . Recorded data were analyzed by using the SPSS software and through the Mann-Whitney u-test, student t-test and chi-square. $P < 0.05$ was considered statistically significant.

Results

The study showed that the age, weight, height, and obstetrical history (gravidity, parity and gestational age) of the two groups were statistically similar. Also, anesthetic time, surgery time, incision length, and hospital stay time were unaffected by patient randomization (Table 1). The number of pump infusions during the 24-hour postoperative period were 9±3 and 6 ± 2 for the bupivacaine and control groups, respectively, and the infusion volume was 68 ± 22 ml vs. 47 ± 16 ml for the two groups, respectively. At all time intervals, the number and volume of pump infusions were greater in the bupivacaine group compared with the control group, which was significant ($P<0.05$) (Table 2).

Table 2: Postoperative drug administration via pump infusion

	Bupivacaine (n=30)	Control (n=30)	P-value
Number of pump infusions			
0-6 h	4±1	3±1	<0.05
6-12 h	3±1	2±1	<0.05
12-24 h	2±1	1±1	<0.05
Total	9±3	6±2	<0.05
Volume infused via pump			
0-6 h	35±10	26±8	<0.01
6-12 h	23±7	18±3	<0.01
12-24 h	10±5	5±5	<0.01
Total	68±22	47±16	<0.01

* Values are mean ± SD

Morphine consumption during the first 24 postoperative hours was considerably less in the bupivacaine group (2.5 ± 2.5 mg) than the control group (7.3 ± 2.7 mg). In the bupivacaine group, 9 patients (30%) didn't require postoperative morphine infusion, while in the control group all the patients needed morphine injection (P<0.001) (Table 3).

Mean VAS for pain was 4.5 versus 6.4 at 6 hours, 3.5 vs. 5 at 12 hours, and 2 vs. 3.7 at 24 hours for the bupivacaine and control groups, respectively. During the entire period, pain scores were lower in the bupivacaine group than the control group, which was a statistically significant difference (P<0.001) (Table 3). Moreover, resting pain scores based on VAS within the first 6 postoperative hours was similar between the two groups. However, in other conditions (coughing and leg raise), pain scores 3 to 6 hours after the surgery were prominently higher in the control group than the bupivacaine group, and the difference was significant (P<0.03) (Fig.1).

Patient satisfaction with the analgesia provided within the first 24 postoperative hours as excellent and good was 94% vs. 46% for the bupivacaine and control groups, respectively. Compared with the case group, most of the control group patients reported their satisfaction with the analgesia as satisfactory and poor (54% vs. 6%), and this difference was quite significant (P<0.01) (Table 4).

With respect to the postoperative pain complications and morphine consumption, a larger number of symptoms such as coughing, vertigo, constipation and dizziness was reported by the control group, thus indicating a significant difference (P<0.006), but there was no significant difference with respect to fever, vomiting and urinary retention (NS).

Ambulation time was 11 ± 5 hours vs. 16 ± 4 hours for the bupivacaine and control groups, respectively. White blood cell (WBC) count before and 48 hours after the surgery to check for leukocytosis showed 11 ± 2.6´10^3 / ml and 12.5 ± 2.5´10^3 / ml, respectively, which was not a significant difference. Additionally, there was no wound infection observed in any of the participating patients one week after the surgery.

Discussion

This study showed that patient-controlled bupivacaine wound instillation decreased postcesarean delivery pain and improved patient satisfaction and comfort. Both objective indicators of pain intensity morphine requirement and actual morphine administration) and subjective pain assessment (pain scores

Table 3: VAS and Postoperative morphine

	Bupivacaine (n=30)	Control (n=30)	P-value
Morphine (mg)			
0-6 h	1.5±1	3.8±1	<0.001
6-12 h	1±1	2.5±0.7	<0.001
12-24 h	0	1±1	<0.001
Total (24 h)	2.5±2.5	7.3±2.7	<0.05
VAS			
0-6 h	4.5±1	6.4±1.2	<0.001
6-12 h	3.5±1	5±0.5	<0.001
12-24 h	2±1	3.7±1.3	<0.001

* Values are mean ± SD

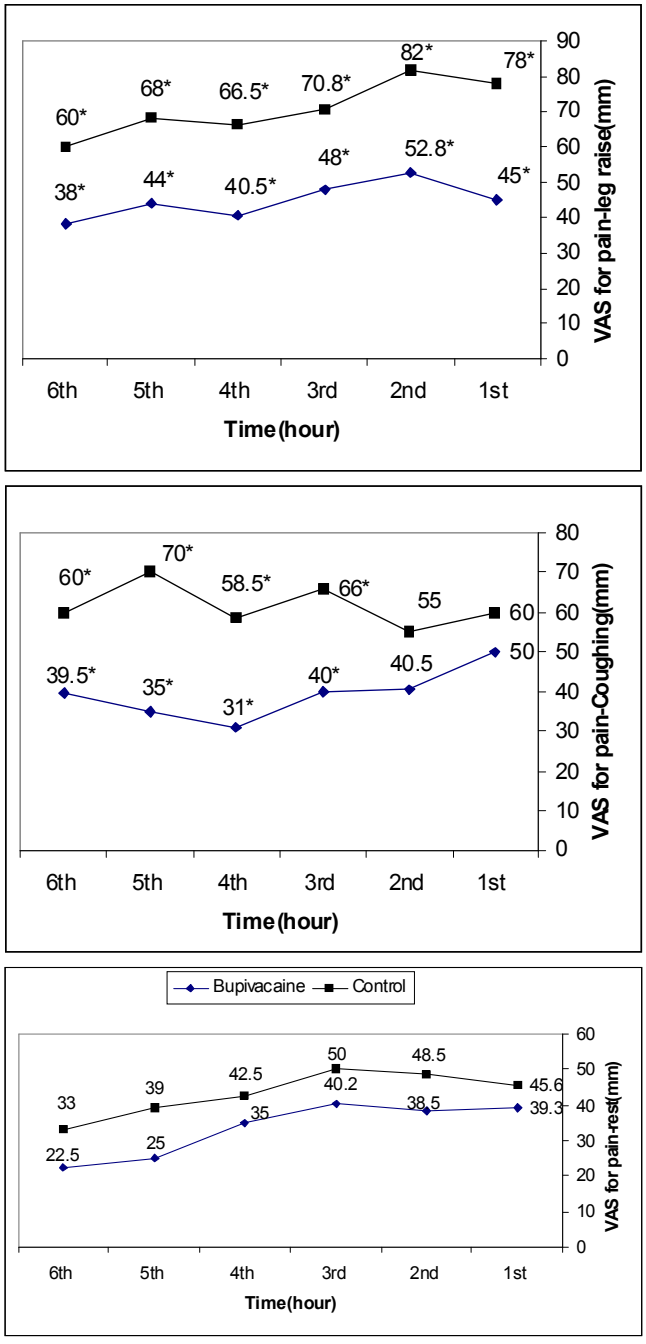

Figure 1: Visual analog scales for pain at rest, on coughing and after leg raise at specified times during the first 6 postoperative hours (P< 0.03).

after coughing and leg raise) were significantly improved in the bupivacaine group as compared with the control group. The study showed that the use of the P.C.A. (Patient Controlled Analgesia) technique with bupivacaine infusion gave rise to longer lasting postoperative analgesia and led to an improvement of

Table 4: Postoperative patient Satisfaction

	Bupivacaine (%)	Control (%)	P-value
Excellent	40	6	<0.01
Good	54	40	NS
Satisfactory	6	50	<0.01
Poor	0	4	<0.01

the patient's general condition as indicated by the early ambulation of the patient, decrease in morphine requirements, and reduction in complications caused by excessive administration of morphine and post-operative pain complications.

Anesthetic drug administration prior to or after the surgical incision provided short relief of postoperative pain in a number of studies. However, few studies have investigated the use of local anesthetic drugs after cesarean delivery and have come up with different results. Despite the difference in the dosage and volume of local anesthetic drugs in various surgeries, a comparison between our study and the previous studies on the efficacy of surgical wound infiltration is at issue here.

In two studies, Fredman B. et al, investigated the efficacy of ropivacaine 0.2% wound instillation after cesarean delivery and efficacy of bupivacaine 0.25% wound instillation after major abdominal surgery. The first study showed that continuous local anesthetic infusion after cesarean delivery proved effective in decreasing postoperative pain and narcotic requirements. However, the second study did not reveal any useful efficacy after major abdominal surgery, which could be attributed to the difference in kind of surgery, longer incision length, surgery period, and perioperative trauma (5, 6).

The study conducted by Vanessa A. Givens et al, on the efficacy of postcesarean wound irrigation with bupivacaine 0.25% showed that local anesthetic wound instillation was effective in pain control ( ). Nevertheless, Kristenson B., who inserted catheters between muscular layers and the peritoneum and administered bolus injections of bupivacaine (15 ml of a 2.5 mg/ml solution), did not observe any reduction in postoperative pain and opioid requirements after abdominal hysterectomy (7). Perhaps, it could be said that, first, the factors determining local analgesic spread and the optimal drug administration site being either above or below the fascia are unknown

in optimizing pain control. Second, because the pump is connected to a catheter, the length of the surgical incision may be greater than the extent of local anesthetic spread, thus limiting the analgesic efficacy of the pump after surgical procedures performed through an extensive incision.

Gambling who investigated the efficacy of pre-cesarean skin infiltration with bupivacaine 0.5% did not observe any difference in the pain scores between the two groups (18). In this study, given that the local anesthetic drug had been administered only once before the surgery and that a PCA system had not been used to provide continuous pain relief, and also considering that the use of sub-arachnoid morphine could have caused interference in the pain intensity between the two groups due to its strong analgesic effect, the results were not reliable.

The efficacy of bilateral ilioinguinal nerve block with bupivacaine 0.5% and 0.375% in postcesarean delivery showed statistically different results in the two studies conducted by Ganta R. and Seah Y. S., respectively. Ganta's study did not show any significant difference between the two groups (9). However, Seah's study revealed a significant difference in reduction of pain score and narcotic requirements (10).

Most of the studies have been performed in a randomized, placebo controlled and double blinded method, and their results can be generalized. Nonetheless, despite its results being different from some of the previous reports, the present study showed that the use of the PCA technique with bupivacaine infusion using an infusion pump not only provides a good and continuous postoperative analgesic effect, but is also inexpensive, and its use for a few days after the surgery is effective and avoid any complications.

Based on the existing data and the opposing results of some of the studies, it has been shown that the spread, intensity and period of postoperative pain is significantly different with respect to the surgical procedure, kind of anesthesia, personal history, patient tolerance, volume and concentration of local anesthetic drug, and that numerous factors affect the intensity, quality and period of postoperative pain such as incision site, period of surgery, amount of perioperative trauma, physiological and psychological condition of patient, preoperative preparatory condition of patient in physical, psychological and pharmacological terms, surgery - induced complications, anesthesia management before, during and after surgery, and the most important the quality of post-operative care.

Despite the favorable results of this study, confirming the efficacy of local anesthetic wound instillation requires further investigation according to the factors interfering postoperative pain assessment and control.

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