ORIGINAL RESEARCH

Local Infiltration of Bupivacaine along the Incision Line following Cesarean Section reduces Postoperative Pain and Analgesia Requirement: A Double-blinded Randomized Controlled Study

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Received on: 07 June 2022; *Accepted on*: 30 July 2022; *Published on*: 16 November 2022

Abstract

Introduction: Cesarean delivery commonly induces moderate to severe pain lasting for 48 hours. Any form of intervention that leads to improvement in pain relief can positively impact ability to breast feed early. Infiltration of local anesthetics (LAs) into the surgical wound is a simple, safe, and low-cost technique for postoperative analgesia. Systemic side effects seen with central neural blockades are avoided. Analgesic requirements are also reduced. Risks of LA toxicity are very low or negligible.

Aims and objectives: To compare the effect on postoperative analgesia of bupivacaine (BP) infiltration into the incision line vs normal saline (NS) infiltration after cesarean section (CS) by analyzing pain-free interval, pain score, and overall analgesic consumption in first 24 postoperative hours.

Materials and methods: A prospective, double-blinded, randomized controlled study was conducted in the Department of Obstetrics and Gynecology, RG Kar Medical College and Hospital over 1 year including 130 patients undergoing cesarean delivery under spinal anesthesia. Before skin closure, 30 mL 0.25% BP or NS infiltration was infiltrated over incision line (10 mL in rectus sheath; 10 mL for each upper and lower subcutaneous flap). Postoperatively, the patients were evaluated at 2, 4, 6, 12, and 24 hours. Analgesic drugs were considered on pain score above 4 on visual analog scale (VAS). Diclofenac intramuscularly 75 mg was given on the first request and tramadol on second, if VAS was above 4 within 12 hours.

Results: Mean time of first analgesic demand was 274.30 minutes in BP group whereas 149.15 minutes in NS group (p <0.0001). Pain scores (on VAS) were significantly reduced for up to 6 hours postoperatively in BP group as compared to NS group (at 2 hours, p = 0.000 and at 6 hours, p = 0.007). There was no statistical difference in pain scores in two groups beyond 6 hours. In BP group, 58.46% patients required only 75 mg of intramuscular diclofenac and 41.54% patients required 150 mg of diclofenac in two divided doses whereas in NS group; only 23.08% patients had pain control by 75 mg of intramuscular diclofenac and 76.92% required 150 mg (p = 0.0001). In addition to diclofenac, 26.15% patients in NS group required 100 mg of tramadol vs only 7.7% in BP group (p = 0.0101).

Conclusion: Direct infiltration of 0.25% BP along incision line following cesarean delivery under spinal anesthesia prolongs pain-free interval, provides adequate analgesia for 1st few postoperative hours, reducing requirement of systemic analgesic in first 24 postoperative hours with negligible side effects.

Keywords: Analgesia, Bupivacaine, Cesarean section, Infiltration, Local, Obstetric, Postoperative pain, Randomized trial.

Journal of South Asian Federation of Obstetrics and Gynaecology (2022): 10.5005/jp-journals-10006-2114

Introduction

Cesarean section is the most common obstetric operation performed.[1] Cesarean delivery commonly induces moderate to severe pain lasting for 48 hours.[2] Any form of intervention that leads to improvement in pain relief can positively impact on early breastfeeding. A prompt and adequate postoperative pain relief is therefore an important component of cesarean delivery that can make the period immediately after the operation less uncomfortable and more emotionally gratifying.[3] Spinal anesthesia is the most commonly used anesthesia for CS.

The drugs most commonly used for postoperative analgesia are opioids, either by intrathecal administration prior to CS or by parenteral administration postoperatively; tramadol; a centrally acting analgesic; or non-steroidal anti-inflammatory drugs (NSAIDs). Each of them is associated with their set of side effects on mother and baby.[4]

Infiltration of LAs into the surgical wound is a simple, safe, and low-cost technique for postoperative analgesia. Due to the local application, transmission of pain from the wound is

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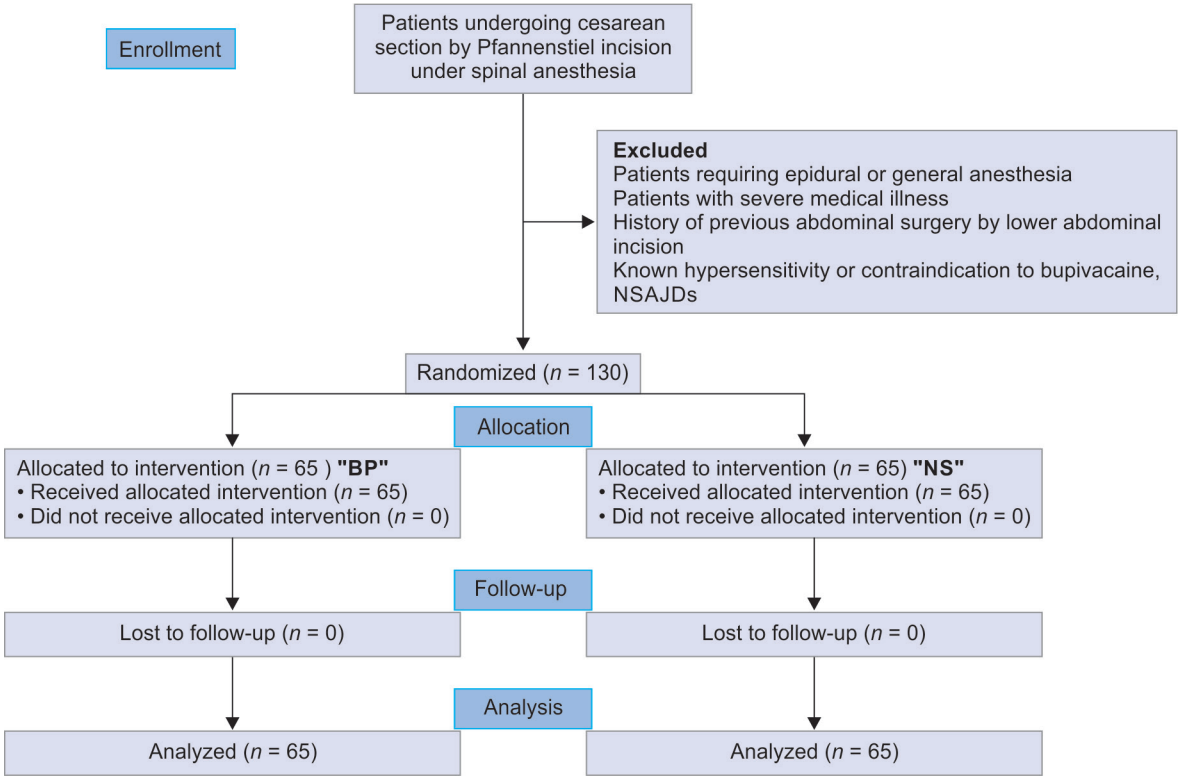
How to cite this article: Saboo V, Biswas D, Naz A, *et al*. Local Infiltration of Bupivacaine along the Incision Line following Cesarean Section reduces Postoperative Pain and Analgesia Requirement: A Double-blinded Randomized Controlled Study. J South Asian Feder Obst Gynae 2022;14(5):596–601.

Source of support: Nil

Conflict of interest: None

Flowchart 1: The CONSORT flow diagram of the study



reduced, and the local inflammatory response to the injury is suppressed. Consequently, sensitization of nociceptive receptors, and the ensuing hyperalgesia may be prevented.[5] The LA may be administered by pre- or post-incisional abdominal nerve block or pre- or post-incisional abdominal wound infiltration.[6–8] It may also be administered by continuous wound irrigation at the end of the procedure.[9] Systemic side effects seen with central neural blockades (e.g., motor blockade, hypotension, nausea, and vomiting) are avoided.[4] Analgesic requirements are reduced. The risks of LA toxicity and wound infection have consistently been low or negligible.[10]

Materials and Methods

This study was a prospective, randomized, double-blinded comparative study carried out at RG Kar Medical College and Hospital, which is a tertiary care medical college and hospital in Kolkata, in eastern India. The data collection was carried out from March 2013 to April 2014. A total of 130 subjects were included (Flowchart 1).

All patients (irrespective of their age) undergoing CS by Pfannenstiel incision under spinal anesthesia without past abdominal operation by lower abdominal incision were included in the study. The patients undergoing both elective and emergency CS were included. Patients who required epidural or general anesthesia, patients with severe medical illness (e.g., cardiac disease, pulmonary disease, diabetes, hypertensive disorders, etc.) or history of the previous abdominal surgery by lower abdominal incision or who had known hypersensitivity or contraindication to BP infiltration or administration of NSAIDs were excluded from the study.

The objective of the study was to examine the quality of analgesia provided by the infiltration of a solution of 0.25% BP over the incision line (in the rectus sheath and the subcutaneous plane) in Pfannenstiel incision for CSs and by comparing it with the infiltration of NS (placebo), in order to show whether 0.25% BP infiltration leads to a reduction in the need for postoperative analgesic medication.

The primary objective was to compare the time of first demand of analgesia (pain-free interval) following cesarean delivery among two groups.

The secondary objectives were to compare pain on VAS, total dose of diclofenac and rescue analgesic (tramadol) consumption in first 24 hours and time of onset of breast feeding among both groups. In addition, incidences of postoperative pulmonary complications due to delayed mobilization, incidence of wound gaping were noted.

Sample size was calculated on the basis of mean time interval to first analgesic request as primary outcome measures with 80% power and 5% probability of type I error. Calculation assumes a standard deviation of 1 hour and 30 minutes of first analgesic requirement on the basis of the previous study and two-sided testing rounded to 65 subjects per group as target sample size. Patients were randomized into the following two groups: (1) Group I, "BP" (Case) – Incision line (subcutaneous plane) and rectus sheath were infiltrated with 0.25% solution of BP; (2) Group II, "NS" (Control) – Incision line (subcutaneous plane) and rectus sheath were infiltrated with NS.

All patients underwent lower section CS under spinal anesthesia (L3–L4 with 8–10 mg of hyperbaric BP 5 mg/mL solution, according to height and the weight of the patient). Both elective and emergency CSs were included. Operation was performed by surgeon of senior resident level or consultants in all cases. A urinary catheter was inserted systematically before the CS and was left in

place for 24 hours. After the confirmation of level of anesthesia up to T6 by anesthesiologist, CS was performed using a Pfannenstiel incision, with peritoneal opening. Before skin closure, infiltration with 30 mL of 0.25% BP was done with 23G needle in group I: 10 mL in the rectus sheath, 20 mL (total) in the subcutaneous plane, 10 mL for the upper abdominal flap, and 10 mL for the lower flap. Group II: 30 mL of NS infiltration in the same plane and in the same manner as that of group I before skin closure. Skin closure was done in single layer mattress with (2–0) nylon suture. Further postoperative analgesia was administered on demand by the patient and/or when pain score, evaluated systematically at 2, 4, 6, 12, and 24 hours, was more than 4 on the VAS. Injection diclofenac was administered intramuscularly (75 mg/3 mL) and then, if required, repeated at every 12 hours for the first 24 hours. The time of administration of first analgesic was noted calculating from the time of last skin suture. Intravenous tramadol at a dose of 100 mg was administered secondarily every 8–12 hours, if the patients requested further pain relief and if the VAS score was more than 4 (within 12 hours of administration of last dose of diclofenac). Time of onset of breast feeding was noted to see any delay in the initiation of breast feeding due to postoperative pain and discomfort. Any evidence of postoperative pulmonary complications which may occur due to delayed mobilization was looked for. Incidence of wound gaping was noted which may indicate wound site infection due to local infiltration. Blinding during outcome measurement was ensured by pain assessment by inpatient nursing personnel unaware of which group the patient belonged.

Informed consent was taken from all patients and the study was cleared by local institutional ethics committee.

Results

The test and the control groups were similar with respect to baseline characteristics. Most patients belonged to third decade age wise (range, 19–43 years) and had normal body mass index (BMI). Most of the subjects were primigravida. Indications for undergoing lower segment CS were varied with fetal distress being the most common indication. Duration of surgery was calculated from the making of the skin incision to the application of the last skin suture. The various demographic characteristics and duration of surgery can be compared in Table 1.

Pain experienced by the participants was assessed by VAS at 2, 4, 6, 12, and 24 hours (Table 2). There was a significant reduction in the VAS score for up to 2 hours postoperatively in BP group compared to NS group. Median of VAS score at 4 hours was found to be more in BP group. The difference in the VAS score between the two groups was found to be significant for first 6 postoperative hours after which the VAS scores were comparable in the two groups, the difference being statistically insignificant.

No analgesia was routinely given to either group unless demanded by the patient. Time to first demand for analgesia from the completion of surgery was noted (Table 3).

The mean time of first demand of analgesia; taking the reference point as the moment when the skin closure was done; in BP group was 274.30 (±94.42) minutes whereas that in group NS was 149.15 (±46.25) minutes signifying that there is prolongation of pain-free interval by 125.15 minutes in BP as compared to NS. It was found that p = <0.0001 and thus statistically significant.

Table 4 shows that out of 65 patients in group BP, 38 (58.46%) required only 75 mg of intramuscular diclofenac vs only 15 (23.08%)

Table 1: Comparison of baseline demographic characteristics, indication of CS, and duration of surgery

Parameter	*BP (N = 65)*[¥]	*NS (N = 65)*[¥]	*p-value*
Age (in years)	21.86 ± 3.36	22.14 ± 3.96	0.67[*]
BMI (in kg/m^2)	22.67 ± 0.91	22.60 ± 0.86	0.6524[*]
Gravida/Parity			
G_1	50 (76.92)	49 (75.38)	0.9945[#]
G_2A_1	4 (6.15)	3 (4.62)	
G_3A_2	1 (1.54)	1 (1.54)	
$G_2P_1L_1$	6 (9.23)	7 (10.77)	
$G_3P_1L_1A_1$	2 (3.08)	2 (3.08)	
$G_3P_2L_2$	2 (3.08)	3 (4.62)	
Indication of CS			
CPD	6 (9.23)	9 (13.85)	0.6694[#]
Fetal distress	16 (24.62)	16 (24.62)	
Induction failure	7 (10.77)	8 (12.38)	
IUGR	4 (6.15)	5 (7.69)	
Malpresentation	6 (9.23)	9 (13.85)	
Non-progress of labor	10 (15.38)	5 (7.69)	
Oligohydramnios	6 (9.23)	6 (9.23)	
PROM	5 (7.69)	1 (1.54)	
Others	5 (7.69)	6 (9.23)	
Duration of surgery			
≤45 min	31 (47.69)	33 (50.77)	0.8361[#]
>45 min to ≤60 min)	31 (47.69)	28 (43.08)	
>60 min	3 (4.62)	4 (6.15)	

Table 2: Comparison of pain scores (VAS)

VAS score at (hours)	*BP (N = 65) Median (interquartile range)*	*NS (N = 65) Median (interquartile range)*	*p-value*[@]
2	2 (1–2)	4 (3–4)	0.000
4	4 (3–4.5)	2 (2–3)	0.000
6	2 (2–3.5)	3 (3–4)	0.007
12	3 (3–5)	4 (3–5)	0.210
24	2 (2–2)	2 (2–3)	0.084

[@]Mann–Whitney *U* test

Table 3: Time to first demand of analgesia

Variable	*BP (N = 65) Mean ± SD*	*NS (N = 65) Mean ± SD*	*p-value**
Time to first demand for analgesia from end of surgery (minutes)	274.30 ± 94.42	149.15 ± 46.25	<0.0001

*Student's unpaired *t*-test

Table 4: Requirement of NSAID and rescue analgesia and duration of immobilization due to pain

Parameter	*BP (N = 65) n (%)*	*NS (N = 65) n (%)*	*p-value*
Diclofenac requirement in first 24 hours			
75 mg	38 (58.46)	15 (23.08)	0.0001[#]
150 mg	27 (41.54)	50 (76.92)	
Rescue analgesia (Tramadol) requirement in first 24 hours			
Not required	60 (92.3)	48 (73.85)	0.0101[#]
100 mg	5 (7.7)	17 (26.15)	
Duration of postoperative immobilization due to pain			
≤12 hours	56 (86.15)	53 (81.54)	
>12 hours to ≤24 hours	8 (12.31)	11 (16.93)	0.7572[#]
>24 hours	1 (1.54)	1 (1.54)	

[#]Chi-squared test

Table 5: Comparison of secondary study outcomes

Variable	*Outcome*	*BP (N = 65) n (%)*	*NS (N = 65) n (%)*	*p-value*[#]
Postoperative pulmonary complications		0 (0)	0 (0)	
Time to initiation of breast feeding	≤12 hours	57 (87.69)	62 (95.38)	0.2147[#]
	>12 hours to ≤24 hours	3 (4.62)	2 (3.08)	
	>24 hours	5 (7.69)	1 (1.54)	
Postoperative wound gaping		0 (0)	0 (0)	

[#]Chi-squared test

out of 65 patients in group NS. Only 27 (41.54%) patients required 150 mg in group I as compared to 50 (76.92%) patients in group II. The *p*-value was found to be 0.0001 which is statistically significant.

Also, the comparison of the two groups with respect to the need of rescue analgesic; intravenous tramadol; when pain was not controlled adequately by diclofenac shows only 5 (7.7%) patients in group BP required one dose of 100 mg of rescue analgesia in addition to diclofenac as compared to 17 (26.15%) patients in group NS. The difference was statistically significant ($p = 0.0101$).

Majority of the patients, that is, 56 (86.15%) patients in group BP and 53 (81.54%) in group NS were mobilized in less than or at 12 hours postoperatively as they were relatively pain free. 8 (12.31%) patients in group BP and 11 (16.93%) patients in group NS were mobilized between 12–24 hours postoperatively. Only 1 (1.54%) patient in each group was immobilized for more than 24 hours postoperatively. The difference was statistically insignificant ($p = 0.7572$).

Postoperative pulmonary complication and wound gaping was not seen in any patient in the study population in either of the two groups. A total of 57 (87.69%) patients in group I and 62 (95.38%) patients in group 2 initiated breast feeding in less than 12 hours. In most of the patients in whom breast feeding was delayed for more than 12 hours was because the baby was sent to sick neonatal care unit because of some perinatal complication. The difference in time of onset of breast feeding was statistically not significant ($p = 0.2147$). Secondary outcomes are summarized in Table 5.

Discussion

Minimizing pain after CS can be best achieved using a multimodal approach and is a component of various enhanced recovery after cesarean (ERAC) protocols being proposed, although there is still no consensus.[11,12] Use of LA is one of the important components often included in the ERAC protocols,[13]

The procedure specific postoperative pain management (PROSPECT) Working Group of the European Society of Regional Anaesthesia and Pain Therapy supported by the Obstetric Anesthetists' Association had in 2020 issued guidelines[14] for optimum pain management during cesarean delivery. Among the many recommendations, use of LA for wound infiltration and NSAIDs have also been advocated.[14]

The findings from our study agree with the above recommendations. In our study, the local infiltration of 0.25% solution of BP along the incision line in the rectus sheath and in the subcutaneous plane, significantly prolonged the pain-free interval following cesarean delivery ($p < 0.0001$). The BP group had significantly reduced pain intensity; as assessed on VAS at 2 and 6 hours after operation, $p = 0.000$ and $p = 0.007$, respectively. A greater VAS score at 4 hours in group BP compared to group NS can be explained by the fact that by this time the effect of locally infiltrated BP had started to fade away and most of the patients in group NS had already received one dose of additional analgesia by this time which had led to reduction in their pain intensity. There was no statistical difference in the pain score in the two groups beyond 6 postoperative hours.

One of the main advantages of local infiltration of anesthetic agent is the reduced demand for postoperative analgesia by the patient. The adverse effects of using opioids like tramadol such as nausea and vomiting, dizziness, constipation, and headache are well known. Serious side effects such as respiratory depression can also happen.[15] The NSAIDs have their unique set of adverse effects and

may be responsible for adverse perinatal outcome.[16] Paracetamol while being innocuous in itself with regards to adverse effects, may be dangerous in patients with acute fatty liver of pregnancy.[17] While all of these drugs have been recommended[15] for the post cesarean pain control and their use is somewhat inevitable, the reduction in their requirement due to local wound infiltration is always beneficial. In our study there was significant difference in the amount of postoperative analgesic requirement in two arms in our study. In group BP, only 27 patients (41.54%) required 150 mg of diclofenac in two divided doses whereas in group NS, majority of patients, that is, 50 (76.92%) required 150 mg ($p = 0.0001$). In addition to diclofenac, 17 (26.15%) patients in group 2 required 100 mg of rescue analgesic (tramadol) for adequate pain relief in contrast to only 5 (7.7%) patients in group I. The difference was statistically significant ($p = 0.0101$). Pain control by local infiltration at the time of surgery is also more feasible in resource limited settings[18] compared to other methods of analgesia which might require continuous monitoring.

Finally, there has been several studies documenting the presence of BP (and ropivacaine) in low concentrations in breast milk when administered to mothers as epidural or transverse abdominis plane blocks. Although the concentrations found were unlikely of significance, further research in this regard is warranted.[19–22]

Limitations

Pain being a subjective feeling; pain threshold may differ from one patient to another. Furthermore, some of the patients could not explain if it was a true pain (at the surgical wound incision) or the colicky abdominal pain which normally occurs due to contraction of the uterus making interpretation difficult at times. Second, there was a chance of interpersonal variation during drug infiltration as infiltration was done by different clinicians. Third, peritoneal spraying of the drug (BP or NS in the respective groups) was not done. The parietal peritoneum though pain sensitive was not anaesthetized and therefore postoperative pain control may be potentially suboptimal.[23] We did not include peritoneal spraying as the amount of BP absorbed from peritoneum is not well established. However, it has also been said that preperitoneal LA might not have added benefit over subcutaneous infiltration.[24] Also, subgroup analysis was not done on the basis of whether the patient had experienced labor pain before undergoing CS or not. Lastly, a cost–benefit analysis is needed as theatre time will be increased and there is a cost attached to the LA and accessories.

The generalizability of our study is reduced because the study included only those patients without any past history of lower abdominal surgery. The post-CS patients and those who had other previous lower abdominal surgery who form a large proportion of patients undergoing CS were thus excluded from the study for which the result of the study cannot be applied.

Although this study was double-blinded, the data analysis was done by authors who were among the treating clinicians; there is a chance of some degree of assessment bias during outcome analysis.

Strengths of the Study

Because epidural analgesia and patient-controlled analgesia is not in vogue in our study setting, therefore control of post cesarean delivery pain by wound infiltration with LA may be safe and effective (as found in our study) alternative to systemically used analgesics each one of which has its own set of adverse effects on the mother or the baby or both. No case was lost to follow-up and there was no need to unblind any case at any point of time during the study.

A future study may be undertaken including the post cesarean and repeat cesarean patients and the patients with other comorbidities. A study may be undertaken comparing different LA available to find out the best anesthetic available for the purpose of wound infiltration. Peritoneal spraying may be included in the study.

Conclusions

Direct local wound infiltration of 0.25% BP along the incision line in the rectus sheath and subcutaneous plane provides good pain relief following cesarean delivery done via Pfannenstiel incision under spinal anesthesia. It prolongs the pain-free interval following cesarean delivery prolonging the time of demand of first analgesia and providing adequate pain control for the first few postoperative hours which are crucial for developing maternal-new born bonding. It significantly reduces the requirement of systemic analgesic (diclofenac and tramadol in our study) in the first 24 postoperative hours with negligible side effects. This technique can contribute to early rehabilitation in sectioned mothers.

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