

Local Injection of Bupivacaine Hydrochloride to Reduce Postoperative Pain in Obstetrical and Gynaecological Surgical Incision

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Abstract

Background and objectives: The post-operative pain experienced by patients after abdominal surgery is significant and this has necessitated studying the efficacy of local injection of Bupivacaine to decrease severity of this pain.

Patients and methods: A prospective, randomized, comparative clinical trial was conducted on 800 women admitted to Maternity Hospital, Erbil, Iraq, for either Caesarean section or any gynaecological abdominal surgery. All were classified as American Society of Anesthesiologists (ASA) physical status I-II. The sample was divided in two groups by systematic random sampling (400 each). Group A was designed to receive 25 mg of Bupivacaine hydrochloride as infiltration at the site of the incision after skin closure and Group B was treated with standard of care. The degree of pain was assessed after 6, 12, 24, 48, 72 and 96 h from the operation by using defense and veterans pain rating scale (0-10). The amount and type of systemic painkiller medicine used during the operation day and the first three post-operative days were recorded. Patient satisfaction, time of first mobilization, h of confinement to bed per day and complication rates were compared in both groups. Chi-square (χ^2) test and Fisher's exact test Student's t-test was used in data analyses. p value of ≤ 0.05 was considered statistically significant and p value of ≤ 0.01 was considered highly significant.

Results: The group treated with post-operative wound infiltration with bupivacaine hydrochloride had lower pain score ($p > 0.001$), earlier mobilization ($p < 0.001$), fewer h of confinement to bed ($p < 0.001$), better patient satisfaction ($p < 0.001$), lower consumption of painkiller medicine ($p < 0.05$, but no significant difference in complication rates ($p = 0.158$).

Conclusion: Instillation of Bupivacaine hydrochloride into the surgical incision is a safe, well-tolerated treatment and it is superior to traditional systemic pain medication in both self-reported and clinical outcomes.

Keywords: Bupivacaine hydrochloride; Caesarean section; Gynecologic surgery; Local anesthetic injection; Pain management; Post-surgical pain; Post-operative narcotic requirement

Abbreviations GA: General Anesthesia; Gp A: Group A; Gp B: Group B; I.V.: Intravenous; tab.: Tablet; gm.: Gram, HCl: Hydrochloride; mg: Milligram; Op: Operation; Pn: Per need.

Introduction

Pain is "an un-pleasant sensory and emotional experience associated with actual or potential tissue damage" [1]. It is well documented, that post-operative pain is undertreated and several studies have shown that over half of all the patients experience moderate to severe pain after surgery [2]. The most appropriate method for the treatment of post-operative pain after Caesarean section remains uncertain [3]. Physiologically, pain leads to a stress response, which, in turn, leads to retention of sodium, water and increase in metabolic rate in addition to other systemic complications [4]. This is, of course in addition to the significant discomfort of the patient in the vulnerable post-partum period. In this context effective

post-operative analgesia is important from a patient perspective and can also improve clinical outcome. Recent surveys report only modest success in providing suitable analgesia, as 30% to 86% of patients report moderate to severe pain after surgical procedures [5]. Opioids are the mostly used medicine for post-surgical pain control [6]. They are, however, associated with unwanted side effects that can lead to increased hospitalization and costs, and opioid-related adverse event rate is correlated to dosage [7]. As an alternative, several studies have evaluated the use of local anaesthesia after abdominal hysterectomy or caesarean delivery with conflicting results [8,9].

Infiltration of wounds with local anesthetics not only provides analgesia but also appears to reduce the local inflammatory response to trauma or surgery, and in 2011, the FDA approved bupivacaine liposome injectable suspension (Exparel) for use in surgical pain [10]. Instillation of surgical wounds with local anesthetics in response to post-operative pain has now been found to be effective in several studies [11-14]. New evidence suggests that the combined use of general and local anesthesia may be effective in reducing postoperative pain preemptively [15,16].

Bupivacaine HCl is indicated as a local or regional anesthesia or analgesia during surgery. Only the 0.25% and 0.5% concentrations are indicated for obstetrical anesthesia [17]. The safety and effectiveness of local anesthetics depend on proper dosage, correct technique, and readiness for emergencies [18,19]. The rate of systemic absorption of local anesthetics is dependent upon the total dose and concentration of drug administered, the route of administration, the vascularity of the administration site, and the presence or absence of epinephrine in the anesthetic solution [19]. There is no lower limit for the effective dosage of Bupivacaine HCl given as local infiltration.

In the current study, we aimed to find the role of least possible dose of Bupivacaine HCl injection in decreasing post-operative pain in Kurd women, who are generally hesitant with regards to surgery because of their fear of post-operative pain.

Objectives

We wanted to assess the viability of Bupivacaine HCl versus standard of care treatment in reducing post-operative pain. Further, we aimed to assess economic advantages, if any, by comparing complication rates and consumption of post-operative painkillers.

We present a prospective, randomized, comparative study to answer these questions.

Material and Methods

Study setting

This prospective, parallel, comparative, randomized study was carried out on women admitted to surgical wards at Maternity Teaching Hospital in Erbil, Iraq from April 1st, 2013 to February 1st, 2014. The sample size was 800 women admitted for either Caesarean section or any gynaecological abdominal surgery performed as emergency or elective procedures.

The patients were divided into two groups by systematic randomization in to two groups, (400 each). Group A (Gp A) received 10 ml of 0.25% Bupivacaine HCl as a single dose by infiltration subcutaneously at the site of incision after skin closure, while the patients were still anesthetized. Group B (Gp B) was treated with standard of care post-operative systemic pain medication. Patients and

the post-operative health providers were blinded for the treatment modality. Data were collected through a specially designed questionnaire by direct interview and later through telephone contact. Defence and Veterans Pain Rating Scale (DVPRS) was used for scoring pain from 1-10, where pain score 1-4 equates to mild pain, 5-6 moderate pain and 7-10 the severe pain. Women marked on the designed scale and numerical value for pain was recorded [20].

The following parameters were registered for each patient and compared between the two groups:

- a) Type of operation and anesthesia; b) severity of pain on the day of operation and the first three post-operative days; c) time of first mobilization; d) h of confinement to bed during the daytime; e) patient satisfaction regarding pain relief through a simple question whether they were satisfied or not satisfied with the pain relief treatment; f) consumption of pain medication in the first three post-operative days; g) formation of hematoma, wound infection or any other post-operative complication.

The 1st 24 h after the operation was regarded to be the operation day followed by the 1st post-operative day.

Data analysis: Data were analyzed using the statistical package for social sciences program (SPSS, version 19). Chi-square test (χ^2) of association was used to compare the proportion of two study groups. Fisher's exact test was used when the expected count of more than 20% of the cells of the table were less than five and Student's t-test was used to compare between means. p value of ≤ 0.05 was considered statistically significant, and p value of ≤ 0.001 was considered highly significant.

Ethical considerations: Scientific and Ethical Committee at College of Medicine, Hawler Medical University approved the study protocol (Number 1970/2, Date June, 6th 2013) and a verbal informed consent was obtained from each patient prior to participation in the study.

Results

There was no significant difference between two groups ($p=0.058$) with regards to types of surgical operations (Table 1). There was a highly significant difference between the two groups regarding type of anesthesia ($p<0.001$) (Table 2).

Type of operation	Gp. A		Gp. B		P- value	Test
	No.	%	No.	%		
Cesarean Section	373	93.25%	374	93.5%	0.058	Fisher's exact test
Hysterectomy	11	2.75%	18	4.5%		
Myomectomy	12	3%	3	0.75%		
Adnexal operations	4	1%	5	1.25%		

Table 1: Comparison between the two groups regarding types of operation and types of anesthesia.

Type of anesthesia	GP. A		Gp. B		P- value	Test
	No.	%	No.	%		
General	360	90%	393	98.25%	<0.001	Chi-Square test

Spinal	40	10%	7	1.75%		
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Table 2: Comparison between the two groups regarding types of anesthesia.

Time of pain Assessment	Gp.A Mean ± SD	Gp.B Mean ± SD	p-value	Test
6 h after op.	2.83 ± 1.09	5.89 ± 0.87	<0.001	Fisher's exact test
12 h after op.	2.96 ± 1.01	4.94 ± 0.68	<0.001	
24 h after op.	2.98 ± 0.89	4.50 ± 0.68	<0.001	
1st Post-operative day	3.03 ± 0.79	3.96 ± 0.67	<0.001	
2nd Post-operative day	2.90 ± 0.73	3.39 ± 0.63	<0.001	
3rd Post-operative day	2.66 ± 0.68	3.10 ± 0.57	<0.001	

Table 3: Comparison between the two groups regarding post-operative pain scoring.

The mean pain score ± SD, was less in Gp A than in Gp B at 6, 12, 24 h after the operation. The same was found during the 1st, 2nd and 3rd post-operative day (p<0.001) (Table 3). Thus Gr. An experienced significantly less pain peri-operatively and this difference remained in the post-operative follow-up period.

The time of first mobilization and h of confinement to bed (h per day) showed highly significant differences between the two groups (p<0.001) for both parameters, where Gp A was more mobile than Gp B (Table 4). Similarly patients in Gp A were more satisfied with post-operative pain management than Gp. B (p<0.001) (Table 5).

Parameters	Gp A Mean ± SD	Gp B Mean ± SD	p-value	Test
Post-operative mobilization time by h	5.79 ± 1.68	6.26 ± 2.07	<0.001	T-Test
Confinement to bed in h per day	5.84 ± 1.79	7.14 ± 1.46	<0.001	

Table 4: Comparison between the two groups regarding the first mobilization time by h after op. and duration of confinement to bed by h per daytime.

Patient Satisfaction	Gp A		Gp B		p- value	Test
	No.	%	No.	%		
Satisfied	381	95.25%	67	16.75%	<0.001	Chi-square test
Unsatisfied	19	4.75%	333	83.25%		

Table 5: Comparison between the two groups regarding patient satisfaction.

In the 1st six and twelve h, Gp A patients had a significantly lower consumption of pain medication (mean of opioids +/- SD) than Gp B (mean +/- SD) (p<0.05) (Table 6). This effect was surprisingly more pronounced between 12 and 24 h post-operation (p<0.001) (Table 6). This difference continued in 1st, 2nd & 3rd post-operative days (p<0.001) (Table 7). In conclusion, fewer number of women in Gp. A received painkiller medicines in comparison to Gp B.

Pain-killer/ 1st six h	Gp. A		Gp. B		p-value	Test
	No.	%	No.	%		
Tramadol injection, 100 mg. i.v. pn	392	98%	400	100%	0.008	Fisher's exact test

Paracetamol tab. 1 gmx4	8	2%	0	0%		
No pain killers needed	0	0%	0	0%		
Pain killer medicine in the 2 nd six h						
Tramadol capsule 50 mg pn.	8	2%	8	2%	0.012	Fisher's exact test
Paracetamol tab. 1 gmx4	0	0%	8	2%		
No pain killers	392	98%	384	96%		
Pain killer medicine in the 2 nd 12 h						

Tramadol capsule 50mg pn	388	97%	365	91.25 %	<0.001	Chi-square test
Paracetamol tab. 1 gm.x4	0	0%	35	8.75%		
No pain killers	12	3%	0	0%		

Table 6: Comparison between two groups regarding types of painkiller in 1st 24 h after operation

1st post-operative day	Gp A		Gp B		p-value	Test		
	No.	%	No.	%				
Tramadol capsule 50 mg. pn.	12	3%	36	9%	<0.001	Chi-square test		
Paracetamol tab. 1gm. x4	369	92.25 %	356	89%				
No pain-killer medicine	19	4.75%	8	2%				
2nd post-operative day								
Paracetamol tab. 1gm. x4	377	94.25 %	400	100 %	<0.001		Chi-square test	
No pain-killer medicine	23	5.75%	0	0%				
3rd post-operative day								
Paracetamol tab 1 gm. Pn.	381	95.25 %	400	100 %	<0.001			Chi-square test
No pain-killer medicine	19	4.75%	0	0%				

Table 7: Comparison between the two groups regarding needs for and types of painkiller on 1st, 2nd, and 3rd post- operative day.

Regarding post-operative complications. There was no significant difference in the numbers of hematoma and wound infection in Gp A than in Gp B, but the difference was not significant (p=0.158) (Table 8).

Post-operative complications	GP. A		GP.B		P-value	Test
	No.	%	No.	%		
No complications	352	88%	359	89.8 %	0.158	Fisher's exact test
Hematoma	4	1%	0	0%		
Wound infection	44	11%	41	10.3 %		

Table 8: Comparison between the two groups regarding post-operative complications.

Discussion

Post-operative pain is usually greatest in thoracic, abdominal, head, neck, and orthopedic surgeries [21], and it is most intense during the first or second day after any procedure [22,23]. An important number of patients, however, experience moderate to severe pain in the postoperative period even after 4 days [24]. After discharge, pain can

continue to interfere with daily activities for several days [21,25]. Unrelieved pain has negative physical and psychological consequences, and aggressive pain prevention and control that occurs before, during, and after surgery can yield both short- and long- term benefits [26]. Controlling acute post-surgical pain is also important because the intensity of acute pain is a predictor of ongoing chronic pain post-surgery [27]. In multimodal pain treatment, Local, regional and pharmacological techniques with different mechanisms of action were used to get an additive or synergic effect, thus using relatively lower doses of each of the items, achieving better effect and less side effects [28], and one of the earliest studies on the effect of incisional bupivacaine on postoperative narcotic requirements was in 1990 [29].

In the current study, it is demonstrated a safe, and efficient regime for the prevention and treatment of post-operative pain. The mean pain severity was assessed in the h and days after surgery and significant differences were found between the two groups, where the intervention group experienced less pain. Previous studies have alluded to the benefits of bupivacaine instillation, however with shorter follow-up period.

Russel et al. concluded that participants who had the bupivacaine instillation experienced reduced pain intensity, which lasted until six h postoperatively, and also had reduced pain intensity when moving around 30 h after the operation [30]. Modares et al. concluded that injection of Bupivacaine into the Caesarean section incision might reduce post-surgical pain in the mothers [31].

In the current study, there was a significant difference between the two groups regarding time of first mobilization, post-operatively, confinement to bed in h per day and also regarding number of patients using systemic painkiller medicine. This has also been demonstrated earlier in a number of studies mentioned below. Samreen et al. concluded that the amount of tramadol required to give the same degree of postoperative pain relief was significantly less when Bupivacaine was used as local anesthesia than in control group at all time intervals [32]. In a double blind randomized trial study carried out by Tan et al. an elective infiltration of abdominal rectus muscle opened during abdominal hysterectomy was performed by using 20 ml of Bupivacaine 0.5% versus normal saline 0.9% in both case and control groups and it was found that the Morphine dosage was reduced in the group using Bupivacaine [8]. These were comparable to the results in the current study.

In the current study, we used a smaller dose of Bupivacaine than previous aforementioned study protocols. A single study by Helvacioğlu et al. used 25 mg Bupivacaine at the site of incision safely with effective reduction of postoperative pain in the recovery room [14]. Only one study used smaller doses of 10 mg of 0.5% Bupivacaine with good effect, but this was in relation to a much gentler procedure with single incision laparoscopy [33].

Regarding data analysis of demographic characters in the current study, there was statistically significant difference between two groups for the age average p<0.05, while statistically non-significant difference for body mass index (p=0.953), marital status (p=0.124), house-ownership (p=0.101), and the type of operation (p=0.058), but highly significant difference for type of anesthesia p ≤ 0.001. Similar demographic differences have been reported in in other studies and may be due to different sample sizes [8,31,32]. In this study, a significantly higher number of patients in Gp.A had spinal anesthesia this may have its impact on our results and thus is one of limitations,

because type of anesthesia may have some role in the severity of pain experienced in the h after operation.

In the current study the operation day was regarded to be the 1st 24 h following surgery, as interventions were performed during different times of the day.

Limitations of the study: We found a significant difference in type of anesthesia, because only a small number of anesthetists were well trained in giving spinal anesthesia, this may skewer the data in one or another direction. (Age difference; it is plausible that patients of different ages, experience pain differently). It would have been valuable to assess the absolute amount of pain medication consumed per patient, however this was not possible because of lack of patient cooperation. Therefor we only recorded the number of patients needing pain medication rather than recording the net consumption of pain medication.

Conclusion

It is concluded that sub-cutaneous injection of least possible dosage of Bupivacaine HCl (25 mg) in to the incision per-operatively reduces post-operative pain after Caesarean section and gynecological abdominal operations, it promotes early mobilization, reduces h confined to bed per day and leads to better patient satisfaction. While having a positive effect on pain-control there seems to be no detrimental effect on complication rates. Fewer patients are in need of post-operative systemic pain medication and it may reduce overall consumption of painkillers.

We recommend futures studies to investigate the cost/benefit of such a protocol and to compare Bupivacain HCL treatment with other analgesics and anesthetic compounds thus may be used as an effective adjuvant pain control without having any impact on post-operative complication rates.

Recommendations

We recommend futures studies to investigate the cost/benefit of such a protocol and to compare Bupivacain HCL treatment with other analgesics and anesthetic compounds thus may be used as an effective adjuvant pain control without having any impact on post-operative complication rates.

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