

**Original Article**

Comparison of the Effect of Intrathecal Hyperbaric 0.5% Bupivacaine Alone and With Addition of Dexmedetomidine on First Analgesic Request in Post-Operative Care Unit Following Elective Cesarean Section

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ABSTRACT

Spinal anesthesia has been considered preferred method of anesthesia for patients undergoing elective cesarean sections. Dexmedetomidine (DXM) is relatively a newer drug in Pakistan as compared to conventional used drug i.e. Bupivacaine (BPV) and that's why the local data regarding its efficacy in cesarean section is lacking. **Objective:** To compare the mean duration of spinal anesthesia between hyperbaric bupivacaine 0.5% alone versus hyperbaric bupivacaine 0.5% with dexmedetomidine on first analgesic request for women undergoing elective cesarean section under subarachnoid block. **Methods:** Spinal anesthesia was performed in the sitting position under sterile conditions with 25G pencil point needle. After successful intrathecal injection, patient was placed in the supine position with left tilt. The cases in Group A received hyperbaric 0.5% BPV (2.25ml) with 5ug DXM (0.25ml) and those in Group B received only 0.5% BPV (2.25ml) with 0.25ml normal saline under full aseptic measures. These patients underwent cesarean section and were assessed in post-operative time after every 30 minutes to first request of analgesia which were given if there was pain of 4 or more on visual analogue scale. **Results:** In Group A, mean and SDs for duration of analgesia was 359.73±8.021 minutes. In Group B, mean and SDs for duration of analgesia was 182.30±7.720 minutes. **Conclusions:** In this study, hyperbaric bupivacaine 0.5% with DXM in spinal anesthesia for patients undergoing caesarean section significantly prolonged the duration of analgesia.

INTRODUCTION

Pain has been a scourge for humankind and much effort has been done to understand it and thereby control it. Postoperative pain by virtue of its unique transient nature is more amenable to therapy [1]. The rate of cesarean deliveries has increased globally over recent years. Adequate postoperative pain relief after cesarean section avoids the adverse effects of pain on various systems in the mother and facilitates early mobilization and better nursing of the baby. It is inevitable that the mode of analgesia should be safe and effective, which will not interfere with the mothers' ability to take care of her baby along with zero adverse effects to the newborn.

The population of women giving birth by cesarean section (C-section) has increased in both developed and developing

countries. Spinal anesthesia has been considered a preferred method of anesthesia for patients undergoing elective c-sections because risk of maternal and fetal complications associated with spinal anesthesia is less than general anesthesia [2,3]. Bupivacaine (BPV) is amide local anesthetic used in spinal anesthesia for c-section but it has side effects like hypotension, bradycardia etc. due to increased dose requirement and less efficient pain control in post-operative care when used alone [4]. Intrathecal adjuvant such as ketamine, opioids, Alpha 2 agonists and neostigmine has been used to enhance the effect of spinal anesthesia [5,6].

In the modern world the role of Dexmedetomidine (DXM) as adjuvant to spinal anesthesia is emerging. DXM can

effectively prolong the duration of spinal anesthesia and also provide effective pain control in postop period. DXM is Alpha 2 agonist which when combined with BPV intrathecally enhance the sensory blockade by depressing the release of c fiber neurotransmitter and by hyperpolarization of postsynaptic dorsal horn neurons. DXM is considered more effective than clonidine for its better analgesic effect, and it is associated with hemodynamic stability and better quality of anesthesia and analgesia during and post-surgery with lesser side effects [7,9].

Subarachnoid block (SAB) has become the preferred anesthetic technique for patients undergoing elective cesarean delivery [10]. Opioids remain the mainstay among the various adjuvants to local anesthetics (LAs) in SAB primarily by virtue of its various properties such as reducing the dose of LA, minimizing side effects, and prolonging the duration of anesthesia [4]. American Society of Anesthesiologists (ASA) recommends neuraxial opioids over intermittent administration of parenteral opioids for postoperative analgesia after neuraxial anesthesia for caesarean section [11]. As smaller doses are used intrathecally, neonatal drug transfer is negligible compared to epidural or parenteral opioids. Although morphine is the gold standard for postoperative analgesia, its use is associated with inherent side effects such as delayed respiratory depression, nausea, vomiting, and pruritus. Moreover, developing countries face a limited supply of preservative-free preparation. Al-Mustafa et al., indicated that the onset time of BPV together with DXM was shorter than that in the control group, the duration of anesthesia was longer and the dose was lower. The duration of motor block was longer in the DXM group than control group (199 ± 42.8 min versus 138.4 ± 31.3 min, $P < 0.05$) [8].

It will be the first study to the best of our knowledge, comparing the duration of anesthesia between two groups: one with conventional drug BPV and the other with DXM. It will be providing information to the other surgeons and anesthesiologists regarding the new drug, its efficiency and comparison with the conventional one.

M E T H O D S :

It was a Randomized controlled trial conducted at the Department of Anesthesiology, Rehman Medical Institute (RMI), Peshawar from 15 Aug, 2020 to 15 Feb, 2021. The sample size was calculated as 60 (30 in each group) by keeping the confidence interval equal to 95% power equal to 80% and the anticipated duration of analgesia with BPV alone vs BPV with DXM as 187.32 ± 16.45 minutes as compared to 357.46 ± 30.64 minutes respectively in a previous study [9]. Non-probability consecutive sampling technique was applied. Women with age 20-40 years, American Society of Anesthesiologists (ASA) classification I, II and pregnant females with singleton pregnancy irrespective of parity and

admitted for elective c-sections were included. Documented cases of any bleeding disorder i.e. factor deficiencies (assessed by history and medical record), documented cases of allergy to any of the study drugs. (assessed by history and medical record) and documented cases of end stage renal failure (creatinine > 3 mg/dl) and liver failure (ALT, AST > 60 IU/L) were excluded.

Data Collection

After approval of synopsis and approval from the ethical review committee of the hospital, 60 cases (30 in each group) fulfilling the inclusion criteria was selected. An informed written consent was taken from those to include in the study and to collect demographic and clinical data in the form of age (years), height (meters), weight (kg), BMI, ASA class, parity and h/o prior spinal anesthesia and was recorded on a pre-designed proforma. Then these cases were divided by using random numbers and patients were divided into two equal groups with a ratio of 1:1, labelled as A and B. After confirmation of fasting intravenous catheter was placed and patient was preloaded with ringer lactate solution (@15ml/kg) before induction of spinal anesthesia. Spinal anesthesia was performed in the sitting position under sterile condition with 25G pencil point needle. After successful intrathecal injection patient was placed in the supine position with left tilt. The cases in Group A received hyperbaric 0.5% BPV (2.25ml) with 5ug DXM (0.25ml) and those in Group B received only 0.5% BPV (2.25ml) with 0.25ml normal saline under full aseptic measures. These patients then underwent cesarean section and were assessed in post-operative time after every 30 minutes to first request of analgesia which was given if there was pain of 4 or more on visual analogue scale. During surgery monitoring was done for pulse rate, Blood pressure, ECG and SpO₂.

Data Analysis

The data was analyzed by using SPSS version 24.0. Quantitative data like age, height, weight, BMI, duration of surgery, parity and duration of analgesia was presented as means and standard deviations (SDs). The qualitative data like ASA Class and history of prior spinal anesthesia was presented as frequency and percentage. Both the groups were compared by using Independent sample t test taking p value ≤ 0.05 as significant. Data was stratified for age, BMI, duration of surgery, ASA Class, parity, history of prior C-section to see its effect on outcome i.e. duration of analgesia with the help of independent sample t test and post stratification p value ≤ 0.05 was considered as significant.

R E S U L T S :

The study was carried out at the Department of Anesthesiology, Rehman Medical Institute (RMI), Peshawar

on 60 (30 patients). In Group A, mean and SDs for age was 26.80±4.278 years. Mean and SDs for weight was 70.27±4.051 Kg. Mean and SDs for height was 5.4±0.056 ft. Mean and SDs for BMI was 25.66±1.52 Kg. Mean and SDs for duration of surgery was 43.70±7.49 minutes. Mean and SDs for parity was 2.43±0.858. Mean and SDs for age duration of analgesia was 359.73±8.021 minutes. In Group B, mean and SDs for age was 27.80±4.582 years. Mean and SDs for weight was 70.20±4.318 Kg. Mean and SDs for height was 5.4±0.06 ft. Mean and SDs for BMI was 25.57±1.553 Kg. Mean and SDs for duration of surgery was 46.00±9.09 minutes. Mean and SDs for parity was 2.57±0.728. Mean and SDs for age duration of analgesia was 182.30±7.720. In Group A, 24 (80.0%) patients were recorded in 20-30 years age group while 06 (20.0%) patients were recorded in 31-40 years age group. In Group B, 22 (73.3%) patients were recorded in 20-30 years age group while 08 (26.7%) patients were recorded in 31-40 years age group. In Group A, 16 (53.3%) patients had ASA Class I while 14 (46.7%) patients had ASA Class II. In Group B, 19 (63.3%) patients had ASA Class I while 11 (36.7%) patients had ASA Class II (Table 1). In Group A, 12 (40.0%) patients were recorded with previous history of c-section while in Group B, 10 (33.3%) patients were recorded with previous history of c-section. Duration of analgesia was stratified with age (Table 2), ASA Class (Table 3), history of previous c-section (Table 4) and duration of surgery (Table 5) respectively.

Treatment Group	ASA Class	Frequency	Percent %
Group A (BPV+DXM) (n=30)	ASA Class I	16	53.3
	ASA Class II	14	46.7
	Total	30	100.0
Group B (BPV) (n=30)	ASA Class I	19	63.3
	ASA Class II	11	36.7
	Total	30	100.0

Table 1: Frequencies and Percentages for ASA Class

Age Groups (n=60)	Treatment Group	N	Mean	SD	S.E. Mean	P Value
20-30 Yrs	Duration of Analgesia Group A (BPV+DXM)	24	359.04	7.888	1.610	0.000
	Group B (BPV)	22	180.14	7.815	1.666	0.000
31-40 Yrs	Duration of Analgesia Group A (BPV+DXM)	6	362.50	8.689	3.547	0.000
	Group B (BPV)	8	188.25	2.915	1.031	0.000

Table 2: Stratification of Duration of Analgesia with Age

ASA Class (n=60)	Treatment Group	N	Mean	SD	S.E. Mean	P Value
ASA Class I	Duration of Analgesia Group A (BPV+DXM)	16	359.06	6.638	1.659	0.000
	Group B (BPV)	19	182.26	8.027	1.841	0.000
ASA Class II	Duration of Analgesia Group A (BPV+DXM)	14	360.50	9.566	2.557	0.000
	Group B (BPV)	11	182.36	7.540	2.273	0.000

Table 3: Stratification of Duration of Analgesia ASA Class

Previous C Section (n=60)	Treatment Group	N	Mean	SD	S.E. Mean	P Value
Yes	Duration of Analgesia Group A (BPV+DXM)	12	361.08	9.737	2.811	0.000
	Group B (BPV)	10	181.90	7.094	2.243	0.000
No	Duration of Analgesia Group A (BPV+DXM)	18	358.83	6.802	1.603	0.000
	Group B (BPV)	20	182.50	8.185	1.830	0.000

Table 4: Stratification of Duration of Analgesia with Previous C-Section

Duration of Surgery (n=60)	Treatment Group	N	Mean	SD	S.E. Mean	P Value
≤ 40 Min	Duration of Analgesia Group A (BPV+DXM)	10	359.80	7.177	2.270	0.000
	Group B (BPV)	9	178.67	8.231	2.744	0.000
> 40 Min	Duration of Analgesia Group A (BPV+DXM)	20	359.70	8.591	1.921	0.000
	Group B (BPV)	21	183.86	7.129	1.556	0.000

Table 5: Stratification of Duration of Analgesia with Duration of Surgery

DISCUSSION :

Obstetric anesthetists are faced with the unique situation of providing anesthesia for c-sections, where anesthetists have to provide care for both the mother and the unborn baby [12]. A team approach is vital to ensure optimal outcome while ensuring that the labour process is a safe and pleasant experience for the parturient. There has been a move towards more c-sections being performed under regional anesthesia compared to general anesthesia [13]. New techniques for regional anesthesia, such as the combined spinal epidural (CSE) anesthesia and the continuous spinal anesthesia, offer specific advantages. There has also been recent interest in the use of supraglottic airway devices for c-section under general anesthesia, especially when difficult airway is encountered [14]. Maternal comorbidities such as obesity and pre-eclampsia also present a challenge to the obstetric anesthetists [15].

Subarachnoid block can be used as the sole source of anesthesia. Alternatively, spinal and epidural anesthesia can be used jointly, taking advantage of the qualities of both techniques: the rapid, dense sensorimotor blockade of a spinal anesthetic and the opportunity to redose the patient with an epidural catheter anesthetic [3]. In another study done by Kamat SD et al., mean duration of analgesia with BVP alone was seen as 187.32±16.45 as compared to 357.46±30.64 minutes with BVP with DXM which was in agreement to the findings of this study, where in Group A, mean and SDs for duration of analgesia was 359.73±8.021. In Group B, mean and SDs for duration of analgesia was 182.30±7.720 [9].

Major advances in obstetric anesthesia have resulted in improved maternal outcomes [16-18]. As women are delaying child bearing, and both obesity and Cesarean delivery rates continue to rise in developed countries [19,20], research must continue to reduce maternal mortality and improve peri-partum care for mother and child. Providing safe perioperative care for cesarean delivery requires a detailed understanding of the physiologic changes associated with pregnancy with particular attention to changes in airway, cardiovascular, respiratory and gastrointestinal systems. Neuraxial anesthesia for cesarean delivery is preferred to general anesthesia because it minimizes the risk of failed intubation, ventilation and aspiration [21]. As we move forward in this field, multimodal analgesia regimens after cesarean delivery for prevention of chronic pain would benefit from additional research. In addition, lack of hospitals able to meet current guidelines and accommodate women who would like to attempt trial of labour after c-section (TOLAC) represents a barrier to equal access to women's health care and is a necessary focus for further study [22].

Researchers are ongoing to explore the efficacy and

analgesic effects of different drugs during c-section. In a very recent study a randomized double-blind clinical trial was conducted by giving spinal anesthesia in two groups of patients (30 in each group) undergoing elective c-section: one with 12.5mg meperidine and other with sufentanil, both were added in 0.5% 10mg BVP. The main outcome measure was to estimate the first analgesic request time and then to assess the analgesic requirement during the initial 24 hours post-operative and also to evaluate the side effects. Meperidine had longer first analgesic request time (400.0 ± 142.1 min) compared to sufentanil (274.0 ± 104.1 min). Approximately 73% of the participants in the latter group required analgesics at 4 hours as compared to 13% in the other (meperidine) group. There was no difference in side effects in both groups. However, meperidine was found to be better in terms of improved analgesia, intra-operative postoperative pruritus, shivering and more satisfaction level among surgeons [23].

BVP provides a longer duration of motor block and is associated to maternal hypotension. In another recent prospective, randomized, double-blind, controlled trial from Belgium, hyperbaric prilocaine (50mg) was compared with BVP (10mg) (both given along with sufentanil, 2.5 µg and morphine, 100 µg) in terms of shorter motor block and recovery. There were 40, ASA II participants undergoing c-section. Prilocaine was found to be superior in terms of recovery and haemodynamic stability. Median motor block was significantly shorter in prilocaine group [24].

Limitations existed in the current study. First, we only observed one dose of IT DXM. Further studies should focus on whether a further increase in the dose of IT DXM can decrease the ED₉₅ of spinal BVP and subsequently decrease the incidence of hypotension. Secondly, we did not observe the duration the motor block. However, the primary purpose of this study was to determine the ED₉₅ of IT BVP. Third, the IT application of DXM was off-label use. Further studies using large, multi-center populations are needed to determine the safety of IT DXM.

CONCLUSION :

In this study, hyperbaric bupivacaine 0.5% with dexmedetomidine in spinal anesthesia for patients undergoing caesarean section significantly prolonged the duration of analgesia.

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