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A randomized controlled study of intrathecal hyperbaric bupivacaine and hyperbaric bupivacaine with fentanyl in caesarean section, government medical college, Suryapet

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Abstract---Background: Spinal anesthesia with hyperbaric bupivacaine and adjuvants such as Fentanyl is now the preferred technique for spinal anesthesia, and is the gold standard for caesarean section. The common procedure is to add such adjuvants in a two-syringe before intrathecal injection into hyperbaric bupivacaine. Drug mixing may alter anesthetic solution density and baricity and may change the distribution of medication in cerebrospinal fluid (CSF). Objectives: In this study, we aimed to assess the effect of comparing block characteristics, intraoperative hemodynamics, and postoperative pain relief in Caesarean section under the subarachnoid block (SAB), following administration of hyperbaric bupivacaine and Fentanyl as a mixture. Methods: The research population consisted of 100 patients parturient women undergoing elective caesarean section under spinal anesthesia with the age ranges aged 20-52 years. By using computer-generated random numbers to obtain they were allocated to one of the two classes of an evenly sized group (50 each). This is a forward-looking, comparative analysis using an inclusive protocol framework for similarly sized classes. Group A received intrathecally 2ml of 0.5% hyperbaric Bupivacaine (10 mg) and Group B received intrathecally 2ml of 0.5% hyperbaric Bupivacaine (10 mg) + 0.5ml of Fentanyl (25 µg) as a concurrent process. Results: The mean age of the cases in categories A and B was 32.5 years and 28.6 years respectively, the anthropometric parameters of both groups showed no statistically meaningful variations ($p>0.05$). The ASA classification of

ASA category I physical status (Group A & B; 38 (76%)) and II (Group A & B; 12 (24%)) was comparable between all categories and there was no statistically meaningful difference ($p=1.0$). The mean onset of the sensory block in group B (52.12 ± 2.64 sec.; $p<0.001$) was comparatively group-A quicker, but the discrepancy was statistically significant. At baseline and in all subsequent measurements ($p>0.05$), the mean arterial pressure, respiratory rate, and partial oxygen concentration were similar between the two classes. None of the cases in any group experienced nausea, vomiting and respiratory depression. Conclusions: Sequential fentanyl administration reduces the time needed for maximum sensory and motor block accomplishment and substantially prolongs the overall analgesic duration. We found that the sequential procedure did not raise the degree of sedation and occurrence of hypotension or bradycardia as compared with drug administration as a mixture.

Keywords---Fentanyl, hyperbaric bupivacaine, spinal anesthesia, randomized controlled.

1. Introduction

Due to its simplicity and efficacy, as well as the speed with which significant rates of analgesia may be developed, spinal anesthesia is presently the preferred method and the gold standard for caesarean delivery [1, 2]. Several intrathecal medications have been tried to extend analgesia, including opioids (morphine, creatine, sufentanil, buprenorphine), and non-opioids (clonidine, dexmedetomidine), benzodiazepines (midazolam), ketamine, and others [3]. Delivery of opioids intrathecally as adjuncts to provide sustained postoperative analgesia has several adverse effects, including pruritus, nausea, vomiting, urine retention, and unexpected respiratory depression [4, 5]. When a long-acting local anesthetic, such as bupivacaine, is utilized, the duration of spinal anesthesia is reduced, and the postoperative period necessitates larger analgesic dosages. High intrathecal bupivacaine dosages have also been linked to severe hypotension [6, 7]. To improve the antinociceptive impact of local anesthetics, opioids have been used in regional (intrathecal and epidural) anesthesia. In caesarean delivery, intrathecal morphine and fentanyl [8], as well as local anesthetics, are utilized.

Before injecting the medications intrathecal, adjuvants are frequently mixed with local anesthetics (LA) in a single syringe. The combination of the two medications changes the constitution of all pharmaceuticals, affecting their distribution in the cerebrospinal fluid. When LA and adjuvants are given separately, the effect of density changes, and therefore their activities, is reduced. Intrathecal addition of opioids such as morphine to hyperbaric bupivacaine as a combination and sequentially exhibited a substantial difference in the duration of analgesia in previous studies [10, 11]. Density is known to influence the spread of LA, but there was no extensive study of the effect of adjuvant solution density on its movement in the CSF. We hypothesized, therefore, that if we administer LA and the adjuvants separately, it could minimize the effect of density changes and hence also their actions. Thus, in the present study, we aimed to compare block

characteristics, intraoperative hemodynamics, and post-operative pain relief in parturients undergoing Caesarean section under the subarachnoid block (SAB), after administering hyperbaric bupivacaine (HB) and Fentanyl as a mixture.

2. Material and Methods

After approval by the institutional ethical committee and signing of informed consent, the Department of anesthesiology, Government Medical College, Suryapet, The trial group was comprised of 100 women aged 20 to 32 who were undergoing an elective caesarean delivery under spinal anesthesia from September 2020 to November 2021. They were assigned to one of two classes of evenly sized groups using computer-generated random numbers (50 each). This is a forward-looking, comparative study for similar-sized classes employing an inclusive protocol architecture. Intrathecal, Group A got 2 ml of 0.5 percent hyperbaric Bupivacaine (10 mg) and Group B received 2 ml of 0.5 percent hyperbaric Bupivacaine (10 mg) + 0.5ml of Fentanyl (25 mg) in consecutive order.

Patients with multiple pregnancies, Pregnancy-induced hypertension, Placenta previa, acute fetal distress, bodyweight > 80 kg, refused informed consent, some contraindication for spinal anesthesia, allergy to local anesthetics, ASA status more than 2, Gross spinal deformity or prior lumbar spinal surgery were excluded from the study. Inclusion Criteria were considered as parturient women with ASA grade I or II, Parturient women term gestation, parturient women between the ages of 20 years to 32 years, parturient women who were willing to give written informed consent.

All patients had to get clearance from the preoperative examination clinic (PAC) before being taken for a C-section. After clearing out of PAC, patients were maintained nil by mouth for 6 hours. All moms were examined under conventional hematological and urological circumstances, including hemoglobin level, blood group, pacing, urinalysis, blood sugar, blood urea, serum creatinine, HIV, HBS Ag, and so on.

An 18-gauge cannula was inserted to protect the intravenous line upon arriving in the operating room, and an infusion of Ringer's lactate was started. Heart rate (HR), non-invasive measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), continuous electrocardiographic (ECG) monitoring, and oxygen saturation were all monitored during the perioperative period (SPO₂). To ensure the block was blinded by the anesthetist, study medication was produced by someone who was not involved in patient care or monitoring. Both studies were carried out by a single reviewer who was likewise unaware of the drugs administered.

The patients and anesthesiologists in the study were completely unaware of the medicine utilized in the study. The patient was in a seated position. Intrathecal block performed at L3-L4 or L4-L5 interspinous space with a spinal needle of 27 G whit acres under strict aseptic conditions. Once the block was completed, patients were made to lie in the supine position. All the necessary equipment and drugs required for general anesthesia and resuscitation administration were kept ready to manage procedural failure and any complications.

We measured different parameters; the emergence of the sensory barrier was measured bilaterally by impairment of the sense of the pinprick along the mid-clavicular axis. The dermatomal level was tested every 2 minutes after SAB until four consecutive readings had stabilized the level. The period had been noted from intrathecal injection to the highest sensory level (maximum block height). In addition, a degree was checked every 30 min before regression was noted from peak to T4 and T6 dermatomes. Sensory blockade was assessed using the cold sensation test on each side of the midclavicular line. The degree of motor blockade was scored from 0 to 3 by the Bromage scale (0-no motor effects, 1-a decrease in muscle strength with the ability to move the leg against pressure, 2 - inability to move the leg against pressure without complete paralysis, and 3 - unable to move feet or knees) at 1 h, 2 h, 4 h, 8 h, 12 h, and 24 h. Heart rate & blood pressure was tracked directly after injection and then for the first 30 minutes after every 3 minutes, then every 10 minutes afterward during the procedure and every hour before full recovery from the block. The record of anesthesia was maintained and the heart rate changed, blood pressure was noted. Any drop in heart rhythm below 60 beats/min was called bradycardia and Atropine was treated with 0.6 mg. Likewise, any decrease in systolic blood pressure of more than 20 percent of the baseline is known as Hypotension has been diagnosed with quick crystalloid infusion and 6 mg bolus, ephedrine if hypotension continues. Sedation was assessed to the Adjusted Sedation Scale of Ramsey. Postoperatively, for the first 2 hours, every 60 min for the next 6 hours and at 12 and 24 hours after arrival in the recovery room, pain, sensory level, and motor block were assessed every 30 minutes. A digital-analog scale measured pain level, first for 2 hours every 1 hour, for the next 8 hours every 2 hours, and then every 4 hours. till 24 hrs. Inj tramadol 2mg / kg iv (max 100 mg) was administered as a relief analgesic when the VAS level was above / equal to 4 (VAS ranking: 0 = no pain and 10 = the worst pain imaginable). All the parameters were reported and statistically analyzed according to the performance.

2.1. Statistical Analysis

The quantitative figures were represented as their mean \pm SD. It represented categorical and nominal data in percentage. The t-test was used to analyze quantitative data, or Mann Whitney test analyzed non-parametric data and evaluated categorical data using chi-square testing. The *p*-value meaning limit was set at < 0.05 . All the analysis was conducted using version 2.1 of the SPSS software.

3. Results

A demographic detail is comparable for both groups in terms of age, weight, height, and length of the surgery. The median age of cases in categories A and B was 32.5 years and 28.6 years respectively ($p=0.94$), and the anthropometric parameters in both groups demonstrated no statistically meaningful variations ($p>0.05$). The ASA classification of ASA category I physical status (Group A & B; 38 (76%)) and II (Group A & B; 12 (24%)) was comparable between all categories and there was no statistically meaningful difference ($p=1.0$).

The mean onset of the sensory block in group B (52.12 ± 2.64 sec.; $p < 0.001$) was comparatively group-A quicker, but the discrepancy was statistically significant. Time for the maximal sensory block was slightly shorter in group B (3.42 ± 0.95 min vs. 4.41 ± 0.95 min; $p < 0.01$), although time was substantially longer for 2 section regression (89.12 ± 6.41 vs. 83.24 ± 5.21 min) and overall analgesic length (314.00 ± 8.72 vs. 289.21 ± 11.41 min) (Table 1).

Table 1: Mean comparison of sensory block parameters between study groups

Variables	Group-A (N=50)	Group-B (N=50)	p-value
The onset of Sensory Block (sec)	59.22 ± 3.54	52.12 ± 2.64	<0.001
Time for max. Sensory Block (min)	4.41 ± 1.15	3.42 ± 0.95	<0.001
Time for 2 segment regression (min)	83.24 ± 5.21	89.12 ± 6.41	<0.001
Duration of Analgesia (mins)	289.21 ± 11.41	314.00 ± 8.72	<0.001

* p-value is a result of t-test and chi-squared and Mann Whitney test analyzed categorical variables, respectively

T4 was the highest block point achieved in group A cases of 86 percent (43) compared with group B cases of 96 percent (48) and there was no statistically meaningful discrepancy ($p = 1.0$). The onset of Motor Block was significantly faster in group B (72.0 vs 75.23 sec; $p < 0.001$) while the duration of motor block was significantly longer (185.87 vs 192.5 min; $p = 0.13$). At baseline, the two groups' mean heart rates were equal ($p = 0.52$) (Figure-1). However, starting at the 9th minute, the mean heart rate in group B was considerably lower than baseline and also when compared to group A, whose heart rate was higher than baseline until the 60th-minute reading ($p < 0.001$).

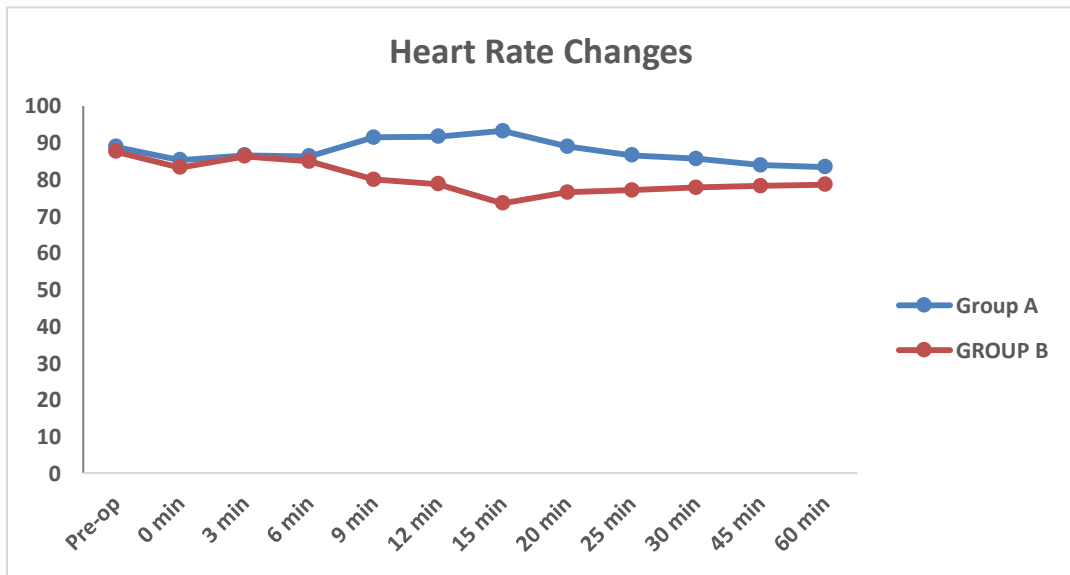


Figure 1: Mean heart rate comparison between study groups

Mean arterial pressure was comparable between the two groups at baseline and in all subsequent readings ($p > 0.05$) (Figure-2).

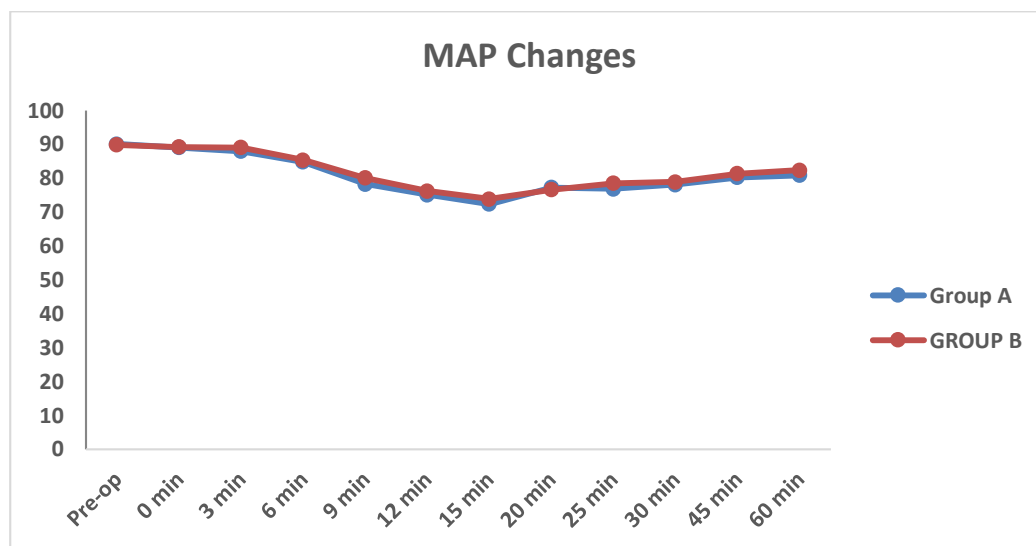


Figure 2: Mean arterial pressure comparison between study groups

The mean respiratory rate was comparable between the two groups at baseline and in all subsequent readings ($p > 0.05$). Mean oxygen partial pressure was comparable between the two groups at baseline and in all subsequent readings ($p > 0.05$) (Figure-3).

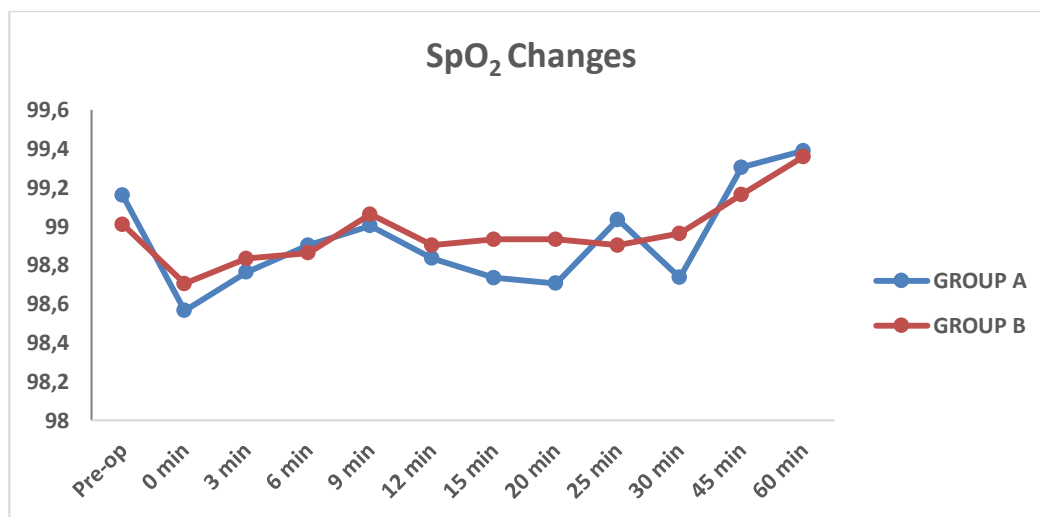


Figure 3: Mean comparison between study groups as per partial pressure of oxygen

There was no statistically significant difference in the adverse effects between the two groups ($p > 0.05$). A total of 30% of patients in Group A and 28% in group B had episodes of hypotension. One patient in Group A and two patients in group B had bradycardia and they were treated with inj. Atropine 0.6mg (Table 2). Two patients in groups A and B had nausea and vomiting. None of the cases had respiratory depression in any group.

Table 2: Distribution of cases as per incidence of adverse events

Adverse Effects	Group-A (N=50)	Group-B (N=50)	Total	<i>p</i> -value
Bradycardia	1 (2%)	2 (4%)	3 (6%)	0.36
Hypotension	15 (30%)	13 (26%)	28 (28%)	1.00
Nausea/ Vomiting	2 (4%)	2 (4%)	4 (4%)	NA
Resp. Depression	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA

** p-value is a result of t-test and chi-squared and Mann Whitney test analyzed categorical variables, respectively*

4. Discussion

A spinal anesthetic is the favored approach for elective caesarean sections because it is simple to administer, inexpensive, and provides fast anesthesia with complete muscular relaxation. This results in increased efficiency, fewer medication dosages, less infant distress, and fewer cases of pneumonitis aspiration. However, this leads to a predetermined anesthetic time, decreased block height control, post-dural puncture headache, and hypotension [12-14], however. Hypotension is also considered to result in maternal morbidity; diarrhea, vomiting, and dizziness, by reducing uteroplacental blood supply, may also specifically affect the well-being of neonates [15]. The connection between the magnitude of the sympathetic block and the occurrence of hypotension has contributed to multiple attempts to reduce the dosage of local anesthetic and also to attach opioids due to their synergistic activity with local anesthetics on the sensory block without the sympathetic block for cesarean section [16, 17].

In the delivery of caesareans, several researchers have utilized varied doses of local anesthetics and the quantity of spinal anesthetic required. According to Nagata et al., [18], 8 mg of hyperbaric bupivacaine is preferred to 10 mg of hyperbaric bupivacaine in caesarean section spinal anesthesia to produce adequate analgesia and avoid maternal hypotension. They employed 5 mg of isobaric bupivacaine with 25 g of fentanyl intrathecally in the Ben David study, although a few patients suffered transient and mild intraoperative discomfort, which was inappropriate. The comparably modest amount of bupivacaine utilized reduced sections of the spinal block and therefore the size of the sympathetic barrier, improving the safety margin of hemodynamic effects found following spinal anesthesia, according to Subedi et al.,[19]. As a result, we were involved in investigating the potency of a low-dose (7.5 mg) combination of (0.5%) hyperbaric bupivacaine and 25 g fentanyl in spinal anesthesia in our study. The research included patients who were planned for a caesarean section since abdominal nausea and discomfort under spinal anesthesia are well-known [20].

The time required for the beginning of sensory blockade up to T4 was statistically insignificant [*p* less than 0.05] in our investigation, and the mean onset time of sensory block was identical in both groups. However, according to research by Heo et al., [21], the start of the sensory block did not improve after a specific dosage. The researchers recommended a statistically negligible premixed medication of bupivacaine 10mg and fentanyl sequential group [22].

The time it took for group A to reach the full sensory block point was 4.33 minutes, whereas group B took 3.46 minutes. [$p < 0.001$] Differences between the two subjects are statistically significant. The time to establish complete sensory block height was marginally shorter in Group B (sequential medications) than in Group A in this research [22] (Mixed drugs). In this examination comparing two classes, researchers discovered evidence that these findings were statistically highly significant [$p < 0.001$]. Consequently, it is possible that concurrent administration of local anesthetic and adjuvant drugs would take less time to reach the maximum level of the sensory block, and the gap in length to reach the maximum level of the sensory block would rely on the dose of fentanyl and hyperbaric bupivacaine used, physiological improvements in pregnancy and more trials with a greater number of patients for evaluation.

Mean heart rate was comparable between the two groups at baseline ($p = 0.62$). However, from the 9th minute onwards, the mean heart rate was significantly lower in group B than baseline and also as compared to group B, where the heart rate was more than baseline till the 60th-minute reading ($p < 0.001$). In our investigation, however, two patients in group B and one patient in group A had bradycardia and were treated with inj. Atropine 0.6 mg ($p = 0.36$). They determined that the highest decline in heart rate when compared to baseline in the sequential and mixed groups was statistically significant ($P < 0.001$). Fentanyl reduces heart rate by neither inhibiting norepinephrine production via presynaptic inhibition nor by directly depressing atrioventricular nodal conduction following systemic absorption [22].

In our study, there is no significant difference between the groups concerning intraoperative and post-operative mean arterial pressure ($p > 0.05$). In our study, a total of 30% of patients in Group A and 26% in group B had episodes of hypotension. similar reported that the, they concluded that a significant fall in arterial blood pressure after SAB was observed in their study, There was statistically insignificant between both the groups [24]. There was no major variation in respiratory rate and oxygen saturation between the two groups ($P > 0.05$), and no episode of respiratory failure existed in both groups. The application of intrathecal fentanyl in other trials did not negatively impact the neonatal result [10. 25]. In our study, when intrathecal fentanyl was provided with hyperbaric bupivacaine, none of the patients needed additional analgesics to achieve a sufficient block of the senses. No patient reported nausea, diarrhea, respiratory depression, and dry mouth.

5. Conclusion

Sequential fentanyl administration decreases the time needed for maximum sensory and motor block accomplishment and substantially prolongs the overall analgesic duration. The addition of fentanyl to hyperbaric bupivacaine provided dense surgical anesthesia regardless of the administration technique. We found, however, that the sequential technique did not raise the degree of sedation and frequency of hypotension or bradycardia when contrasted with drug administration as a combination. Newborn findings were also untouched. The drawback of our analysis was that we calculated in vitro solution densities; however, when injected into the CSF, we did not quantify the densities. Therefore,

we do not intrathecally determine what happens to the product densities. Similarly, the effects of the temperature of drugs when injected were not considered.

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Ethical approval: The study was approved by the Institutional Ethics Committee of Government general hospital, Suryapet, Telangana, India.

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