

Analysis of the Addition of Clonidine and Fentanyl Addition to the Bupivacaine for Caesarean Section

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Received: 15-04-2022 / Revised: 18-05-2022 / Accepted: 01-06-2022

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Conflict of interest: Nil

Abstract

Background: Intrathecal opioids enhance analgesia from subtherapeutic dose of local anesthetic and make it possible to achieve successful spinal anaesthesia using otherwise inadequate doses of local anesthetic. Hence the aim of the present study was to evaluate the effects of fentanyl and clonidine added to Bupivacaine, for caesarean section in spinal Anaesthesia.

Materials & Methods: Patients were randomly allocated into 3 groups of 80 each. A- Control Group - Injection (0.5%) Bupivacaine 1.8 ml + 0.4 ml NS, B- Study group 1 inj. (0.5%) Bupivacaine 1.8 ml + Clonidine 30 µg + 0.2 ml NS, C- Study group 2 Inj (0.5%) Bupivacaine 1.8 ml + Clonidine (30 µg) +fentanyl (10µg). Total duration of analgesia was taken as the period from the time of giving subarachnoid block till the patient's first requirement of analgesic medication.

Results: The pain free time between the groups were compared in the table 1. The means of three groups were 131.5 ± 25.5 , 182.6 ± 18.3 and 224.2 ± 29.2 respectively. They were significantly differed between them. The sedation levels of three groups were associated in the above table 2. The sedation level 1 was associated with groups A and B. The sedation level 2 was associated with group C. The above associations were statistically very highly significant.

Conclusion: The above study bears out the following facts. Intrathecal clonidine and the clonidine fentanyl combination, both improved quality of Intra Operative analgesia. Combination of clonidine with fentanyl increased the intra operative analgesic efficacy and significantly prolonged postoperative analgesia compared with clonidine alone.

Keywords: Fentanyl, Clonidine, Bupivacaine, Caesarean section

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Introduction

The aim of anesthesiology as a science is the removal of pain temporarily started initially with pain relief for surgeries, extending now to post operative pain relief, relief of chronic pain and cancer pain. Spinalanesthesia plays

in important role of alleviating pain intraoperatively, extending sometime into postoperative period also [1, 2]. The entry of Corning's needle in 1885-into the subarachnoid space paved the way for the

greatest leap into spinal anaesthesia. His words “Be the density of this observation, what it may have seemed to me on the whole, worth recording. This opened the prologue for the word “spinal anaesthesia”. Cocaine was the drug first used experimentally in dogs [3].

In men the first spinal anaesthesia was conducted by “August Bier” on 16.8.1898 with cocaine 3 ml as 0.5% solution followed by Matas in America and Tuffier in France. Spinal anaesthesia for caesarean section has always enjoyed popularity as it eliminates the complication of pulmonary aspiration and avoids the problem of difficult tracheal intubation observed with general anaesthesia. Other advantages of this technique are its simplicity, rapid onset and dependability. The demonstration of opiate receptors in substantia gelatinosa of spinal cord (Yaksh and Rudy 1976) has created interest in the intrathecal administration of opiates [4].

The use of intrathecal morphine for providing postoperative pain relief in caesarean section was started in the year 1988 by EzzazAboulesish et.al. The advantages of neuraxial opioids over neuraxial local anaesthetics are that it produces prolonged, intense, selective, segmental analgesia without motor blockade and sympathetic dysfunction. Opioids and local anaesthetics administered together have a potent synergistic analgesic effect [5-7].

Intrathecal opioids enhance analgesia from subtherapeutic dose of local anaesthetic and make it possible to achieve successful spinal anaesthesia using otherwise inadequate doses of local anaesthetic. The α_2 adrenergic mechanism have been exploited for more than 100 yrs. Veterinarians have used α_2 agonist for many years for regional analgesia, but the experience with these agents in humans, dates back only slightly more than 10 years [8]. Hence the aim of the present study was to evaluate the effects of fentanyl and clonidine added to Bupivacaine, for caesarean section in spinal Anaesthesia.

Materials and Method

The present prospective study was done at the medical college and hospital. A total of 240 patients undergoing elective or emergency caesarean section were included in the study. The included patients were explained in detail about the procedure and the written informed consent was signed. The present study was a randomized prospective comparative study. The ethical committee was informed about the study and the ethical clearance certificate was obtained prior to the start of the study.

Inclusion and Exclusion Criteria:

Patients with ASA I and ASA IE who were fit to undergo spinal anaesthesia for caesarean section, age between 18-35 yrs were included in the study. Patients with medical and obstetrical complications and impaired placental function were excluded; patients who were converted to general Anaesthesia were also excluded from the study.

Preoperatively all patients were seen by the anaesthetist. The procedure was explained in detail and informed consent was obtained. No premedication was given. Patients were randomly allocated into 3 groups of 80 each.

A- Control Group - Injection (0.5%) Bupivacaine 1.8 ml + 0.4 ml NS

B- Study group 1 inj. (0.5%) Bupivacaine 1.8 ml + Clonidine 30 μ g) + 0.2 ml NS.

C- Study group 2 Inj (0.5%) Bupivacaine 1.8 ml + Clonidine (30 μ g) + fentanyl (10 μ g)

On arrival to operation theatre, basic monitoring was applied to all patients and basic pulse rate, blood pressure, oxygen saturation and respiratory rate were recorded. TM Intravenous line with 18 g canula was established and preload of 250-300 ml of crystalloid was given to all patients.

Following resuscitative measures were kept ready before the start of the procedure: Boyles machine with oxygen source, laryngoscope and appropriate size blades, suction apparatus, vasopressors (Ephedrine), naloxone and other

emergency drugs. TM The subarachnoid block was performed in right lateral position with 23 G spinal needle through L3, 4 space. Free flow of CSF was ensured before introducing the drug.

The drug injected was according to the group assigned. A- Injection (0.5%) Bupivacaine 1.8 ml + 0.4 ml NS, B- inj. (0.5%) Bupivacaine 1.8 ml + Clonidine 30 µg) + 0.2 ml NS. C-Inj (0.5%) Bupivacaine 1.8 ml + Clonidine (30 µg) + fentanyl (10µg) Drugs were measured in a sterile tuberculin syringe. Thorough aseptic precautions were taken during the addition of injection and making the final injection.

Immediately after the Intrathecal injection the patients were gently turned to supine position with leftward tilt by a wedge under right buttock 100% oxygen was given through Magills breathing system till the delivery of baby. Assessment of Patient and Recording of Data Time of subarachnoid block was noted. Following observations were made 1. Time of onset of analgesia 2. Time of maximum cephalic spread 3. Upper level of sensory block. 4. Grade of motor block obtained according to Bromage motor scale.

Bromage motor scale 0- No paralysis 1- Inability to raise extended legs. 2- Inability to flex the knee joint 3- inability to flex the ankle joint After the establishment of an adequate level of analgesia, the surgeons were allowed to operate and the time of beginning of surgery was noted. Blood pressure, pulse rate, respiratory rate and Spo2 were monitored intraoperatively every 2 minutes for the first 10 minutes and every 5 minutes till the end of surgery. Patients were watched for side effects like hypotension, bradycardia, and vomiting, itching and respiratory depression. Any hypotension (30 % fall from base line) was treated with oxygen, intravenous fluid and inj. ephedrine. Any bradycardia (pulse rate < 60 mt) was treated with inj. Atropine.

Nausea and vomiting were treated with inj. metaclopramide Pruritis if complained was treated with inj. chlorpheniramine maleate. Time to decrease from maximum sensory level to 2 segments below that level was noted. Sedation state was assessed by Brain and Ready sedation score: 1. Awake and alert 2. Drowsy 3. Sleepy but easily arousable on call. 4. Sleepy but difficult to arouse.

In the postoperative period, any complications to the mother and baby, especially that is attributed to opioids like respiratory depression, nausea, vomiting, pruritus were noted.

Total duration of analgesia was taken as the period from the time of giving subarachnoid block till the patient's first requirement of analgesic medication. Pain was evaluated using 10 cm linear visual analogue scale (VAS) with 0 for no pain and 10 for worst pain. If VAS was more than 6, supplementary analgesia was given and the study was assumed to be concluded at that point. Results were expressed as mean ± standard deviation. Statistical significance was determined by Anova table.

Results

The three groups were namely A (Bupivacaine only), B (Bupivacaine + intrathecal clonidine) and C (Bupivacaine + intrathecal fentanyl + Clonidine). Each group 40 Caesarean Sections were selected and data were collected before during and after surgery. For Randomization the three groups were matched according to their selected and related demographic characteristics and base level Physiological characteristics. The three groups were matched in respect of their age, weight and height. They were not significantly differed between them ($P>0.05$).

The Physiological characteristics of three groups were matched and stated. There was no significant differences were observed between groups in respect of their base Physiological characteristics ($P>0.05$).

The sensory time between the groups were compared. The mean time of A was 3.8 ± 0.8 minutes with mean time of B (3.6 ± 0.7) and C (4.3 ± 0.8) not differed significantly ($P > 0.05$). But the means of B (3.6 ± 0.7) and C (4.3 ± 0.8) were differed significantly ($P < 0.01$).

The pain free time between the groups were compared in the table 1. The means of three groups were 131.5 ± 25.5 , 182.6 ± 18.3 and 224.2 ± 29.2 respectively. They were significantly differed between them ($P < 0.001$)

Table 1: Pain free time comparison between the groups

Groups	n	Mean	SD	Test
A	80	131.5	25.5	181.95
B	80	182.6	18.3	
C	80	224.2	29.2	

The sedation levels of three groups were associated in the above table 2. The sedation level 1 was associated with groups A and B. The sedation level 2 was associated with group C. The above associations were statistically very highly significant.

Table 2: Sedation comparison between the groups

Sedation level	A	B	C	Total
0	34	4	0	38
1	46	56	6	108
2	0	20	58	78
3	0	0	16	16
Total	80	80	80	240

Nausea and vomiting occurred in 5% of patients in group A and group B and 2.5% in group C and they were treated with inj. Metaclopramide. Pruritus occurred in 2.5% of patients in group B and 7.5% of patients in group C and they were treated with inj. chlorpheniramine maleate.

Discussion

The mechanism by which intrathecal α_2 -adrenoceptor agonists prolong the motor and sensory block of local anesthetics is not well known. They act by binding to presynaptic C-fibers and postsynaptic dorsal horn neurons. Their analgesic action is a result of depression of the release of C-fiber transmitters and hyperpolarisation of postsynaptic dorsal horn neurons [9]. Local anesthetic agents act by blocking sodium channels. The prolongation of effect may result from synergism between local anesthetic and α_2 -adrenoceptor agonist, while the prolongation of the motor block of spinal anesthetics may result from the binding

of α_2 -adrenoceptor agonists to motor neurons in the dorsal horn [10]. Intrathecal α_2 -receptor agonists have been found to have antinociceptive action for both somatic and visceral pain. Fentanyl is a lipophilic μ -receptor agonist opioid. Intrathecally, fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of spinal cord and may have a supraspinal spread and action [11].

For Randomization, the three groups were matched with their age, height, weight, pulse, SBP, respiration and SPO2 and found that there was no significant difference between them ($P > 0.05$). Hence, there groups were comparable groups. The sensory level T4 was obtained by A group 2(2.5%), B group 4(5%) and C group 20 (25%). The above attainment by C group was significantly greater than the other A& B groups.

The pain free time of C group was significantly greater than B group and B

group was significantly greater than A group. The sedation level of A (57.5%) and B (70%) groups was associated with level 1 and C (72.5%) was associated with level 2. The improvement was very highly significant. The α -2 adrenergic agents also have antishivering property as observed by Talke *et al* [12] We too did not find any incidence of shivering in the two groups.

From the above results it was found in the study that C group administration is better than the above two groups namely A and B groups. Evidences to conclude, improved quality of analgesia is the post-operative period. There is not of much difference in the onset of analgesia, which was found to be similar to studies by Singh Harbhej *et al*.

Conclusions

The above study bears out the following facts. Intrathecal clonidine and the clonidine fentanyl combination, both improved quality of Intra Operative analgesia. Combination of clonidine with fentanyl increased the intra operative analgesic efficacy and significantly prolonged postoperative analgesia compared with clonidine alone.

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