Original Article

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Comparison of Intrathecal Clonidine and Fentanyl in Hyperbaric Bupivacaine for Spinal Anesthesia and Postoperative Analgesia in Patients Undergoing Lower Abdominal Surgeries

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Abstract

Introduction: Fentanyl and clonidine both prolong sensory and motor block of spinal anaesthesia and duration of postoperative analgesia when used as an adjuvant to intrathecal bupivacaine. Lack of studies that directly compare them regarding their efficacy prompted us to compare both drugs as an adjuvant to intrathecal bupivacaine for spinal anaesthesia and postoperative analgesia in patients undergoing caesarian section**. Subjects and Methods:** It was a prospective randomized study in which eighty patients posted for lower limb orthopedic surgery were divided into two groups of forty each. Group C – Received intrathecal hyperbaric bupivacaine (2.5 ml) +50 μg clonidine (diluted to 0.5 ml). Group F – Received intrathecal hyperbaric bupivacaine (2.5 ml) + fentanyl 25 μg (diluted to 0.5 ml). Duration of postoperative analgesia, sensory and motor block characteristics, hemodynamic parameters, and side effects were recorded and analyzed. **Results:** Both the groups were comparable in demographic data, onset and duration of sensory and motor blockade, hemodynamic parameters, but the duration of analgesia is significantly longer in clonidine group when compared with fentanyl group. Sedation score is more in clonidine group. **Conclusion:** Addition of clonidine to intrathecal bupivacaine offers longer duration of postoperative analgesia than fentanyl but with higher sedation.

Keywords: Bupivacaine, Clonidine, Fentanyl, Intrathecal, Postoperative Analgesia.

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Introduction

Spinal anaesthesia and postoperative analgesia can be prolonged by using adjuvants to local anaesthetics like adrenaline, midazolam, opioids, neostigmine and clonidine. Administration of opioids as adjuvants to local anaesthetics intrathecally results in both synergistic and multimodal analgesia.[1] The successful use of intrathecal morphine in human beings was first described by Wang et al in 1979. Since then, almost all opioids have been used via this route. Fentanyl citrate, a μ-1 and μ-2 agonist is a very potent drug because of its high lipophilicity. It is preferred as an adjuvant in spinal anaesthesia because of its rapid onset and short duration of action with lesser incidence of respiratory depression.[2]However, pruritus, nausea, vomiting, activation of herpes labialis, urinary retention and late and especially unpredictable, respiratory depression of other opioids have directed pain research towards non-opioids. Clinical studies have suggested that intrathecal clonidine prolongs sensory and motor block of spinal anaesthesia. It decreases local anaesthetic requirements, and provides prolonged postoperative analgesia. Other beneficial effects are antiemesis, reduced post spinal shivering, anxiolysis and sedation. Unlike spinal opioids, clonidine does not produce pruritus or respiratory depression.[3] In this study we have compared intrathecal clonidine with fentanyl in regard to their efficacy and safety as an adjuvant to intrathecal bupivacaine for spinal anaesthesia and postoperative analgesia in patients undergoing caesarian section.

Subjects and Methods

This randomized controlled study was carried out from January 2016 to January 2017, after obtaining approval from the Hospital Ethics Committee and written informed consent from the patients. Eighty patients of the American Society of Anesthesiologists Classes I or II of either sex and of age 20–60 years of age posted for lower limb orthopedic surgery were randomly divided into two groups (n = 40)

using computer-generated program. Assigned random group was enclosed in a sealed envelope to ensure concealment of allocation sequence. The anesthesiologist, who was not involved in the study, opened the envelope in operation theater and prepared the drug accordingly. The observation was done by the anesthesiologist who was blinded to the drug. Patients having severe systemic disorders such as diabetes mellitus, hypertension, heart disease, allergy to bupivacaine, spine deformity, increased intracranial pressure, neurological disorders, hemorrhagic diathesis, and infection at the puncture site were excluded from the study. Group C – Received hyperbaric bupivacaine (2.5 ml) +50 μg clonidine (diluted to 0.5 ml) administered intrathecally. Group F – Received hyperbaric bupivacaine (2.5 ml) + fentanyl 25 μg (diluted to 0.5 ml) administered intrathecally. Total volume of study drug was 3 ml. Preanesthetic checkup was done, and visual analog scale (VAS) was explained to all patients. All the patients were kept nil orally for 6 h before surgery. After shifting the patients to operation theater, intravenous (IV) cannula was inserted, and preloading was done with Ringer solution (10 ml/kg). Preoperative parameters such as pulse rate, oxygen saturation, and blood pressure were recorded. Under all aseptic precaution, spinal anesthesia was administered at the level of L3–L4 intervertebral space in sitting position using midline approach by 25-gauge Quincke spinal needle. The anesthesiologist who administered anesthesia was blinded to the group allocation. Pulse rate, respiratory rate, electrocardiogram, SpO_2, and blood pressure were monitored. Pulse rate and blood pressure variations more than 20% of baseline were noted in both groups. Bradycardia and hypotension were treated with IV atropine and ephedrine, respectively. Sensory and motor block was monitored at 2, 4, 6, 8, 10, 15 min, and after that at 15 min interval. Sensory block was tested by pinprick method. The motor block was assessed according to the modified Bromage scale: Bromage 0: Patients able to move hip, knee, and ankle, Bromage 1: Patients unable to move hip but able to move the knee and ankle, Bromage 2: Patient unable to move hip and knee but able to move the ankle, Bromage 3: Patient unable to move hip, knee, and ankle. The onset of sensory block was taken from the time of intrathecal injection till loss of pin prick sensation at T10. Duration of sensory block was taken as time from maximum height of block till regression to Level 1. The onset of motor block was defined as time from intrathecal injection to motor blockade Level 2 in Bromage scale. Duration of motor blockade was taken as time from intrathecal injection till no motor weakness (Bromage 0). Duration of analgesia was defined as time from intrathecal injection till administration of first rescue analgesic. Any side effects such as nausea, vomiting, pain, shivering, pruritus, sedation, hypotension, bradycardia, and respiratory discomfort were noted. Patients were assessed for degree of sedation, and scoring was done with Campbell sedation score as: 1: Wide awake, 2: Awake and comfortable, 3: Drowsy and difficult to arouse, and 4: Not arousable. Postoperatively, the pain score was recorded by using VAS between 0 and 10 (0 = no pain, 10 = severe pain). Injection paracetamol (1 gm) was given intravenously as rescue analgesic when VAS was >5. Time of administering the first dose of rescue analgesia was noted.

Power analysis suggested that a sample size of forty patients per group was required to achieve a power of 80% and a level significance of 0.05 to be able to detect a difference in the mean duration of analgesia by 60 min between the groups. Interpretation of the data was carried out and analyzed using statistical package for social sciences (SPSS version 19, IBM Corp, NY, USA). Data was represented as mean ± standard deviation for continuous data and frequency (percentage) or median (range) for nonparametric (categorical) data. The two groups were compared using analysis of variance. The proportion of adverse effects was compared using Chi-square test. $P < 0.05$ was considered statistically significant. $P < 0.001$ was considered highly statistically significant.

Result

In our study, we observed that demographic data (age, height, weight, ASA grade, gender, and duration of surgery) were comparable with $P > 0.05$ (statistically not significant).

Similarly, in our study, there is no statistically significant difference in hemodynamic parameter (blood pressure and heart rate) is observed in both groups. Hypotension is not observed in any of the cases in both the groups. Incidence of bradycardia was similar in two groups, and only one patient in BC group developed bradycardia requiring treatment with injection atropine. [Table 2] shows the comparison of blockade in terms of onset, duration, wearing off, and need of rescue analgesia. Both the group were comparable in terms of onset and offset of sensory and motor blockade, peak of sensory blockade, regression of sensory blockade whereas the analgesic duration is prolonged in BC group as compared to BF group, and the time for the requirement of first analgesic dose is longer for BC group as compared to BF group ($P < 0.05$).

In our study, we observed more sedation in BC group as compared to BF group. On Campbell sedation score, we observed sedation score of 1 in 48 patients of BF group whereas only five patients in BC group have sedation score 1. Sedation score of 2 is observed in only two patients belonging to BF group, and it is contrary to BC group where 37 patients have sedation score 2. No patient in BF group demonstrated sedation score more than 2, whereas 8 patients in BC group showed sedation score of 3. From the above observation, we conclude that more patients are sedated in BC group as compared to BF and this difference is statistically significant ($P < 0.05$). [Table 3] depicts the sedation scoring

Table 1: Demographic data

Characteristics	BF Group (n=50)	BC Group (n=50)
Age in years	42.53±15.43	44.76±14.20
Height	154.75±9.54	153.25±8.59
Weight in Kg	64.54±12.50	61.80±8.38
Sex of patients (male: female)	16:18	18:16
ASA grade	1-2	1-2
Duration of surgery	120.47±54.63	128.65±7.10

Values are mean ±SD. P>0.5 not significant. ASA: American Society of Anesthesiologist; SD: Standard deviation.

Table 2: Comparison of blockade (onset and regression of sensory and motor block) and analgesic duration

Parameters	Mean ±SD		P-Value
	BF Group (n=50)	BC Group (n=50)	
Time in min to onset of sensory blockade	0.90±0.19	0.91±0.18	0.82
Time in min to onset of motor blockade	1.58±0.45	1.71±0.49	0.44
Time in min for peak of sensory blockade	7.34±0.96	7.56±1.78	0.94
Two segment regression time in min for sensory blockade	132±14.56	136.56±12.67	0.35
Time in min for weaning offer motor block	190.50±18.65	184.58±12.07	0.23
Time in min for first dose rescue analgesic	416.87±105.67	497.20±139.78	0.0004

and percentage of patients in both the groups showing the sedation scores.

Apart from sedation, other complications and side effects are similar in both the groups and are not significant statistically (P > 0.05) and these complications are depicted in [Table 4].

Discussion

Both clonidine and fentanyl when used in lower dose are safe and prolongs the postoperative analgesia of intrathecal bupivacaine, and there is a paucity of studies comparing the safety and efficacy of these two drugs.[4] In our study, we compared intrathecal clonidine and fentanyl in terms of safety and efficacy, and to compare the efficacy, we used the effective analgesia duration measured in minutes for requirement of rescue analgesia. In consistent with several other studies, we found that both drugs are effective as adjuvants to intrathecal bupivacaine in prolonging the analgesia duration. Duration of analgesia was significantly higher in clonidine group (497.20 ± 139.78 min) than in fentanyl group (416.87 ± 105.67), (P < 0.05). Augmented analgesia duration due to fentanyl and clonidine in our study was different as compared to other studies but is consistent with the study conducted by Shidhaye et al. The reason for this may be because of the usage of doses of clonidine, fentanyl, or bupivacaine similar to those used by Shidhaye et al.[5,6] Systemic side effects such as bradycardia, hypotension, or sedation are usually not associated with small dose of intrathecal clonidine or fentanyl and hemodynamic stability observed in both groups of our study confirms this. Only one patient had significant bradycardia requiring treatment with IV atropine. Similarly, Sethi et al. and Shah et al.[7,8] observed very few incidences of hypotension and bradycardia by using 1 mcg/kg of intrathecal clonidine for nonobstetric surgeries, whereas Kothari et al.[9] found the increased incidence of both hypotension and bradycardia in bupivacaine group than in bupivacaine with clonidine group. Bajwa et al.[10] did not observe bradycardia by addition of clonidine even up to 45 μg in 9 mg of bupivacaine. Similar hemodynamic stability was observed by Biswas et al. and Agrawal et al.[11,12] while using 12.5 μg and 25 μg of intrathecal fentanyl. In our study, both the groups are similar regarding onset, peak, and duration of sensory and motor block, but the duration of analgesia is significantly higher in

Table 3: Campbell Sedation score

Sedation Score	Group BF (n=50) (%)	Group BC (n=50) (%)
Wide awake	48 (96)	5 (10)
Awake and comfortable	2 (4)	37 (74)
Drowsy and difficult to arouse	0	0
Not arousable	0	0

P<0.05

Table 4: Other complications and side effects

Side Effects	BF group (n=50)	BC group (n=50)
Nausea	1	0
Vomiting	0	1
Pruritis	0	0
Hypotension	0	0
Bradycardia	0	1
Respiratory depression	0	0
Shivering	7	6

clonidine group than in fentanyl group (P < 0.05). Sedation scores in our study were more in clonidine group than in fentanyl group (P < 0.05). Similarly, in consistent with our study, Kothari et al. reported 35–45% of patients drowsy by addition of 50 μg of clonidine to bupivacaine but Bajwa et al. [13] did not report any sedation by addition of up to 45 μg of clonidine to bupivacaine. From the above observation, we can make out that the sedation with clonidine is dose dependent. In our study, we observe no sedation in fentanyl group and these findings are consistent with study conducted by Biswas et al., and Hunt et al. [14,15]

Conclusion

Addition of 50 μg clonidine to intrathecal bupivacaine offers longer duration of postoperative analgesia than 25 μg of fentanyl but with higher sedation. Both the drugs offer similar surgical conditions and prolongs postoperative analgesia (clonidine more than fentanyl), so we suggest fentanyl as better choice when sedation is not desirable and clonidine is recommended where sedation is acceptable.

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