To Determine the Role of Clonidine as an Adjuvant to Intrathecal Bupivacaine in Patients Undergoing Lower Abdominal Surgery

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Abstract

Background: Clonidine is an alpha-2 adrenergic agonist with various actions, one of which enhances the effectiveness of local anaesthetics. For patients undergoing lower abdominal surgery, we examined the effect of adding intrathecal clonidine to hyperbaric bupivacaine on postoperative pain relief and side effects, if any.

Aim: To assess the efficacy of intrathecal clonidine along with hyperbaric Bupivacaine in patients undergoing lower abdominal surgeries.

Method: It was a retrospective study carried out under spinal anaesthesia on 80 patients undergoing lower abdominal surgery. The research population was assigned randomly to two groups; group B- received 15 mg bupivacaine+ 0.4mi Normal Saline and group C received 15 mg bupivacaine + 60mcg clonidine.

Results: Addition of 60mcgs of intrathecal clonidine to 0.5% hyperbaric bupivacaine significantly prolonged the duration of motor & sensory blockade along with the duration of effective postoperative analgesia. The demand for rescue analgesic was earlier in group B as compared to group C. Both groups were matched for the side-effects like hypotension, bradycardia, nausea, vomiting, and shivering.

Keywords: *Spinal Anaesthesia, Clonidine, Lower Abdominal Surgeries, Post-op Analgesia.*

Introduction

Neuraxial blockage is more preferred mode of anaesthesia for lower abdominal surgeries. It has gained prominence since the introduction of spinal anaesthesia by "August bier" in 1898 due to its ease, minimal implementation ability, optimal operating environment, reduced risk of aspiration, low intraoperative blood loss, prolonged postoperative analgesia and minimal postoperative morbidity. Thus it was mostly used in sub-umbilical surgeries such as orthopedic lower extremity, arthroscopic, lower abdominal surgery[1]. Sub-arachnoid block (SAB) is one of the earliest known types of regional anaesthetic techniques.[2] This technique, however, suffered a significant setback shortly after it was described,[3] is now commonly used by anaesthetists[4] and clonidine has been introduced with newer hopes. Amide local anaesthetic, hyperbaric bupivacaine is most widely used for spinal anaesthesia. A small dose of hyperbaric bupivacaine produces a short lasting spinal anaesthesia,

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which may be clinically useful in ambulatory surgical procedures[5].

One drawback with spinal anaesthesia using bupivacaine alone is the relatively short duration of action, which means the postoperative period required early analgesic intervention. Potentiation of the effect of subarachnoid block and prolongation of postoperative analgesia can be achieved by using adjuvants to local anaesthetic agents such as Midazolam, Ketamine, Phenylephrine, Neostigmine, Clonidine, and Opioids.[6-12] out of which opiods are the most popular one's. Nevertheless, addition of opioids as adjuvant to local anaesthetic agent is associated with side effects[13] such as nausea, vomiting, pruritus, urinary retention, herpes labialis activation, and respiratory depression which directed the research in favour of non-opioid adjuvant and resulted in the introduction of clonidine as adjuvant to local anaesthetic agent.

Clonidine Hydrochloride is an imidazoline derivative with á2- adrenergic agonistic activity with a selectivity ratio of 200:1 in favour of á2 receptors. Intrathecal clonidine is demonstrated to potentiate the effect of subarachnoid block as well as reducing the local anaesthetic agent requirement.[14] Intrathecal clonidine also offers prolonged postoperative analgesia,[15,16] reduced shivering associated with subarachnoid block, and is devoid of side effects associated with intrathecal opioids. This research was therefore conducted to determine the degree of postoperative analgesia in patients undergoing lower abdominal surgery by intrathecal clonidine admixed with bupivacaine compared to bupivacaine alone.

Materials and Method

A cross sectional, prospective, observational study was conducted in the department of Anaesthesiology at Datta Meghe Medical College, Shalinitai Meghe Hospital and Research Centre, (DMIMS), Hingna Nagpur, in collaboration with Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi Meghe, Wardha, Maharashtra after obtaining permission from the Institutional Ethical Committee and written informed consent.

The study was carried out in the department of Anaesthesiology, Shalinitai Meghe Hospital and Research Centre Annexed to, DMMC, Wanadongari, Nagpur. Eighty patients with ASA physical status I or II in the 20-60 year age range, scheduled for lower abdominal surgery under spinal anaesthesia, have been enrolled in the study. Exclusion requirements included rejection of patients, age less than 20 years and older than 60, any contraindication to spinal anaesthesia or any patient with history of allergy to local anaesthetics. Patients were assigned randomly to two groups of 40 each to obtain either 15 mg of Bupivacaine (H) + 60mcg of clonidine (measured with insulin syringe) (group C) and 15 mg of Bupivacaine (H) + 0.4ml of regular saline in (group B). All of the research drugs were intrathecally added, and the total amount of administered agents was 3.4 ml. Preloading was performed with 10–15 ml/kg of ringer lactate. Monitoring parameters such as heart rate, ECG, oxygen saturation, and blood pressure were recorded. Under all aseptic precautions, subarachnoid block was given with 25 gauge Quinckie needle in L3-L4 space in sitting position and depending upon the groups, either 60 mcg clonidine or 0.4ml normal saline admixed with 3.0ml of 0.5% hyperbaric bupivacaine resulting in total volume of 3.4ml.

The primary outcome of this randomized observational study is to determine the time required for the first analgesic supplement and total analgesic intake post-operatively in the first 24 hours.

The secondary findings included the assessment of sensory block onset time, onset of motor block, duration of blockade, hemodynamic variables, the incidence of hypotension, mephentermine requirements, bradycardia, and adverse events such as and postoperative nausea, vomiting and shivering. Sensory and motor block was monitored every 5 mins for first 15 mins. Pinprick method was used to check the sensory block. The motor block was measured 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.[17] The onset of sensory block was taken from the time of intrathecal injection untill loss of pin prick sensation at T10. Sensory block length was taken as time from maximum height of block till regression to Level 1. The onset of motor block was described as time from intrathecal injection to motor blockade Level 2 in Bromage scale. Duration of motor blockage was taken as time from intrathecal injection untill no motor weakness (Bromage 0). Analgesia duration was described as time from intrathecal injection till administration of first rescue analgesic. The pain score

was measured postoperatively by using VAS between 0 and 10 (0 = no pain, 10 = extreme pain).[18] Injection diclofenac (75mg) was intramuscularly administered as rescue analgesic when VAS was >5. The time when the first dose of rescue analgesic was administered was noted. Data analysis was performed and analyzed using statistical package for social sciences (SPSS version 17.0) and GraphPad Prism 5.0 and $p<0.05$ is known as the degree of significance ($p<0.05$).

Observations And Results

Both groups were comparable in terms of demographic data, hemodynamic parameters. The observations are recorded in following tables:

Table 1: Comparison of initial block features in both categories

Initial Block Characteristics	Group C (n=40)	Group B (n=40)	t-value	p-value
OSB(sec)	87.75±14.40	96.25±16.66	2.440	<0.0169, S
DSB (min)	340±28.69	250.62±30.98	-13.388	<0.0001, HS
OMB(sec)	110.75±23.46	122.25±18.04	2.458	0.0162, S
DMB(min)	262±27.36	219.12±28.34	-6.885	<0.0001, HS
T2SR(min)	156.50±20.45	110.9±23.75	-9.202	<0.0001, HS
TDA(min)	270.75±29.71	222.87±32.38	-6.891	<0.001,S

Statistically significant difference was observed in total duration of analgesia between both groups. In group C it was 234.75±29.71 (min) while in group B it was 170.87±32.38 (min), (p value 0.000,S).

Table 2: Comparison of Time for First Rescue Analgesia in both the groups

Group	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Group C	40	357.00	54.26	8.57	9.19	0.000 S,p<0.05
Group B	40	259.50	39.35	6.22		

The above table and graph show the mean time required for rescue analgesia in both groups. Mean time for rescue analgesia in clonidine group was 357.00 minutes which was significantly higher compared to plain Bupivacaine group which was 259.00 minutes (p-value>0.05, NS).

Table 3: Total number of rescue analgesic in both the groups

	Clonidine (Mean)	Plain Bupivacaine (Mean)	t-value
Mean	1.5	2.15	2.51 p=0.045 S, p<0.05
SD	0.64	0.23	

The above table and graph shows the mean number of rescue analgesics that were required in both the groups. In clonidine group mean no of rescue analgesics that were required were 1.5 and in plain Bupivacaine group mean number of rescue analgesics that were required were 2.15. The difference was statistically significant. (p value 0.045, <0.05, S).

Table 4: Comparison of side effects in both the groups

Complications	Clonidine		Plain Bupivacaine		χ^2-value
	No	%	No	%	
Bradycardia	12	30	3	7.5	15.72 P<0.0001,S
Hypotension	4	10	2	5	0.68 P=0.40,NS
Nausea/Vomiting	0	0	5	12.5	13.90 P=0.0002,S
Shivering	0	0	12	30	12.77 P=0.0007,S

The above table and graph shows the incidence of side effects that were observed in both groups. 30% patients in clonidine group had bradycardia while only 7.5% patients in plain Bupivacaine group had bradycardia. The difference was significant (p-value <0.05, S). 10% patients in clonidine group had hypotension while only 5% patients in plain Bupivacaine group had hypotension. The difference was non-significant (p-value 0.40, NS). None of the patients in clonidine group suffered from shivering while 30% patients in plain Bupivacaine group had shivering. Difference was statistically significant (p-value 0.0007, S). None of the patients in clonidine group suffered from nausea and vomiting while 12.5% patients in plain Bupivacaine group had nausea and vomiting. Difference was statistically significant (p-value 0.0002, S).

Discussion

Clonidine is an α_2-agonist that block the conduction of Aδ and C fibers, thus prolonging the local anaesthetic action. It stimulates the postsynaptic α_2-receptors in substantia gelatinosa of spinal cord when used intrathecally and induces analgesia[15,19]. Roh et al.,[20] recently indicated that its ability to modulate spinal cord N-methyl-D-aspartate receptor activation through the suppression of NR1 phosphorylation is one of the mechanisms for enhanced intrathecal clonidine administration in a rat model of neuropathic pain.

Our observational research results highlight some main findings. First, the administration of intrathecal clonidine was associated with an increase in postoperative analgesia, as demonstrated by the significant decrease in rescue analgesic intake of Inj diclofenac 75 mg IM in 24 hours and the extension of time to the first analgesic application. Tuijl et al[21] observed the total duration of analgesia up to 120mins by using 75 μgs of clonidine in their study while in our research we found that it was 270.75±29.71mins. The mean time in the clonidine group for two segment regression (T2SR) was also 156.50 minutes, while in the control group it was 110.9 minutes. This was in line with Rajan et al's analysis where similar results were found as T2SR was 137.00 ± 10.42.[22] in the clonidine group.

Second result that should be noted is that the length of both the sensory block and the motor block is clearly enhanced by intrathecal clonidine. The mean length of sensory and motor block with clonidine group was 340±28.69 minutes and 262±27.36 minutes respectively, and 250.62±30.98 minutes and 219.12±28.34 minutes in simple Bupivacaine group. The disparity was extremely statistically significant. This result is also consistent with previous studies.[(11),(23),(24)] The mechanism of sensory block potentiation induced by clonidine in spinal anesthesia is stated to be based on the action of presynaptic (decrease in transmitter release) and post-synaptic (increase in hyperpolarisation)[25,26] Bhure et al. demonstrated that adding clonidine, morphine, and midazolam to bupivacaine substantially enhances the onset and length of sensory and motor block with greater hemodynamic control, prolongs the length of surgical analgesia and successful post-op anaesthesia, and decreases the intake of systemic analgesics compared to bupivacaine alone. They concluded that clonidine is an excellent addition to bupivacaine in spinal anaesthesia and offers extended analgesic time with no deleterious effects on mother and baby when used in the delivery of cesarean section[27.]

Third result that we found was that in the plain Bupivacaine group the mean time for rescue analgesia was 259 minutes while in the clonidine group it was 357 minutes. Rescue analgesic was issued at a score of 5 and more than 5 in the VAS.

Fourth thing we found was linked to intrathecal clonidine-induced side effects. We found in our analysis that systemic side effects such as bradycardia and hypotension were more in the clonidine group relative to the plain Bupivacaine group. Although bradycardia was more important than hypotension in the clonidine population, there is no other obvious explanation available except for the sympatholytic action of clonidine and profound analgesia which also reduces sympathetic function. Sethi et al.[15] and Shah et al.[16] reported very little occurrence of hypotension and bradycardia using 1 mcg/kg of intrathecal clonidine in non-obstetric surgery.

One major side effect that we observed in our study was shivering which is common during spinal anaesthesia. It is observed that around 30% patient under regional anaesthesia develop shivering either intra or post operatively[28]. Surgery and anaesthesia induce shivering as a compensatory mechanism due to thermal dysregulation, which is exacerbated by spinal anaesthesia vasodilatation that redistributes core body heat. We also found in our sample that the number of patients complaining of shivering in the simple Bupivacaine group was significantly high compared to the clonidine group[29]. Few studies also reflected on anaesthetics used lower abdominal surgeries [30-32].

Conclusion

We concluded by this that intrathecal clonidine 60 mcg with bupivacaine prolonged intraoperative anaesthesia and postoperative period for first analgesic request compared to plain Bupivacaine, as well as postoperatively less total analgesic intake in the first 24 hr in clonidine community.

Limitation of the study:

Need to study a larger sample size

The side effects like bradycardia & hypotension need more e attention & need to be evaluated more

Ethical Clearance: Taken from institutional ethics committee.

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Conflict of Interest: Nil.

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