

Intrathecal Bupivacaine vs Bupivacaine and Clonidine in Paediatrics Age Group: A Comparative Evaluation

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Abstract

Context: spinal anaesthesia is advantageous in that it uses small dose, simple to perform and offers a rapid onset of action, reliable surgical analgesia and good muscle relaxation. First report of paediatric spinal anaesthesia was published by August Bier in 1899 with Cocaine in 11 year old child for ischium abscess drainage.

Aims: To compare the efficacy, duration, quality and side effects of intrathecal Bupivacaine alone and Bupivacaine plus clonidine in paediatric patients. **Settings and Design:** Patients were randomly allocated in two groups. Group-A received Bupivacaine 0.5% heavy (0.4mg/kg for 5-15kg or 0.3mg/kg for >15 kg) and Group-B received Bupivacaine 0.5% heavy (0.4mg/kg for 5-15kg or 0.3mg/kg for >15kg) and preservative free Clonidine (1 mcg/kg). **Methods and Material:** A prospective randomised double blind study was carried out in 60 ASA-1 paediatric patients undergoing surgeries below T8 dermatome up to 2 hrs duration. Patients were randomly allocated in two groups. Group- A and Group-B comprising 30 patients each. Time of onset of sensory block, maximum level of

sensory block, duration of sensory block, duration of post-op analgesia and side effects were observed.

Statistical analysis used: Data obtained was subjected to statistical computation and analysed using computer programme statistical package for social science (SPSS) ver-16.0 and test performed were unpaired student-t test, nonparametric mann-whitney two samples test and Chi square test. Value of $p < 0.05$ was considered significant and $p < 0.0000001$ highly significant. **Results:** addition of preservative free clonidine (1mcg/kg) to 0.5% hyperbaric Bupivacaine provides prolonged spinal anaesthesia, superior pain relief and better sedation without causing severe adverse effects compare to Bupivacaine alone. **Conclusions:** Clonidine is better adjuvant to Bupivacaine in spinal anaesthesia as far as patients comfort is concerned. It decreases the time taken for onset, produces longer duration of both surgical anaesthesia and postoperative analgesia and better quality of sedation with no added side effects as compare to Bupivacaine alone, in paediatric patients undergoing surgeries below T8 dermatome.

Keywords: Bupivacaine; Clonidine; Paediatric spinal.

Introduction

Pain is a major concern of human kind since our beginning and object of ubiquitous efforts to understand and to control it. Paediatric pain management is challenging and one of the frontiers of modern anaesthesia. First report on paediatric spinal was published by AUGUST BIER in 1899, when the technique was performed with cocaine in an 11 yr old boy for ischium abscess drainage.

Spinal anaesthesia is advantageous in that it uses small dose of anaesthetic, easy to

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perform and offer a rapid onset, reliable surgical analgesia and good muscle relaxation. Advantages sometime offset by relatively short duration of action and complaints of postoperative pain when it wears off. Spinal anaesthesia with hyperbaric Bupivacaine hydrochloride is popular for longer procedure due to its prolonged duration but there is need to intensify and increased duration of sensory blocked without increasing the intensity and duration of motor blocked and thus prolong the duration of postoperative analgesia.

Various studies have shown that 1mcg/kg clonidine provides a significant improvement in spinal anaesthesia quality, duration and reduces the need of post-operative analgesic requirement without a significant side effects. [1,2,3,4,5,10,11] There is adequate evidence that α -2 adrenergic agonist clonidine given intrathecally produces anti nociceptive effects without any neurotoxicity and useful in the treatment of somatic pain.[1,2,3,4] However unlike spinal opioides clonidine does not produce pruritis and respiratory depression. The rationale behind intrathecal administration of clonidine is to achieve a high drug concentration in the vicinity of α -2 adrenoreceptors in spinal cord by blocking pain conduction of C and A-delta fibres. It increases potassium conductance in isolated neurons in-vitro and intensifies conduction block of local anaesthetic.[7] A α fibres are myelinated afferent sensory nerve fibres, which conduct pain, cold, temperature and touch sensation, and C fibres are nonmyelinated postganglionic sympathetic fibres which conduct pain, warm temperature and touch sensation.[8] Clonidine is now an acceptable adjuvant to local anaesthetic for epidural route nevertheless clinical trial provide evidence that less clonidine is needed intrathecally than epidural to

produce same analgesic effect with fewer side effects.

In the present study we tried to find out effectiveness of 1mcg/kg intrathecal clonidine added to hyperbaric Bupivacaine on onset, quality, duration of analgesia and side effects if any in paediatric patients undergoing surgeries below T8 dermatome

Subjects and Methods

After approval from local ethical committee of institute and written valid informed consent from parents/guardians of all the patients with grade ASA 1 of physical status weight 5-30 kg and age 3-10 years and surgeries below T8 were enrolled for the study except those patients with known sensitivity to the drugs, gross spinal deformity and peripheral neuropathy. Patients were randomly allocated into two groups in a double blinded fashion based on computer generated code. Group-A (0.5% hyperbaric Bupivacaine (0.4 mg/kg for 5-15 kg or 0.3mg/kg for >15kg) and Group-B (0.5% hyperbaric Bupivacaine (0.4 mg/kg for 5-15 kg or 0.3mg/kg for >15 with 1 mcg/kg preservative free clonidine). Detailed preoperative evaluation carried out in all patients and vital parameters noted, Routine investigations like complete blood count, BT, CT, random BSL, urine routine microscopy done. Patients were properly monitored in operation theatre and baseline parameters were noted. Monitoring commenced with pulse-oximeter (spo2), NIBP. peripheral venous access with 22/24 G cannula was secured on dorsum of the hand but there was no fluid preloading. They were premedicated with Glycopyrrolate 4mcg/kg iv before lumbar puncture. Patients were induced with O2 and sevoflurane for 3 mins. Lumbar puncture done in L4-

L5 interspace with disposable hypodermic needles (27G *1.5 inches). Correct needle position confirmed by free CSF flow and the calculated dose of drug i.e. either Bupivacaine alone (Group-A) or Bupivacaine plus clonidine (Group-B) injected intrathecally without barbotage. Patients then immediately placed in supine position with slight head elevation. Intra-operative fluid is given by using 4-2-1 formula, i.e. Holiday seggar. After blocked following parameters related to sensory level were noted.

1. Time of onset of sensory blocked.
2. Maximum level of sensory blocked achieved.
3. Duration of sensory blocked.

Onset of block was defined as loss of sensitivity at the same dermatome level as lumbar puncture. The level of sensory block was determined by attempting to elicit grimace or acknowledgement of pain to bilateral pin prick at each dermatome from caudal to cephalad direction every 2 minutes. The adequacy of spinal anaesthesia was determined by the presence of profound motor block at ankle, knees and hip joints. Patients with failed spinal block were excluded from this study and surgery was performed under general anaesthesia. Vital parameters like HR, BP, RR, peripheral O2 saturation, sedation score noted every min for 5 mins thereafter every 5 min for 30 min, then every 30 min till 2 hrs. Then at 3rd hr and then every 2 hourly for 12 hours. Intraoperatively sedation is graded as follows:

0. eye opening spontaneously
1. eye opening to speech
2. eye opening when shaken
3. unarousable

Duration of surgery was noted. At the end of surgery, no prophylactic pain relief was given and patients were transferred to post anaesthesia care unit and monitoring was continued for vital parameters, Sedation score and level of sensory blocked was noted every 30 minutes for first 2 hours, every hour for next 12 hours. Duration of sensory blockade was defined as - the time from injection of subarachnoid drug till the level of regression up to L5-S1 and it was assessed by reappearance of sensation on heel and sole of foot.

Postoperative pain was assessed by – Modified objective pain score[11,13], given maximum score of 10. Modified objective pain score is used to assess the pain over 5 min. period every hourly. Higher the score greater the pain experience for the child. When objective pain score is more than 4, end point of observation and rescue analgesic will be given.

Duration of analgesia was considered as interval from time of intrathecal injection to the time of rescue analgesic demanded postoperatively. The total numbers of analgesic doses needed in the first 12 hours were noted. All the patients were observed for any side effects or complications in the post-operative period for 12 hours and following complications if occurred were

Variable	Score 0	Score 1	Score 2
Crying	None	Consolable	Not consolable
Movement	None	Restless	Thrashing
Agitation	Asleep/calm	Mild	Hysterical
Posture	Normal	Flexed	Holds injury site
Verbal	Asleep/no complain	Complains but cannot localize	Complains can localize

noted and treated with conventional methods.

Hypotension: fall of blood pressure >20% from baseline was considered as hypotension. It was treated with intravenous fluid administration, raising the foot end, oxygen inhalation and Vasopressor agents. Physiological impact of sympthectomy is minimal or none in small age groups.[16]

Bradycardia: fall of heart rate >20% from baseline was considered as bradycardia and was treated with inj. atropine 10mcg/kg administered intravenously watching for other vital parameters.

Desaturation: saturation <90% was treated with oxygen supplementation.

High spinal level.

Urinary retention.

Excessive Sedation.

Post-Dural puncture headache (PDPH): for prevention of PDPH – use of smaller gauge spinal needle and good hydration (preoperative and intraoperative) though PDPH is low in pediatric patients. [16,18,19,20]

Transient neurological syndrome or other neurological disorder/deficit.

Results

The present study was conducted in 60 ASA-I paediatric patients undergoing surgeries below T8 dermatome to compare the efficacy, duration, quality of spinal blockade and side effect if any

between intrathecal Bupivacaine alone and clonidine added to intrathecal Bupivacaine. Thirty patients were randomly allocated in each of the following two groups.

Demographic profile of the patients is comparable with respect to age and weight. Distribution per ASA status is similar in both the group.

Addition of clonidine to Bupivacaine as an adjuvant result in earlier onset of sensory block (3.1667 ± 1.4162) and more duration of sensory block (168.63 ± 7.0783) compare to Bupivacaine alone i.e. (4.8 ± 1.54) and (110.07 ± 10.8) respectively. [11] All these initial block characteristics turn out to be statistically significant values on comparison i.e. $P < 0.0000001$.

The changes in objective pain score for pain were noted. Comparison was done by applying unpaired t 'test. Significant difference was found from 30 min after shifting up to 12 hours. Objective pain score were low in Group B as compared to Group A.

The above table shows that, Sedation score is significant right from 15 minutes to 3 hours after subrachnoid block. It is significant statistically. It shows Group B patients are more sedated than Group A patients. Clonidine is a popular sedative agent nowadays. Similar findings are observed in our study. Mean sedation scores were higher in Group B than Group A [10,12,13,14] and significant statistically i.e. $P = < 0.0000001$.

Findings of table 5 reveals statistically significant values on comparison of post

Table 1: Demographic data and duration of surgery

	Age (years)	Weight(kg)	m	f	Duration of surgery
Group A (n=30) (mean±SD)	5.83±2.7678	19.06±6.7565	27	3	46.3±13.1
Group B (n=30) (mean±SD)	6.2±2.329	17.56±6.8101	27	3	52.83±16.272
P value	0.586	0.395	1.000		0.093

For age and weight $P > 0.05$ non- significant.

Table 2: Comparison of initial block characteristics

	Group-A (n=30) (mean±SD)	Group-B (n=30) (mean±SD)	P value
Onset of sensory block	4.8±1.54	3.1667±1.4162	<0.0000001
Duration of sensory block	110.07±10.8	168.63±7.0783	<0.0000001
Two segment regression	82.3±11.13	112.8±9.58	<0.0000001

P-value < 0.0000001 i.e. highly significant.

Table 3: Comparison of modified objective pain scores between Group A and Group B

Duration	Group A mean±SD	Group B mean±SD	P value	Sign
Shift	0	0	-	NS
30min	0.2333±0.5683	0	0.02836	Sign
1hr	2.266±1.38	0.333±0.711	<0.0000001	Sign
2hr	5.4±1.1919	1.767±1.278	<0.0000001	Sign
4hr	4.3333±1.02833	3.27±1.2	0.0004868	Sign
6hr	3.7±0.7497	2.87±0.78	0.000084	Sign
8hr	3.266±0.5833	2.2±0.71	<0.0000001	Sign
10hr	2.8333±0.5921	1.8±0.48	<0.0000001	Sign
12hr	2.6666±0.6144	1.5±0.51	<0.0000001	Sign

Table 4: Comparison of sedation score

Time	Group A (N=30)		Group B (N=30)		Unpaired t -test	
	Mean	SD	Mean	SD	P-Value	Sign.
15 min	0	0	0.266	0.305	<0.005	Sign.
20 min	0.1	0.3051	0.7333	0.4498	<0.005	Sign.
25 min	0.2	0.407	0.933	0.365	<0.005	Sign.
30 min	0.3	0.4661	1.13	0.346	<0.005	Sign.
60 min	0.3	0.466	1.2	0.4068	<0.005	Sign.
90 min	0	0	1.06	0.254	<0.005	Sign.
120min	0	0	0.83	0.379	<0.005	Sign.
3 hrs	0	0	0.17	0.38	<0.005	Sign.

Table 5: Post operative block characteristics in mins

	Group A	Group B	P value
2 segment regression	82.3±11.13	112.8±9.58	<0.0000001
Total duration of post-operative analgesia	191±21.551	365±84.578	<0.0000001
Total no of analgesics in 12 hours	2.4666±0.5074	1.5±0.6297	<0.0000001

operative block characteristics. Among the two groups, Clonidine provided the smooth and prolong post operative analgesia as compared to Bupivacaine alone.[9,11] The evidence was very much visible in the prolong time to two

segmental dermatomal regression[11,13] in Group B i.e. 112.8±9.58. As a result time of rescue analgesia[9,11,13] was comparatively shorter 191±21.551 in Group A than Group B. p < 0.0000001.

Table 6: Comparison of Adverse Effects in Both Groups

Side Effects	Group A	Group B
Bradycardia	1	2
Hypotension	0	2
Nausea/ Vomiting	0	0
High spinal	0	0
PDPH	0	0
Urinary Retention	0	0

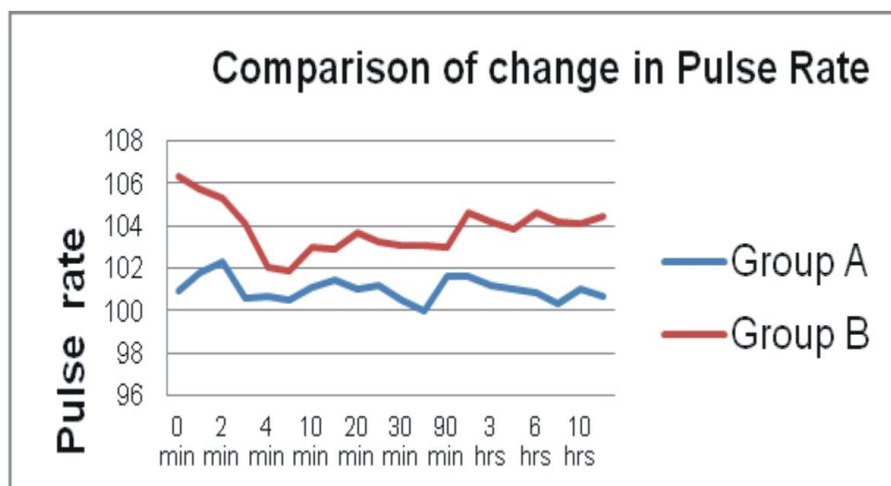
Table 6 shows the incidence of side effects in all groups. Bradycardia was found in 1 cases of group A and 2 cases of Group B, Hypotension was observed in 0 cases of group A and 2 cases of group B. No patient in any group had nausea/ vomiting, PDPH, urinary retention or high spinal level.

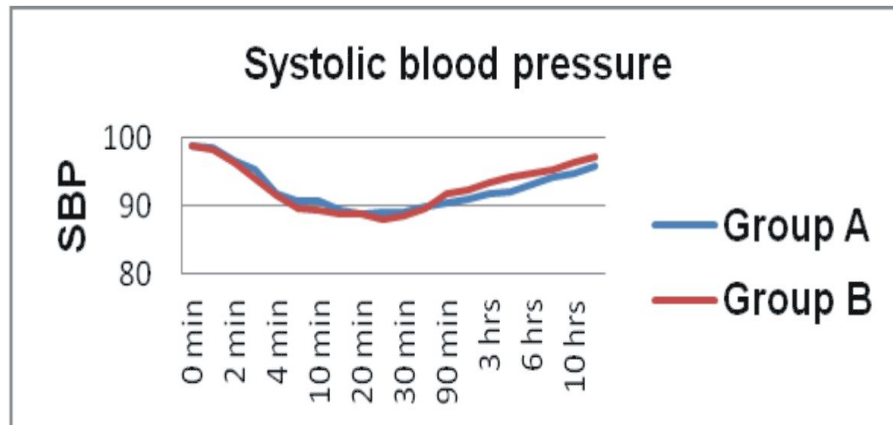
Discussion

The subarachnoid block is a popular, simple and reliable anaesthetic technique for lower abdominal and lower limb surgeries. It has been used widely in clinical practice of anaesthesia because of rapid onset, high reliability and low cost. It produces excellent operating conditions and has high success rate. Though it provides effective analgesia in the initial postoperative period, the effect needs supplementation

of potent opioid analgesics systemically to extend the period. Systemic opioids have been associated with respiratory depression, nausea, and vomiting, itching, and urinary retention. Subarachnoid block last shorter in children than adults because of rapid pharmacokinetics in children as compared to adult. Hence, attempts were made to increase duration of analgesia produced by subarachnoid block by adding various agents intrathecally, like opioids e.g. morphine, buprenorphine, hydromorphone, fentanyl, and non-opioids e.g. ketamine, neostigmine, but none of them have been accepted in clinical practice due to their side effect or non-availability

Spinal anaesthesia is an excellent option in paediatric population as it provides a rapid onset of profound and predictable uniformly distributed analgesia with good neuromuscular blockade. Paediatric spinal anaesthesia has proven to be a safe alternative to routinely administered general anaesthesia as it avoids the polypharmacy associated with the latter technique and also reduces the incidence of post-operative respiratory complications associated with administration of general





anaesthesia.[15] In our study, we evaluate and compare the effects of intrathecal clonidine 1 µg/kg added to hyperbaric Bupivacaine 0.5% and intrathecal Bupivacaine alone on the quality of subarachnoid block, postoperative analgesia and side effects in patients undergoing lower abdominal surgeries. The demographic profile of our patients comparable with respect to age, weight, sex, ASA grading and duration of surgery. Results of study shows that addition of clonidine 1 mcg/kg to Bupivacaine 0.5% hastens the onset of analgesia, increases the time to regression of sensory block, longer duration of sensory block and decreased need of analgesic. Clonidine has a visible edge over Bupivacaine alone as it enables earlier onset and established a sensory time of block.

The results of our study clearly indicate the effectiveness of intrathecal clonidine as a profound sedative [10,12,13] and the patients were arousable by gentle tactile stimulation. Overall sedation scores was highly significant statistically with administration of clonidine. In all patients spo2 maintained more than 90%.

The group-A shown visible superiority over various post operative block characteristics like regression of sensory block, prolonged post-operative analgesia,

lesser amount of analgesic requirement post- operatively. Cardio respiratory parameters as evident from figure 1.

Statistically significant difference was not found in two groups in terms of pulse rate throughout the observation period.

Systolic blood pressure in both the groups fell after induction and return back to near preoperative level. Difference of fall in blood pressures between the groups at different time intervals studied was statistically not significant. No patient in any group had nausea, PDPH, vomiting, urinary retention and high spinal level although one case of bradycardia was found in group-A and two cases of bradycardia and two cases of hypotension were found in group-B. These side effects were not significant on statistical comparison.

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