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The effect of intrathecal clonidine versus intravenous clonidine on duration of spinal anaesthesia with 0.5% hyperbaric bupivacaine, a randomised controlled trial

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Abstract
Background: Spinal anaesthesia can be prolonged after adding adjuvants to local anaesthetics or by intravenous route before the block is performed.
Aim of the work: To prolong the duration of spinal anaesthesia after the block has been performed.
The study was done to compare the effects of intrathecal (IT) and intravenous (IV) clonidine on duration of spinal anaesthesia and to evaluate any advantages or disadvantages of IV over IT clonidine in terms of analgesia, sedation and hemodynamic stability.
Patients and Methods: After ethical clearance, informed and written consent, patients undergoing elective abdominal and lower limb surgeries, were assessed for the inclusion and exclusion criteria. Patients were randomised into two groups of 50 each using computer generated numbers.
Group A: This group of individuals was given intrathecal bupivacaine 15mg + clonidine 1 mcg/kg consisting of 50 patients.
Group B: This group of individuals was given slow intravenous clonidine 1 mcg/kg 15 minutes before spinal anaesthesia + intrathecal bupivacaine 15mg consisting of 50 patients.
Patients were assessed for pain by visual analogue scale (VAS), blood pressure (BP), Heart rate (HR), respiratory rate (RR), oxygen saturation pulse oxymetry (SPO2), sedation, nausea, vomiting at 0 minutes (min), 2 mins, 4 mins, 6 mins, 8 mins, 10 mins, 15mins, 30 mins, 45 mins, 1 hour (hr), 2 hour and 1 hourly until the surgery is over.
Postoperatively assessed for pain VAS, BP, HR, SPO2, RSS 1 hourly till 24 hours.
Results: Intravenous clonidine before bupivacaine spinal anaesthesia has characterstics similar to and comparable with intrathecal clonidine with bupivacaine in terms of sensory and motor onset; maximum sensory and motor block achieved; duration of motor block; duration of analgesia; hemodynamic stability, with an added advantage of significant intraoperative and postoperative sedation.
Conclusion: Our study has demonstrated that addition of clonidine to intravenous and intrathecal spinal bupivacaine significantly increases the duration of analgesia and motor blockade.

Keywords: clonidine, spinal anaesthesia, bupivacaine, motor blockade, analgesia

Introduction

- Spinal anaesthesia is a type of regional anaesthesia used for analgesia during surgeries involving lower limbs and below umbilical level surgeries [1].
- Duration of analgesic action of local anaesthetics can be prolonged by mixing them with certain pharmacological agents called "additives" or "adjuvants".
- Clonidine hydrochloride is an imidazoline derivative and exists as a mesomeric compound commonly used as an adjuvant to local anaesthetics in peripheral nerve blocks where it prolongs the duration of anaesthesia as well as analgesia.

The aim of this study is

1. To compare the effects of intrathecal and intravenous clonidine on duration of spinal anaesthesia.
2. To evaluate any advantages or disadvantages of intravenous over intrathecal clonidine in terms of analgesia, sedation and hemodynamic stability.

Materials and Methods

Ethics: Ethical Committee clearance was obtained as per institution protocol.

Study design

Randomised Controlled Study

Patients undergoing elective surgeries lower limb and abdominal surgeries were assessed for the inclusion and exclusion criteria and were included in the study after obtaining written informed consent.

Inclusion criteria

1. Posted for lower limb surgeries and abdominal surgeries
2. Adult males and females
3. 18 to 45 years
4. ASA I and II
5. BMI < 30 kg/m^2

Exclusion criteria

1. Pregnancy
2. Known sensitivity to clonidine
3. Bradycardia, cardiac dysfunction, renal or hepatic dysfunction
4. Hypotension
5. Polytrauma

Study design

- Sample size: 100 (50 each group)
- Power of study was kept at 80%, levels significance 5% at two tailed test.
- Sampling method: Simple random sampling
- Statistical tests: SPSS version 20 programs were used to enter data and statistical analysis. Data were presented as Mean ± SD,range, number. Comparisons between two groups were performed using unpaired Student's t-test. A P value <0.05 was considered statistically significant. Microsoft word and excel have been used to generate graphs and table.

Method

- All the patients underwent a thorough preoperative assessment on the previous day of surgery, and written informed consent was obtained for participation in the study.
- Randomization was done by computer-generated random numbers. Ringer lactate was infused 15ml/kg within 30 minutes.
- Baseline levels of blood pressure, pulse rate and respiratory rate and oxygen saturation were recorded. The patients was placed in lateral decubitus or sitting position.
- Using full aseptic precautions a midline lumbar puncture was performed through L3-L4 intervertebral space with a spinal needle of 23G.
- The position of the needle in the subarachnoid space was confirmed by free flow of CSF through the needle hub.
- The individuals where divided into two groups

Group A: This group of individuals was given intrathecal bupivacaine 15mg + clonidine 1 mcg/kg consisting of 50 patients.

Group B: This group of individuals was given slow intravenous clonidine 1 mcg/kg 15 minutes before spinal anaesthesia + Intrathecal bupivacaine 15mg consisting of 50 patients.

- The needle was taken out and the patient turned to supine position. Blood pressure, pulse rate, respiratory rate and oxygen saturation was recorded at every 2 minutes for the first 10 minutes then every 15 minutes till 1 hour and 1 hourly thereafter until the surgery is over.
- The time of injection of bupivacaine into sub-arachnoid space was noted. The onset of sensory block was detected by testing the response to pinprick and the onset of motor block by asking the patient to move the legs.
- Post- operative observation was done, blood pressure, pulse rate and respiratory rate was noted and the patient was transferred to the ward.
- The patients were visited at regular intervals of 1 hour in the ward in order to note the time of recovery of sensory, motor paralysis to elicit sensory recovery, heart rate, blood pressure and oxygen saturation.
- Patients were observed constantly for complications. Resuscitative measures were kept.
- Instructions were given to the patient to report whenever they have any difficulties or side effects.
- Neurological function that is sensation of touch, pain, and temperature and muscle power was observed till they will be discharged from the hospital.

Follow Up- 24 hours

Results

All the groups studied were comparable with respect to age, gender, weight and ASA distribution and there were no significant difference in demographic data. All blocks were tested before starting the procedure till deemed adequate for surgery. No patients in any group required conversion to general anaesthesia or required additional analgesics during surgery. There was no significant difference regarding the type and duration of surgical procedures in all group.

Table 1: Patient characteristics

	Group A (IT)	Group B (IV)	P Value
Age	35 ± 3.24	36 ± 2.15	0.07
Weight	55.6 ± 5.6	54.8 ± 3.8	0.40

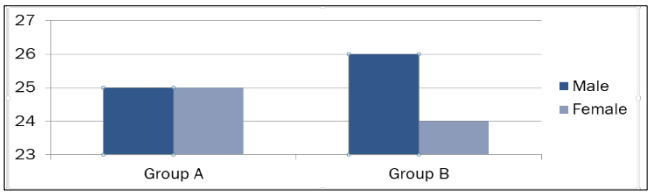

Fig 1

There was no significant difference in mean arterial pressure in Group A (IT) and Group B (IV) clonidine groups. P value > 0.05

Table 2: Mean arterial pressure

Time	Group A (IT)	Group B (IV)	P value
Before drug	79 ± 5.20	77 ± 6.79	0.10
2 min	78 ± 5.70	76 ± 6.78	0.11
4 mins	70 ± 6.25	71 ± 6.29	0.42
6 mins	67 ± 4.25	66 ± 4.20	0.23
8 mins	64 ± 4.83	63 ± 4.71	0.29
10 mins	86 ± 4.71	85 ± 4.89	0.30
15 mins	84 ± 5.94	83 ± 6.72	0.43
30 mins	82 ± 6.89	81 ± 6.89	0.46
45 mins	79 ± 6.59	77 ± 7.1	0.14
60 mins	78 ± 6.79	77 ± 6.89	0.46
120 mins	78 ± 6.66	77 ± 6.62	0.45

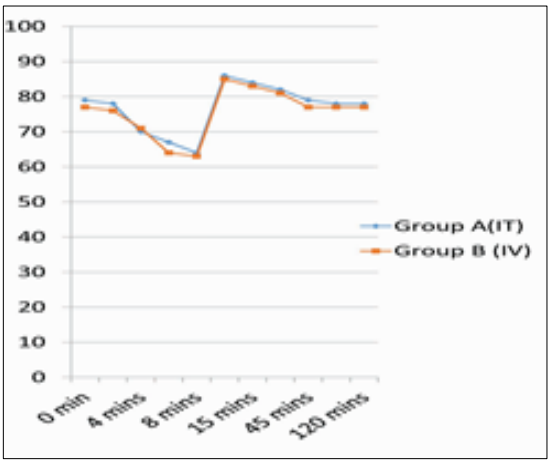

Fig 2

There was no significant difference in Ramsay sedation score in Group A and Group B. P value > 0.05

Table 3: Ramsay sedation score

Time	Group A(IT)	Group B (IV)	P value
Before drug	1.3 ± 0.8	1.5 ± 0.52	0.14
2 mins	1.9 ± 0.41	1.8 ± 0.39	0.21
4 mins	1.8 ± 0.31	1.7 ± 0.37	0.14
6 mins	2.0 ± 0.32	1.9 ± 0.29	0.10
8 mins	2.21 ± 0.42	2.14 ± 0.80	0.58
10 mins	2.11 ± 0.21	2.10 ± 0.50	0.89
15 mins	2.20 ± 0.41	2.11 ± 0.28	0.20
30 mins	2.14 ± 0.42	2.20 ± 0.27	0.39
45 mins	2.20 ± 0.22	2.17 ± 0.41	0.64
60 mins	2.15 ± 0.31	2.11 ± 0.55	0.65
120 mins	1.9 ± 0.72	2.06 ± 0.56	0.21

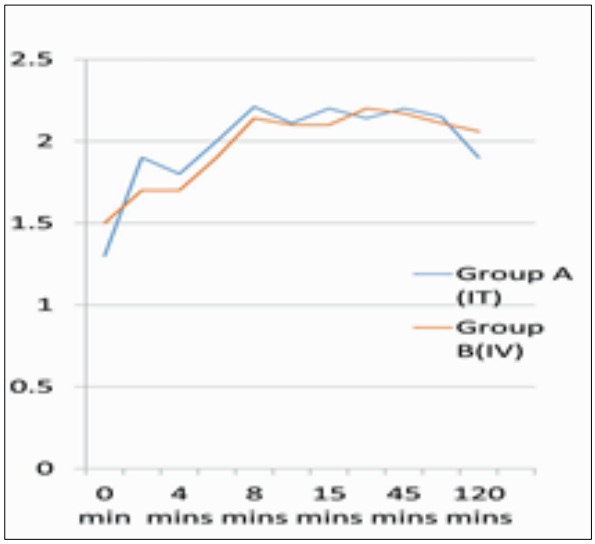

Fig 3

There was no significant difference in VAS in Group A and Group B. P value > 0.05

Table 4: visual analogue scale

Time	Group A (IT)	Group B (IV)	P Value
Before drug	5.1 ± 1.4	5.4 ± 1.3	0.26
2 mins	5.1 ± 1.3	5.3 ± 1.2	0.42
4 mins	5.3 ± 1.0	5.2 ± 1.4	0.68
6 mins	4.8 ± 1.2	4.7 ± 1.6	0.72
8 mins	0	0	-
10 mins	0	0	-
15 mins	0	0	-
30 mins	0	0	-
45 mins	0	0	-
60 mins	0	0	-
120 mins	0	0	

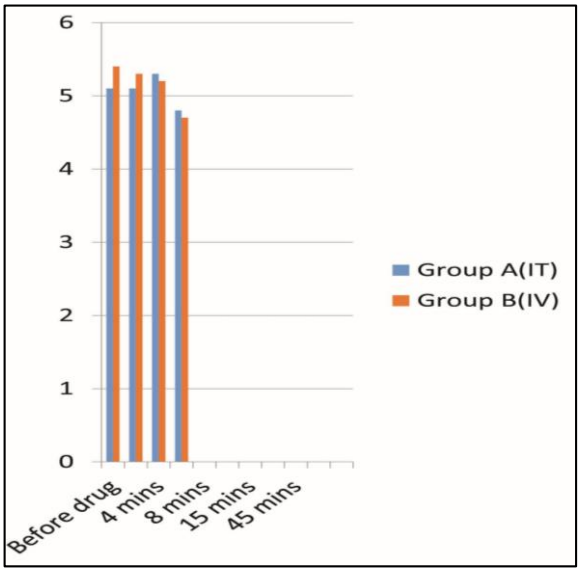

Fig 4

There was no significant difference in HR in Group A and Group B. P value > 0.05

Table 5: heart rate

Time	Group A (IT)	Group B (IV)	P value
Before drug	105 ± 5.2	103 ± 4.8	0.32
2 mins	94 ± 6.3	96 ± 5.2	0.86
4 mins	80 ± 5.9	81 ± 4.12	0.32
6 mins	79 ± 6.0	80 ± 2.42	0.27
8 mins	78 ± 5.98	79 ± 2.20	0.26
10 mins	85 ± 5.98	87 ± 4.12	0.05
15 mins	84 ± 6.10	86 ± 6.02	0.10
30 mins	83 ± 5.72	82 ± 5.20	0.36
45 mins	87 ± 5.62	85 ± 6.56	0.10
60 mins	88 ± 6.08	86 ± 5.72	0.09
120 mins	92 ± 4.92	93 ± 5.26	0.35

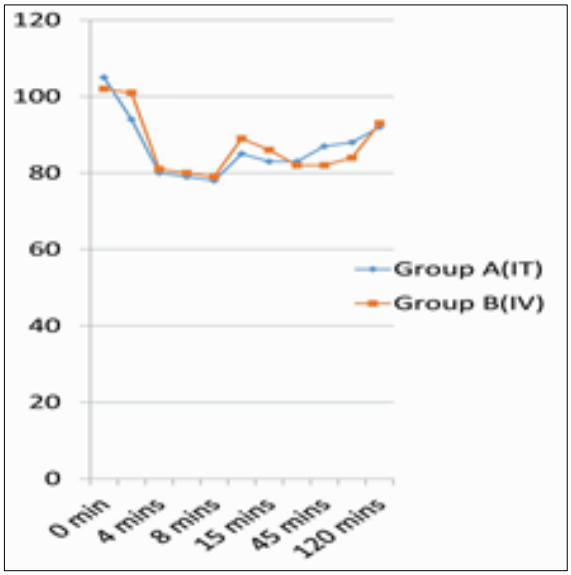

Fig 2

Sensory Characteristics

The duration of sensory analgesia (T 10) sec from the onset to T 10 level in Group A was 210.45 ± 60.17 sec and in Group B was 230.65 ± 75.33 sec there was no significant difference, P Value- 0.14

The duration of maximum level of analgesia (sec) in Group A was 420.60 ± 150.60 sec and Group B was 439.20 ± 98.69 sec there was no significant difference, P Value- 0.46

The total duration of analgesia in Group A was 320.35 ± 90.76 min and Group B was 298.85 ± 31.20 min there was no significant difference, P Value- 0.11

Motor Characteristics

The onset of motor blockade (sec) in Group A was 150.09 ± 99.26 sec and in Group B was 168.14 ± 56.24 sec there was no significant difference, P Value- 0.26

The maximum grade of motor blockage achieved in Group A was 313.74 ± 89.46 sec and Group B was 285.07 ± 90.46 sec there was no significant difference, P value- 0.11

Quality of motor blockade was grade 3 in Group A and Group B.

Intra-operative and postoperative complications

In group A the complications were shivering 4%, bradycardia 4%, hypotension 6 %. There was no nausea and vomiting and other complications like dryness of mouth and respiratory depression. In group B complications were nausea and vomiting 6%, bradycardia 6% and hypotension 8%. All the adverse effects were found to be statistically insignificant.

Table 6

Adverse effects	Group A (IT)	Group B (IV)
Shivering	2 (4%)	-
Nausea and vomiting	-	3 (6%)
Bradycardia	2 (4%)	3 (6%)
Hypotension	3 (6%)	4 (8%)

Discussion

Clonidine is a selective partial agonist for α-2 adrenoreceptors. It is known to increase both sensory and motor block of local anaesthetics [2]. The analgesic effect following its intrathecal administration is mediated spinally through activation of post synaptic α -2 receptors in substantia gelatinosa of spinal cord [3]. The rationale behind intrathecal administration of clonidine is to achieve a high drug concentration in the vicinity of α -2 adrenoreceptors in the spinal cord and it works by blocking the conduction of C and Aδ fibres, increases potassium conductance in isolated neurons in vitro and intensifies conduction block of local anaesthetics.

Clonidine is now an acceptable adjuvant to local anaesthetics for epidural route; nevertheless clinical trials provide evidence that less clonidine is needed intrathecally than epidurally to produce nearly same analgesic effect with fewer side effects.

Dobrydnjov *et al*. in their study in orthopaedic patients, on postoperative pain relief following intrathecal bupivacaine combined with intrathecal or oral clonidine (150 μg), found that addition of intrathecal clonidine prolonged analgesia and decreased morphine consumption postoperatively more than oral clonidine. Hypotension was less pronounced after intrathecal thanss oral clonidine [4]. The data obtained from our study indicate that addition of 1 μg.kg-1 of clonidine to 0.5% bupivacaine significantly prolongs the analgesia and thus reduces the postoperative analgesic requirement. The maximum dose of clonidine used in our patients was 70 μg.

There was no significant difference in mean arterial pressure (MAP), heart rate (HR), visual analogue scale (VAS), Ramsay sedation score (RSS).

Adverse effects such as nausea and vomiting, hypotension, bradycardia was noted but was not statistically significant.

Our study implies that it's possible to achieve equally good analgesia without side effects when clonidine is used in dosages as low as 1 mcg/kg.

Overall as the primary outcome, the study revealed intrathecal and intravenous clonidine to spinal anaesthesia with 0.5% bupivacaine has characteristics similar in terms of sensory and motor onset, maximum sensory and motor block achieved, duration of motor block, duration of analgesia, hemodynamic stability with an added advantage of intraoperative and postoperative sedation.

As a secondary measure the side effects of the drug were found to be minimal in both the Group A and Group B.

Conclusion

From the present study it can be concluded that intravenous clonidine before bupivacaine spinal anaesthesia has characterstics similar to and comparable with intrathecal clonidine with bupivacaine in terms of sensory and motor onset; maximum sensory and motor block achieved; duration of motor block; duration of analgesia; hemodynamic stability, with an added advantage of significant intraoperative and postoperative sedation.

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