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HAEMODYNAMIC AND ANALGESIC PROFILE OF DIFFERENT DOSES OF CLONIDINE WITH SMALL DOSE OF BUPIVACAINE UNDER SPINAL ANAESTHESIA IN LOWER ABDOMINAL SURGERIES.

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ABSTRACT

Objective : To find out the lowest possible dose of Clonidine that can prolong the duration of sensory and motor anesthesia & analgesia with minimal dose of Bupivacaine without undue side effects.

Methods : In this prospective randomized double blind study 90 ASA grade 1 & 2 patients were randomly allocated in 3 groups. All receive 6 mg Bupivacaine with 15ug of Clonidine in group 1, 45ug of Clonidine in Group 2, 75ug of Clonidine in group 3.

Result : Onset of sensory analgesia & motor blockade up to maximal level was achieved faster with 75ug dose (sensory 9.6 ±0.67 min & motor 13.63 ± 0.45 min). The addition of Clonidine to Bupivacaine and increasing its dose delays the time for 2 segment sensory regression (149. ±3.61min), regression to segment L1 (246.72±2.58 min), increases the duration of motor blockade (200.83±2.73 min) & time to walking (320.83 ±3.18min) & voiding (392.47±3.53min). It also increases the time to 1st analgesic requested (339±3.32min). The incidence of postoperative complications was not significantly different in between different doses of Clonidine.

Conclusion : 75ug is the preferred dose, in terms of effect versus side effects, when prolongation of spinal anesthesia is desired as in lower abdominal surgeries.

KEYWORDS : Spinal Anesthesia, Small dose of Bupivacaine, Clonidine, lower abdominal surgeries.

INTRODUCTION

Postoperative pain is due to tissue injury along with muscle spasm after surgery. Central as well as peripheral sensitizations are involved in generation of postoperative pain. It increases the possibility of postsurgical complications, raises the cost of medical care, interfere with recovery and return to normal activities of daily living. So as an anaesthetist our purpose is to provide adequate analgesia as well as early ambulation & discharge from hospital.

These goals can be achieved with right choice of local anesthetics & use of adjuncts to augment spinal anesthesia. Recent dose-response data on the clinical anesthetic characteristic of spinal Bupivacaine indicate that small doses can be used for ambulatory anaesthesia. Hyperbaric Bupivacaine in doses of 6-8 mg has found to be a suitable for surgical procedures of mean duration of about 1 hour. For procedures which last >1 hr many agents are used as an adjuvant to local anesthetic like Epinephrine, Opioids, Non Opioids like Clonidine, Dexmedetomidine etc. Clonidine HCl is a centrally acting selective partial α2 adrenergic agonist. Neuraxial placement of Clonidine inhibits spinal substance P release and nociceptive neuron firing produced by noxious stimulation. It potentiates the effects of intrathecally administered local anesthetics. It also prolongs the sensory blockade and reduces the amount or concentration of local anesthetics required to produce postop analgesia. Intrathecal Clonidine at the usual dose (1-2ug /kg) is associated with bradycardia, relative hypotension and sedation. So there is tendency towards the use of smaller doses (<150ug). Such doses of Clonidine produces minimal side effects that would be a true alternative to other technical or pharmacological procedures aimed at prolonging spinal anesthesia & analgesia such as CSE or intrathecal opioids, which both have adverse effects or risks. So our aim is to see the haemodynamic changes & analgesic profile of different doses of Clonidine with small dose of Bupivacaine. And to find out the dose which has most favorable profile.

METHODS

This prospective randomized double blinded trial, which was approved by the institutional review board, included 90 patients of ASA grade 1 & 2, between the age of 20-50 years and BMI ≥ 25 of either sex undergoing elective lower abdominal surgery will be selected. Written informed consent from all patients is taken. Excluded subjects were the ones who refused to participate, those with ASA physical status ≥ 3, previous surgery on lumbar segments, raised ICT, neurological disorder, obvious skeletal deformity, patients on antihypertensive therapy, significant coagulation disorder, pt with respiratory, cardiac, hepatic, renal disease and known allergy to study drug. Patients were then randomly assigned into 3 groups using closed envelope technique: All receive Intrathecal Bupivacaine (0.5%) 6mg with, Group 1 (n=30) 15ug of Clonidine, Group 2 (n =30) 45ug of Clonidine and group 3 (n=30) 75ug of Clonidine. All were diluted with saline to make a volume of 3 ml.

Intravenous access was established in arm with 18 G cannula and 250ml of Lactated Ringer's solution was given as preload followed by 100 ml/hr. All patients were monitored by non invasive B.P., SpO2 and ECG. All patients received midazolam 1-2 mg i.v. as premedication. Spinal anesthesia was given in sitting position at L2-L3 or L4-L5 interspace using midline approach. Dural puncture was done by 25 G spinal needle. After free flow of clear CSF was obtained, 3 ml of local anesthetic was injected, under all aseptic precautions. The patient was then placed in supine position. The time at which intrathecal injection is given is considered as zero.

Haemodynamic Monitoring- Heart rate and B.P. were measured initially and at 5, 10, 15, 20, 25, 30 min. and then every 15 minutes. SpO2 is measured continuously by pulse oximeter. Hypotension is B.P. decrease >50 mm Hg from initial value or < 70 mm Hg. Bradycardia is H.R. <50 beats /min. Rescue i.v. boluses of Mephentermine (6mg) & Atropine (0.2mg) were given in incremental doses if pt develops hypotension or bradycardia. Side effects nausea or vomiting was treated symptomatically.

Sensory Blockade monitoring – Sensory anesthesia is defined as sharp sensation by pin prick test with 20 G hypodermic needle. This was recorded bilaterally at the mid clavicular level .This assessment was performed at 6,8,10,12,14,16,18,20 and 30 min after intrathecal injection & then every 15 min until regression to L1. Time to 2 segment regression & time to regression to L1 was recorded.

Motor Blockade Monitoring

Motor blockade in the lower limb was assessed bilaterally using a Modified Bromage scale- a). Complete motor blockade b). Almost complete motor blockade, the pt. is able to move only the feet. c).

Partial motor blockade, pt. is able to move the knee. d). Detectable weakness of hip flexion, the pt. is able to raise his leg but is unable to keep it raised. E). No detectable weakness of hip flexion, pt. is able to raise his leg for 10s at least. f). No weakness at all, the pt is able to perform partial knee bend while lying supine.

These measured were performed at 10, 15, 20, & 30 minute and then every 15 min after surgery. If one or more dermatomes (L1-4) were not blocked. It is considered a failed block, and then the pt. was excluded from the further study.

Postoperative Monitoring

1). **Quality of analgesia –** assess by pt. using 4 point scale. For postop analgesia Diclofenac i.m. was given as will be required.
2). **Time to 1st** dose of analgesic requested.
3). **Motor Blockade –** Time elapse between intrathecal injection and walking Time elapse between intrathecal injection and urination.
4). **Sensory Blockade –** we measure full skin sensibility at L1 segment when it is present indicates reversal of sensory blockade.
5). **Side Effects –**Postop nausea, Vomiting, pruritis, headache, low backache, dryness of mouth & cardiotoxicity like hypotension, dysarrythmias & AV block were seen.

The pt. will be transferred from post anesthesia care unit to the surgical unit after complete recovery of motor block, sensory block & stable vital functions.

Statistical analysis was carried out using Mann-Whitney, ANOVA, and Chi-square test and $p<0.05$ is considered significant.

RESULTS

Patient characteristic; mean age & sex (M: F ratio) were same in all groups. Baseline haemodynamic variables (H.R., Systolic & Diastolic B.P.) were statistically insignificant ($p>0.05$). All the groups were comparable with regards to demographic parameters.

The mean time of onset of sensory analgesia was 11.80±0.71 min in group 1, 9.57 ±0.85min in group 2 and 9.60±0.67 min in group 3. So the difference in the time of onset of sensory blockade in the group 1 & 2 is significant, in the group 1 & 3 is significant but in group 2 & 3 is not significant. Showing that increasing the dose of Clonidine from 15ug to 45ug causes early onset of sensory analgesia but further increasing the dose from 45ug to 75ug has no effect on sensory analgesia.

The highest level of sensory analgesia achieved is T6 in all the 3 groups. The time of onset of motor blockade in all the three groups is significant. Showing that increasing the dose of Clonidine from 15 to 75ug causes early onset of motor blockade .We found that differences in the time for 2 segment sensory regression was highly significant b/w group 1&2,and ,1& 3 and 2& 3. Showing that the addition of Clonidine to Bupivacaine delays the time for 2 segment sensory regression thus prolonging the duration of anaesthesia.

Time for regression to segment L1 in all the 3 groups is significant. Showing the addition of Clonidine to Bupivacaine significantly delays the time for regression to L1 segment. So with increasing the dose of Clonidine from 15ug to 75ug causes increase in duration of anaesthesia.

There was a significant difference in onset of sensory analgesia in between group 1& 2 and group 1 & 3. And there was no significant difference in time of onset in between group 2& 3.The onset of motor blockade was comparable in all the three groups. The 2 segment sensory regression was significantly delayed in group 2 ($p<0.001$) and in group 3 ($p<0.001$).The regression to L1 was significantly delayed in group 2 ($p<0.001$) and in group 3 ($p<0.001$) .The duration of motor blockade was comparable in all the three groups. There was significant difference ($p<0.001$) in the time to voiding & walking in between the three groups. There was also significant difference in the time to 1st dose of analgesic requested in between the 3 groups, earlier in group 1 and delayed in group 3.

In group 1 (6.66%) of cases had intraoperative hypotension, bradycardia & nausea- vomiting. While in group 2 (10%) had bradycardia, nausea- vomiting & (6.66 %) had hypotension. In group 3 (10%) had nausea- vomiting & hypotension while (6.66%) had bradycardia. None of patient had cardiotoxicity, respiratory depression, shivering or pruritis.

Postop hypotension is seen only in group 3 (6.66%) cases. Nausea (3.33%) cases in both group 2 & 3. Heavy headedness was seen in (6.66%) cases in group 1 & 2 and (3.33%) cases in group 3. Nobody had shivering, pruritis, low backache or dryness of mouth.

Table No. 1: Patient characteristic and baseline clinical variables.

	Group 1	Group 2	Group 3
Age	*35.33±8.57*	*34.33±10.34*	*33.10±9.14*
Sex M: F	*24:6*	*25:5*	*26:4*
Baseline H.R.	*80.4±9.37*	*87.07±13.76*	*91.03±14.77*
Baseline Systolic B.P.	*121.60±11.75*	*123.6±12.87*	*120.40±12.51*
Baseline Diastolic B.P.	*76.80±8.20*	*82.07±7.23*	*76.6±7.54*

Table 2 shows the number of patients in each group undergoing different types of lower abdominal surgeries

Procedures	Group 1	Group 2	Group 3
Mesh hernioplasty	16	17	16
Lumbar sympathectomy	4	4	4
Lord's plication	5	6	5
Appendicectomy	5	3	5

Table 3 shows the comparison of blockade in terms of onset , duration, wearing off, and need of rescue analgesic .

Parameters				
	Group 1	Group 2	Group 3	P value
1).Time in min to onset of sensory analgesia upto max level	11.8±0.71	9.97±0.85	9.6±0.67	p<0.001
2). Time in min to onset of motor blockade	15.13±0.73	14.27±0.83	13.63±0.49	p<0.001
3). Two segment sensory regression time in min for sensory blockade	96.57±4.07	127.23±3.87	149.97±3.61	p<0.001
4). Time in min for regression to segment L1	182.20±3.56	219±5.45	246.72±2.58	p<0.001
5). Duration of motor blockade	169.38±4.58	188.37±4.33	200.83±2.73	p>0.05
6). Time in voiding in min	349.13±4.42	371.30±4.09	392.47±3.53	p<0.001
7).Time to walking in min	234.90±11.20	302.57±3.45	320.83±3.18	p<0.001
8). Time to 1st dose of analgesic requested in min.	270±4.09	326±4.97	339±3.32	p<0.001

Discussion

The present clinical study encompasses the study of different doses of clonidine 15ug, 45ug & 75ug in respect to time of onset of sensory & motor blockade up to maximal possible level, duration of motor blockade, time to voiding –walking, time to 1st dose of analgesic requested , cardiovascular effects and any side effects due to increase in dose of clonidine. The results of our study show that onset of sensory analgesia & motor blockade upto maximal level was achieved faster with 75ug dose. The highest level of sensory block achieved was T6. The addition of Clonidine to Bupivacaine and increasing its dose delays the time for 2 segment sensory regression

regression to segment L1, increases the duration of motor blockade, increases the time to walking & voiding.

The difference in the time to 1st analgesic request in the three groups is significant. So increasing the dose of Clonidine causes increase in the time to 1st analgesic requested.

Hypotension is more with 75ug Clonidine. But this is not statistically significant. The difference in the incidence of bradycardia in the three groups present in the study is not significant ($p>0.05$). The incidence of post operative complications was not significantly different in between different doses of Clonidine.

CONCLUSION

We conclude that, within the tested dose range, 75ug is the preferred dose, in terms of effect versus side effects, when prolongation of spinal anesthesia is desired as in lower abdominal surgeries.

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Conflicts of interest

There are no conflicts of interest.

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