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Study of Haemodynamic Effects and Side Efeects of Intrathecal Clonidine

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ABSTRACT

Clonidine is a selective partial agonist of α2 adreno receptors. It is known to increase both sensory and motor block of local anaesthetics. Various studies have shown that addition of clonidine with intrathecal bupivacaine prolongs the duration of analgesia significantly thus taking care of post operative pain. The following study was undertaken to observe the effect of intrathecal clonidine on cardiovascular and respiratory system and to study the incidence of complications and side effects of intrathecally administered clonidine . addition of 30 mcg of clonidine to intrathecal Bupivacaine causes statistically significant difference in pulse rate and mean blood pressure at about 90 mins after spinal anaesthesia when compared to intrathecal Bupivacaine alone.Intratheacal Clonidine produces side effects like nausea, vomiting,hypotension bradycardia ,sedation

KEYWORDS : clonidine, intrathecal, complication,hypotension, bradycardia

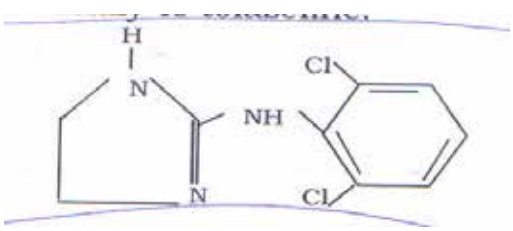
INTRODUCTION

Clonidine is a selective partial agonist of α_2 adreno receptors. It is known to increase both sensory and motor block of local anaesthetics. The analgesic effect following its intrathecal administration is mediated spinally through activation of post synaptic α2 receptors in substantia gelatinosa of spinal cord.

The rationale behind intrathecal administration of clonidine is to achieve high drug concentration in the viscinity of α2adrenoceptors in the Spinal cord and it works by blocking the conduction of C & Aδ fibres, increases potassium conductance in isolated neurons in vitro and intensifies conduction block of local anaesthetics. It can

provide pain relief by an opiod independent mechanisms.

Clonidine is an imidazole derivative closely related chemically to tolazoline.



MECHANISM OF ACTION :

It is a selective α_2 adrenergic agonist that exerts its effects by acting on α_2 adrenergic receptors in the brain stem. It is a partial agonist with higher affinity and intrinsic activity at α_2 receptors.

Stimulation of α_2 receptors.
Situated post synaptically in the medulla (Vasomotor centre)
↓
Decrease in sympathetic outflow
↓
Fall in BP and Bradycardia

Various studies have shown that addition of clonidine with intrathecal bupivacaine prolongs the duration of analgesia significantly thus taking care of post operative pain.

AIM OF THE STUDY

The following study was undertaken

1.) To observe the effect of intrathecal clonidine on cardiovascular and respiratory system
2.) To study the incidence of complications and side effects of intrathecally administered clonidine

MATERIAL AND METHODS

In our study, 60 patients were randomly selected for studying the haemodynamic effects and side effects of intrathecal clonidine (30 ug) bupivacaine heavy(15 mg) combination alone and bupivacaine heavy (15mg) alone.

ASA grade I and II and III patients posted for lower limb orthopaedic surgery were chosen for our study. The study was conducted in Orthopaedic department of TMC and DR.BRAM teaching hospital, hapania agartala. 60 patients were divided in to two groups, having 30 patients in each group.

Group A-Bupivacaine heavy 0.5% 3 cc(15mg) +Inj. Normal saline 0.2 ml.

Group B -Bupivacaine heavy 0.5% 3 cc (15 mg) +Clonidine (30 mcg).

PREANAESTHETIC ASSESSMENT A history of any present or past illness and detailed general as well as systemic examination were done and investigations were checked. After recording baseline vitals, informed written consent was obtained from patient and his or her close relative.

PREMEDICATION : we gave Injection Glycopyrollate 4 µg/kg (0.2 mg) I.V. Vital like pulse, B.P., R.R. and SPO_2 were noted before premedication and after premedication.

PREOPERATIVE OBSERVATION ; For monitoring ,ECG monitor and pulse oxymeter vitals like temperature, pulse, blood pressure and respiratory rate and SPO_2 were used .

EQUIPMENTS : Equipments used in the study consist of - An autoclaved tray consisting of instrument used for painting and draping,Disposable 23 G quinke's spinal needle,Disposable 5 cc syringe for Bupivacaine heavy,Disposable 2cc syringe for clonidine. Drugs :
Inj. Bupivacaine 0.5% heavy 1 ampule. Inj. Clonidine preservative free 1 ampule.

TECHNIQUE About 15 min before the intended time of intrathecal drug administration **e**ach patients was preloaded with 15 ml/kg of Ringer's Lactate solution . After adequate and aseptic precaution, lumbar puncture was performed at L_{3-4} intervertebral space using midline approach with a 23 gauge, quincke spinal needle in the left lateral position. Patients in the group C received a single dose of 15 mg of 0.5% Bupivacaine heavy + 30ug of preservative free clonidine. The patients in the group B received 15 mg 0.5% Bupivacaine heavy only

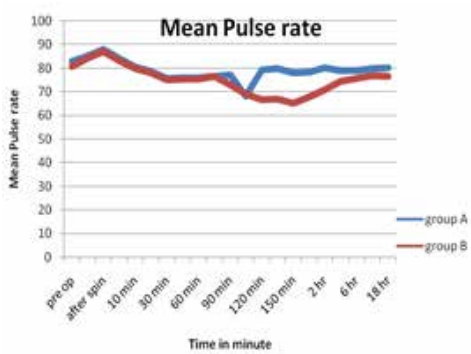
MONITORING : All the patients were monitored in the form of blood pressure, heart rate, respiratory rate and ECG and oxygen saturation (SPO_2) at 1 min, 5 min, 10 min, 15 min and then every 15 min interval.

EVALUATION Side effects like; nausea, vomiting, bradycardia or tachycardia (> 30% decrease or increase above baseline), hypotension (30% fall of blood pressure below baseline) respiratory depression (respiratory rate < 10 /min) and depression in consciousness level were evaluated.

Intraoperative bradycardia was treated with injection Atropine 0.6 mg IV and Hypotension was treated with injection mephentermin 5 mg IV and fast IV fluids.

POSTOPERATIVE MONITORING :
After surgery, patients were shifted to the recovery room and temperature, pulse rate, blood pressure, respiratory rate, SPO_2 were measured every 1 hour for 3 hours and then at three hour interval upto 12 hours and at 18th and 24th hour for 24 hours.

HAEMODYNAMICS – PULSE RATE
In our study, statistically significant difference in pulse rate was observed between the 2 groups at around 90 mins after the spinal anaesthsia was given ($p < 0.01$),which then recovered at around 1 hr post operatively.



Similar findings were found by BS Sethi [1]et al. They carried out a study of 60 patients of ASA Grade I & II on the efficacy of analgesic effect of low dose intrathecal clonidine as adjuvant to bupivacaine. In their study a decrease in mean heart rate was observed from 45 minutes until the end of 6 hrs. in clonidine group compared to control group (p value < 0.001).

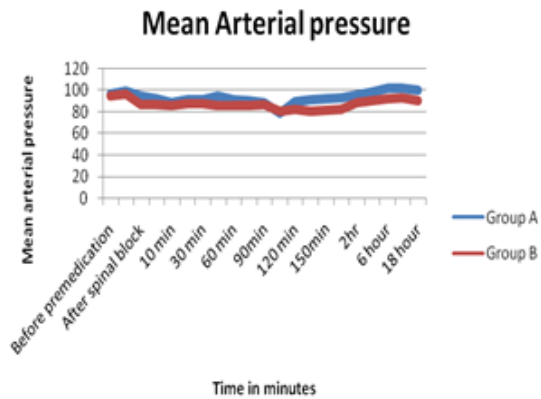
Finding similar to our study is also recorded by Stephen Strebel et al.[2] who carried out a dose response study of small dose of intrathecal clonidine and isobaric bupivacaine for orthopaedic surgery. 80 ASA Grade I, II, III patients scheduled for elective hip and knee arthroplasty were divided in to 4 groups of 20 individuals each. All patients received a total intrathecal drug volume of 4.6 ml. Dose of isobaric 0.5% bupivacaine 18mg was identical in all study groups. The active study groups (group 2 to 4) received clonidine 37.5 mcg (group 2), 75 mcg (group 3) or 150 mcg (group 4) added to bupivacaine. Statistically significant reduction in heart rate was observed in group 3 & group 4.

Similar findings were also reported in another study by I Dobrydnjov et al.[3] Heart rate was significantly lower in Group BC 15 & group BC 30 than in group B. (p value < 0.05) during first 45 to 120 minutes after intrathecal injection.

Finding similar to our study was also reported by Grandhe R P et al.[4] who performed a study for evaluation of bupivacaine – clonidine combination for unilateral spinal anaesthesia in lower limb orthopedic surgery. In their study 45 ASA Grade I & II patients were divided in to three group. Group B received 1.5 ml 0.5% (H) bupivacaine , group BC1 received 1.5 ml 0.5% (H) bupivacaine + clonidine 1 mcg / kg and group BC2 received 1.5 ml 0.5% (H) bupivacaine + clonidine 1.5 mcg / kg. The mean heart rate was significantly lower in group BC2 compared to group B between 105 minutes to 8 hrs following intrathecal drug administration. However bradycardia (heart rate < 60) did not occur in any patient.

HAEMODYNAMICS – MEAN ARTERIAL PRESSURE
In our study mean arterial pressure was recorded preoperatively after giving premedication, after spinal block, 5 mins, 10 mins, 15 mins, 30mins, every 15 mins till the end of surgery and then every 1 hour, 2 hour, 3 hour, 6 hour, 12 hour, 18 hour post operatively.

In our study,statistically significant difference in mean arterial pressure of both the groups were observed after about 15 mins of spinal anaesthesia & which continue post operatively, with group B more prone to hypotension.



Similar findings were reported by B.S.Sethi[1],where low dose intrathecal clonidine when added as adjuvant to bupivacaine causes a decrease in mean arterial pressure from 45 mins until the end of 6 hours (p value < 0.001). in addition the decrease in base line systolic blood pressure value in the patient receiving clonidine was statistically significant at 45 mins to end of 6 hrs (p value < 0.001).

Similar finding were also reported by I. Dobrydnjov[3] et al. In their study mean arterial pressure was significantly lower during first 45 to 120 mins after intrathecal clonidine & bupivacaine administration.(p value < 0.05).

Similar finding were also reported by Grandhe R.P.[4] et al. where average mean arterial pressure of group BC1 & group BC2 were significantly lower compared to group B patient from 45 mins to 8 hours after lumbar puncture (p value < 0.05).

Similar fall in mean arterial pressure was also reported by L. Niemi et al.[5] on addition of intrathecal clonidine to bupivacaine.

In their study Hema Saxena et al.[6] reported that there was 20 % fall in mean blood pressure in all the three groups receiving 15,30,37.5 mcg intrathecal clonidine added to bupivacaine compared to 8% fall in bupivacaine only group 30 mins after the injection.

Similar findings were also reported by Stephen Strebel et al.[2] who noted a small reduction in mean arterial blood pressure with the tested dose range of clonidine.

SIDE EFFECTS
In our study we have monitored the incidence of headache, nausea, vomiting, hypotension, bradycardia & respiratory depression.

In our study it is evident that incidence of nausea, vomiting, hypotension,bradycardia is comparatively more common in group B patients than group A.

Parameters	Group A	Group B
Headache	3	4
Nausea	2	3
Vomiting	2	3
Hypotension	3	5
Bradycardia	0	4
Respiratory depression	0	0

Similar findings were observed in study by Dobrydnjov et al.[3] In their study addition of intrathecal clonidine is usually associated with systemic side effects like vbradycardia, hypotension, or sedation. Although mean systolic & diastolic pressure decrease it was a minor

clinical significance & only one patient required ephedrine for control of hypotention

On the contrary,I.Van Tuiji et al[7]reported that both nausea and vomiting was less in the clonidine and bupivacaine group .Although, mean arterial pressure was less in clonidine group, it was not clinically significant.

Findings in study by Grandhe et al[4] suggest that no significant difference in hypotension and bradycardia was observed in study and control group

Hema Saxena et al[6] also concluded that small doses of clonidine is usually not associated with clinically significant bradycardia, hypotension and sedation.

Sedation

We observed sedation in our study intraoperatively 30 minutes after spinal anaesthesia and postoperatively 30 minutes after shift of patient in th e ward.

In our study it is observed patient receiving intrathecal clonidine and bupivacaine (group B) were more sedated than patients receiving intrathecal bupivacaine alone. In our study out of 30 patients in group A 6 patients had sedation score of 3 intraoperatively and post operatively while 1 patient had sedation score of 1 intraoperatively. Sedation score of 3 and 4 was not observed in any patient of group A. and most patient had sedation score of 0 intraoperatively and postoperatively.

Out of 30 patient of group B, 70 patient had sedation score of 1 intraoperatively and 18 patient had sedation score of 1 postoperatively. Sedation score of 3 and 4 was observed in 6 patient each intraoperatively and postoperatively.

Similar finding were reported by B S Sethi et al.[1] Where sedation score was higher in clonidine group than control group 3 to 6 hours after injection which was statistically significant (p value < 0.001)

Similar finding were also reported by Niemi .L et al.[5] Who showed that patient receiving intrathecal clonidine 3 mcg/kg mixed with15 mg 0.5% bupivacaine (H) remain sedated for 3 to 6 hours after the injection compared to control group receiving bupivacaine alone (p value < 0.04)

In contrast to this study Stebreletal. [2]found no significant intergroup difference in sedation score in patient receiving clonidine and bupivacaine.

CONCLUSION

To conclude addition of 30 mcg of clonidine to intrathecal Bupivacaine causes statistically significant difference in pulse rate and mean blood pressure at about 90 mins after spinal anaesthesia when compared to intrathecal Bupivacaine alone.Intratheacal Clonidine produces side effects like nausea, vomiting,hypotension bradycardia ,sedation. No significant respiratory depression was observed in our study.

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