Original Article

A prospective, comparative, randomised, double blind study on the efficacy of addition of clonidine to 0.25% bupivacaine in scalp block for supratentorial craniotomies

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Access this article online

Website: www.ijaweb.org

DOI: 10.4103/0019-5049.174809

Quick response code

ABSTRACT

Background and Aims: Scalp blocks combined with general anaesthesia reduce pin and incision response, along with providing stable perioperative haemodynamics and analgesia. Clonidine has proved to be a valuable additive in infiltrative blocks. We studied the efficacy and safety of addition of clonidine 2μg/kg to scalp block with 0.25% bupivacaine (Group B) versus plain 0.25% bupivacaine (Group A) for supratentorial craniotomies. **Methods:** Sixty patients were randomly divided into two groups to receive scalp block: Group A (with 0.25% bupivacaine) and Group B (with 0.25% bupivacaine and clonidine (2μg/kg). Bilateral scalp block was given immediately after induction. All the patients received propofol based general anaesthesia. Intraoperatively, propofol infusion was maintained at 75 to 100 μg/kg/h up to dura closure and reduced to 50-75 μg/kg/h up to skin closure with atracurium infusion stopped at dura closure. Heart rate (HR) and mean arterial pressure (MAP) were monitored at pin insertion, at 5 minute intervals from incision till dura opening and again at 5 minute interval from dura closure up to skin closure. Fentanyl 0.5 μg/kg was given if a 20% increase in either HR and/or MAP was observed. Postoperative haemodynamics and verbal rating scores (VRS) were recorded. When the VRS score increased above 3, rescue analgesia was given. Any intraoperative haemodynamic complications were noted. **Results:** Group A showed a significant increase in haemodynamic variables during the perioperative period as compared to group B ($P < 0.05$). Addition of clonidine 2 μg/kg in the infiltrative block also provided significantly prolonged postoperative analgesia. **Conclusions:** Addition of clonidine to scalp block provided better perioperative haemodynamic stability and significantly prolonged analgesia.

Key words: Analgesia, bupivacaine, clonidine, scalp block.

INTRODUCTION

Supplementing general anaesthesia with regional anaesthesia has markedly improved intraoperative haemodynamics, surgical field and postoperative analgesia. Scalp blocks with local anaesthetic agents are increasingly being used along with general anaesthesia in neurosurgical practice to reduce pin and incision response along with providing intraoperative and postoperative analgesia.[1,2] Clonidine, an α2 agonist, has hypotensive and analgesic actions. It has proved to be a valuable tool to anaesthesiologists when used by all routes – oral, intravenous and infiltration.[3-8] Studies have documented potentiation and prolongation of intrathecal, epidural and various peripheral blocks like brachial plexus, peribulbar, etc., with clonidine. The fall in rate pressure product produced by systemic absorption of clonidine can be beneficial in neuro-anaesthesia practice. This pre-emptive analgesia provided by scalp block also

How to cite this article: Wajekar AS, Oak SP, Shetty AN, Jain RA. A prospective, comparative, randomised, double blind study on the efficacy of addition of clonidine to 0.25% bupivacaine in scalp block for supratentorial craniotomies. Indian J Anaesth 2016;60:39-43.

prevents initiation of physiological and neurological responses to noxious stimuli thus reducing the post-operative morbidity and mortality. The benefits of pre-emptive analgesia are speedy recovery, decreased endocrine stress response to surgery, decreased hyperglycaemic response, improvement in respiratory function, early mobilisation, early discharge and reduction in cost of the treatment.[3]

Hence we decided to study the efficacy and adequacy of addition of clonidine 2μg/kg to scalp block with 0.25% bupivacaine versus scalp block with plain 0.25% bupivacaine for supra-tentorial craniotomies.

METHODS

After Institutional Ethical Committee approval and written informed patient consent, 60 patients with ASA grades I and II, age 18 to 65 years, GCS 15/15, scheduled for supra-tentorial craniotomies, with duration lasting 60 to 360 minutes, under general anaesthesia were enrolled for the study. Our exclusion criteria included emergency cases, patients with uncontrolled hypertension or preoperative bradycardia, ischaemic heart disease or cardiac arrhythmias, severe pulmonary, hepatic or renal disease, chronic alcoholism and chronic drug abusers, past history of craniotomy, drug allergy to local anaesthetics and/or clonidine, patients on alpha blockers preoperatively and patient refusal.

Patients were randomly (computer generated tables) divided into two groups of 30 patients each. Group A patients received only 0.25% bupivacaine (20cc) in scalp block and Group B patients received a combination of clonidine (2μg/kg) and 0.25% bupivacaine (total 20 cc) in scalp block. In Group A comparative amount of normal saline in lieu of clonidine was added to maintain blinding. The person performing the scalp block and monitoring intra-operatively and postoperatively was blinded to the drug being used in scalp block. Patient was monitored with electrocardiogram, non-invasive blood pressure, pulse oximetry, end tidal carbon dioxide and temperature. Anaesthesia induction and intubation included use of midazolam 0.03mg/kg, fentanyl 2 μg/kg, lignocaine 1mg/kg, propofol 2mg/kg and atracurium 0.75 mg/kg. Maintenance was done with intravenous propofol infusion 75-100 μg/kg/h with oxygen and nitrous oxide (N_2O) 50:50 mixture and atracurium infusion 5μg/kg/min. At the time of dura closure, N_2O and atracurium were shut off. Thereafter, only propofol infusion was continued at a rate of 50-75 μg/kg/h up to skin closure.

Bilateral scalp block was given immediately after induction with a 25 gauge needle to block supraorbital nerve and supra-trochlear nerve near the supraorbital groove, zygomatico-temporal nerve 1 cm away from outer canthus of eye, auriculo-temporal nerve near tragus, lesser occipital nerve and greater occipital nerve on the line joining mastoid process and occipital protruberance.[9,10] The surgeons also injected adrenaline (1:2,00,000) locally at the incision site to reduce scalp bleeding. Haemodynamics including mean arterial pressure (MAP) and heart rate (HR) were recorded every 5 minutes from pin insertion till dura opening, with special attention given to response to pin insertion and incision times. After dura closure, haemodynamics were again noted every 5 mintues till skin closure. Our primary endpoint was comparison of intraoperative haemodynamic between the two groups. Secondary endpoints studied included postoperative haemodynamics, postoperative duration of analgesia and intraoperative haemodynamic complications (tachycardia, bradycardia, hypotension and hypertension).

Postoperatively, monitoring of haemodynamics was done every hour for the first four hours. Verbal rating scores [VRS scale of 0-no pain to 10-unbearable pain] was recorded every 4 hours up to first 24 hours. When the VRS score increased above 3, rescue analgesia, intravenous paracetamol 1g was given and the time noted and thereafter the patient was discontinued from the study.

Intraoperative decrease in mean arterial pressure (MAP) <20% baseline was treated with decrease in dose of propofol up to 75 μg/kg/h, <30% was treated with ephedrine bolus 6 mg. Increase in MAP and/or tachycardia >20% was treated with increase in dose of propofol infusion up to 100 μg/kg/h, thereafter fentanyl 0.5 μg/kg bolus was injected twice, >30% increase was treated with esmolol 0.5mg/kg. Bradycardia (pulse <50/min) was treated with glycopyrrolate 0.004mg/kg.

Patients requiring postoperative ventilator care, patients with deteriorated glasgow coma scale or patients unable to communicate were withdrawn from the study.

Sample size was calculated by using nMaster 1.0. As per Dash *et al*., the sample size was calculated for a mean change in mean arterial pressure in group A as 7 mm Hg and group B as 7.5 mm Hg, to find a mean difference of 3 mm Hg between both the groups. We required total 45 patients to be enrolled for the study with alpha error

at 5% and 80% power. However, in order to increase the precision in results, we enrolled a total of 60 patients for the study. (30 patients in each arm)

We also calculated the power of the study in the end for the difference we obtained between two treatment arms with respect to MAP, 40 minutes post-incision.

Data was analysed with SPSS 16.0 software. Continuous data was presented as mean +/- SD or median (range) and categorical data as proportions. 95% confidence limits was calculated. Normality of the data was checked by Kolmogorov Smirnov test. Difference in continuous variables was assessed between both the groups by Mann Whitney test. Haemodynamic parameters at different time points were compared by repeated measures ANOVA or Friedman's test with $P < 0.05$ kept as significant for statistical analysis.

RESULTS

The demographic data is comparable in both groups as seen from Table 1. Their preoperative haemodynamic parameters were similar ($P>0.05$). There was a significant reduction in MAP in group B against group A during both pining and incision. During the first 40 mins post incision, MAP was significantly lower in group B as compared to group A, but the pulse rate showed no difference [Figures 1 and 2]. After dura closure, there was a significant difference in pulse from 30 minutes onwards in group B which continued postoperatively up to 120 minutes. Postoperative MAP was also significantly reduced in group B especially at 1 and 3 hours. Intraoperative use of fentanyl was significantly lower in group B as compared to group A [Figure 3]. The most significant difference was seen in the time to rescue analgesia which was almost double the time in group B as compared to group A. [Figure 4]. Also the rate of intraoperative haemodynamic complications were significantly higher in group B. Intraoperatively, in group A, 2 patients had tachycardia and 8 patients had hypertension requiring treatment whereas in group B, only 2 patients had bradycardia and 2 patients had hypotension requiring treatment.

Table 1: Demographics (all values are expressed as mean±SD except sex and ASA status)

Parameters	Group A	Group B
Age in years	41±14	39±14
Weight in kgs	58±9	60±11
Sex (male/female)	20/10	18/12
Surgical duration (min)	154±55	164±60
Anaesthesia duration (min)	231±63	241±65
ASA status (I/II)	21/9	20/10

ASA – American Society of Anaesthesiologists; SD – Standard deviation

We observed a difference between two treatment groups in MAP at 40 minutes post incision as 9 mm Hg with standard deviation of 11.46 mm Hg and 12.04 mm Hg in the two treatment arms respectively. Our study is powered at 84% to detect this difference with 5% significance using two sided test.

DISCUSSION

A combination of regional and general anaesthesia for any surgery has increasingly proved to be beneficial to patients with regard to reduction in perioperative

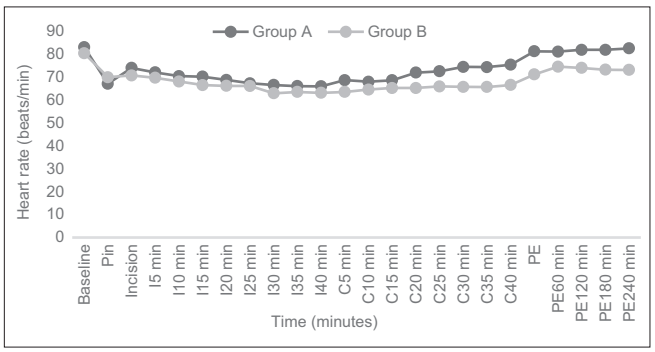

Figure 1: Heart rate graph. (I - Incision, C – Dura closure, PE – Post extubation)

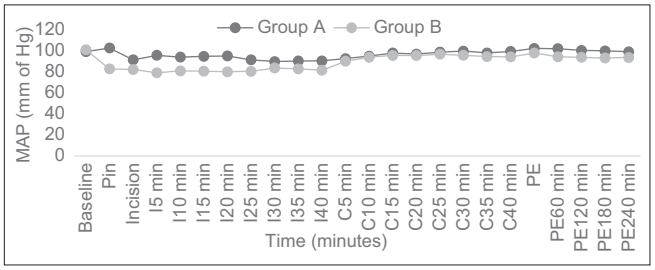

Figure 2: Mean arterial pressure graph. (MAP – Mean arterial pressure, I - Incision, C – Dura closure, PE – Post extubation)

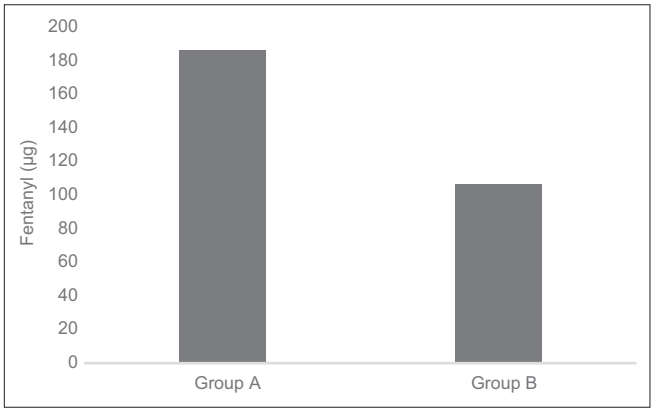

Figure 3: Intraoperative fentanyl use

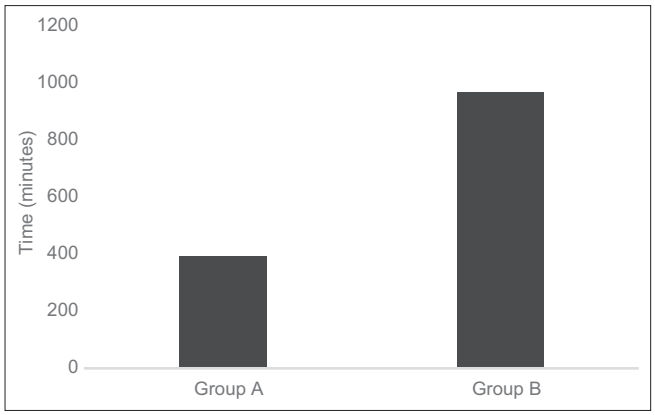

Figure 4: Time to rescue analgesia

stress response, stable perioperative haemodynamics, prolonged postoperative analgesia, early postoperative ambulation, reduction in number of ICU days and hospital stay thus decreasing overall morbidity and mortality.[1]

Scalp block is increasingly being used to attenuate the stress response to pining and incision in neurosurgery.[1] Local anaesthetics like lignocaine, bupivacaine, ropivacaine, etc., are routinely used in scalp block.

Clonidine, an α2 agonist, has become an indispensible adjuvant in anaesthesia. It has been administered by numerous routes such as intravenous, oral, intrathecal, epidural, intra-articular, infiltrative etc.[3-6,11,12] Ghignone *et al*. in 1987, discovered that clonidine acts on presynaptic α2 adrenoreceptors.[13] They postulated that clonidine caused a centrally acting, α2 mediated reduction in systemic vascular resistance and an increase in vagal tone resulting in fall in mean arterial pressure and heart rate. It also caused a reduction in norepinephrine output from peripheral nerve endings thereby reducing the stress response.

A study in 2001, explained the role of α2 agonist in regional anaesthesia and analgesia. Clonidine is not only an antihypertensive, but also provides pain relief by opioid independent mechanism, potentiates the action of local anaesthetics, reduces local anaesthetic amount and concentration and prolongs sensory block. They studied various routes of administration and found addition of clonidine to local anaesthetic opioid mixture caused rapid onset time, improved quality of anaesthesia and prolonged duration of sensory block.[3]

A study done in 2004 found various beneficial effects of clonidine in perioperative period including central sympatholysis, improved hemodynamic stability in response to endotracheal intubation and surgical stress, reduced anaesthetic requirement and opioid requirement, reduced bleeding, sedation, anxiolysis, analgesia as also benefits in prevention and management of perioperative myocardial ischemia.[14]

In our study, we found a significant reduction in MAP at both pin insertion and incision in group B as compared to group A which can be attributed to early onset of scalp block as also systemic absorption of clonidine in group B. Other studies have reported a faster onset of sensorimotor block with the use of clonidine as an adjuvant to local anaesthetics.[4,5] In our study, significant difference in MAP in both groups was found in the first 40 minutes similar to the study by Dash *et al*.[7] Postoperative MAP was also significantly reduced in group B. The half-life of clonidine is 8 hours due to which perioperative haemodynamic monitoring up to approximately 8 hours after block administration is required. The intraoperative use of fentanyl was also significantly higher in group A similar to another study.[7] Use of clonidine can significantly improve the intraoperative haemodynamic profile and help ease the anaesthesia management. According to Ghignone *et al*., clonidine significantly reduces the circulating catecholamine levels both at rest and during stress. It modulates the perioperative haemodynamics reducing the anaesthetic and analgesic requirements.[13]

We found a significant prolongation of analgesia (887.97 ± 398.21 mins in group B vs 408.17 ± 209.81 mins in group A) after neural blockade in our patient. Dash *et al*. did not study this postoperative prolongation of analgesia. They have studied only the intraoperative haemodynamics. Also the rate of intraoperative haemodynamic complications were significantly higher in group A.

Clonidine is also used for treatment of attention deficit hyperactivity disorder in animals and rat pups are found to have better cognitive function post clonidine consumption.[15] Application of this to adult humans especially in the setting of neurosurgery requires further study.

We used nitrous oxide in our study since medical air was not available to us. Hence we shut it off at the time of dura closure. The main limitation in our study is non-availability of depth of anaesthesia monitors because of which propofol dose could not be titrated.

Also we could have monitored the postoperative sedation scores.

CONCLUSION

Addition of clonidine to scalp block offers early onset of block with better perioperative haemodynamic stability. Additionally intraoperative opoid use may be reduced and duration of analgesia prolonged.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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