

The efficacy of intravenous clonidine premedication to reduce surgical area bleeding in posterior lumbar spine fusion surgery

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Abstract

Background: A posterior lumbar spine fusion surgery always associated with significant amount of blood loss and requires blood transfusion. The purpose of this study is to evaluate the efficacy of intravenous clonidine premedication to achieve bloodless surgical field and decrease the need for blood transfusion by controlled hypotension. **Methods:** Sixty patients scheduled for posterior lumbar fusion surgery were included in this randomized placebo controlled trial. Patients were classified into two groups: Group 1 received intravenous clonidine 3 µg/kg by infusion over 15 minutes before surgery and Group 2 received placebo as same. Hemodynamic variables, quality of surgical field by bleeding severity score, estimated amount of blood loss, duration of surgery and any blood transfusion were analyzed. **Results:** Heart rate and mean arterial pressure found less in clonidine group than placebo but not significant. The estimated blood loss (390.8±99.99 mL vs 741.13±79.90 mL; P = 0.001*) and duration of surgery (160.67±16.91 vs 205.9±16.72 min, P=0.001*) were significantly less in clonidine group compared to placebo. The quality of surgical field was better in clonidine group than placebo at all times. No cases of severe bradycardia or clinically significant hypotension were observed in clonidine group. **Conclusion:** Premedication with intravenous clonidine 3 µg/kg found clinically safe & effective drug in controlling blood loss and improves quality of surgical field in posterior lumbar fusion surgeries as a sole agent.

Key words: Clonidine, Bleeding severity score, Posterior lumbar fusion surgery

Introduction

Spine surgeries are significantly associated with major blood loss. The amount of blood loss in spine surgeries can be reduced by different strategies like blood conservation methods (preoperative autologous blood donation), muscle paralysis and proper positioning of the patient to reduce intra-abdominal pressure, infiltration of paraspinal tissues with vasopressors, use of antifibrinolytic agents and deliberate controlled hypotensive anaesthesia [1,2].

Controlled hypotension is the simple and best possible way to obtain bloodless surgical field by reducing intraoperative bleeding. To achieve controlled hypotension various drugs have been studied including vasodilators (sodium nitroprusside, nitroglycerin),

ganglion-blocking agents, beta blockers (esmolol), calcium channel blockers (nicardipine, nimodipine), alpha-2 agonists (clonidine, dexmedetomidine), volatile agents, and magnesium sulphate [3,4]. In recent past the drug clonidine has been widely used in anesthesia as anesthetic adjunct to prevent intubation stress response, sedation, analgesic adjuvant to opioids and to produce hypotensive anesthesia with inhalational agents [5].

The aim of this study is to evaluate the efficacy of intravenous clonidine administered preoperatively as a sole agent for controlled hypotension, to determine the amount of blood loss, quality of surgical field, decrease in the duration of surgery and decrease the need for blood transfusion in adult patients undergoing single level posterior lumbar spine fusion surgery.

Methods and Materials

Manuscript received: 07th Feb 2016
Reviewed: 16th Feb 2016
Author Corrected: 26th Feb 2016
Accepted for Publication: 04th March 2016

This randomized double blind placebo controlled clinical trial was conducted in 60 patients aged between 20 and 60 years classified under American Society of Anesthesiologists (ASA) physical status I-II who were scheduled for posterior lumbar spine fusion surgery for degenerative spine disease in our institute during the period of 2012 to 2013. We excluded patients with cardiac disease (like hypertension, arrhythmia, ischemic heart disease and valve lesions), preexisting coagulation defects, liver disorders, medical renal disease, diabetes mellitus, neuromuscular disorder, and seizure disorder; patients receiving β - blockers, calcium channel blockers, digoxin, anticoagulants or antiplatelets, tricyclic antidepressants, asthmatic patients, patients on long-standing corticosteroids and known hypersensitivity to clonidine.

After obtaining ethical committee approval from our institution and written informed consent from selected patients, they were allocated into two groups by simple randomization using sequentially numbered, opaque sealed envelopes. Group 1 (n=30): received clonidine 3 μ g/kg (diluted with 0.9% Normal Saline) 20 ml by syringe pump infusion over 15 minutes before surgery and Group 2 (n=30): received placebo 0.9% Normal Saline (NS) 20 ml same as treatment group.

On arrival to the operating room, the study drug either clonidine or 0.9%NS (placebo) infusion started after premedication with 0.03 mg/kg midazolam. At the same time all the patients were received 7 ml/kg of ringer's solution by another intravenous line and were monitored for heart rate (HR) and mean arterial pressure (MAP) [invasive and noninvasive], electrocardiography, oxygen saturation (SPO₂), temperature and urine output. Immediately after completion of study drug infusion, anesthesia was induced with fentanyl 2 μ g/kg & propofol 3 mg/kg intravenously. 100% oxygen was administered by mask, atracurium 0.5 mg/kg was used to facilitate intubation and the trachea was intubated after 3-5 minutes. All patients were mechanically ventilated with a tidal volume of 7–10 ml/kg, inspiratory/expiratory ratio of 1:2, and a respiratory rate adjusted to maintain end-tidal carbon dioxide (ETCO₂) concentration of 30-35 mmHg (12–14 breaths/min). General anesthesia was maintained with 1.5% sevoflurane in a mixture of O₂/N₂O (50%/50%) and by intermittent injection of fentanyl 0.5 μ g/kg and atracurium 0.2 mg/kg every 30 minutes. Ringer lactate given as maintenance fluid and normal saline for deficits and losses. All patients were placed prone with a chest and pelvic rolls, leaving the

abdomen hanging free. All patients were positioned and operated by the same surgery team.

Vital parameters were monitored by same system in all patients. The time duration of surgery, estimated amount of blood loss, surgical area bleeding score, and any blood transfusion were recorded.

If any bradycardia <50 beats/minutes was treated by 0.5mg atropine and the same may be repeated when necessary. In case of any decrease in MAP less than 50 mmHg, concentration of inhalational anesthetic stopped and 3 mg of ephedrine was given as incremental doses if needed and the patient was excluded from the study.

Intraoperative blood loss was estimated by calculating blood collection at suction bottle and weighing blood soaked sponges, surgical drapes, and gowns, which was weighed in dry preoperatively to find the difference.

The quality of surgical field assessed every 30 minutes using 5 point surgical area bleeding score given by Dolman et al [6,7]. The surgical area bleeding score was obtained from same surgical team who performed surgery in all patients.

- 1=Minimal bleeding, not a surgical nuisance
- 2=Mild bleeding, but does not affect dissection
- 3=Moderate bleeding, slightly compromises dissection
- 4=Severe bleeding, significantly compromises dissection
- 5=Massive bleeding, prevent dissection.

Blood transfusion was determined when estimated blood loss reaches allowable blood loss, the calculation based on preoperative hematocrit (Hct) with target Hct of 27%.

At the end of the surgery inj. Ondansetron 4 mg given intravenously to prevent postoperative vomiting to all patients and they were extubated after administration of 0.5 mg glycopyrrolate and 2.5 mg neostigmine (1:5) to reverse neuromuscular blockade. Vital parameters observed and patients were shifted to post anesthesia care unit. Inj.diclofinac 75mg i.v twice a day and inj. paracetamol 1gm (100ml) i.v infusion twice a day given alternatively for postoperative pain relief.

Statistical Analysis: Sample size was calculated based on previous study values that mean bleeding in the control group = 749.2±304.5mL and mean bleeding in the clonidine group = 422.3 ±139ml (Anvari et al[14])

with the assumption that clonidine reduces 20% of blood loss, arrived a sample size of 12 in each group, for 80% power and 5% level of significance. For the consistency of results 30 patients were studied in each group.

Data were analyzed using SPSS version 17. Results were presented as mean ±(SD), number, and percentage.

Results

Sixty patients undergoing posterior lumbar spine fusion were divided equally to either the clonidine group (n=30) or the placebo group (n=30). There was no statistically significant difference between the two groups with regard to demographic characters or ASA physical status. There were no statistically significant differences in basal heart rate (HR), mean arterial pressure (MAP) and hematocrit (Hct) between the two groups.[Table 1]

Comparison of demographic data, preoperative vital parameters, Hct, estimated blood volume, duration of surgery and amount of blood loss between groups were done by Student’s *t* test. Analysis of variance was used to analyze hemodynamic variables at different time points. Mann– Whitney *U* test was used to compare the quality of surgical field. *P*<0.05 was considered significant.

Table 1: Demographic and clinical characters - comparison

Characters	Group 1	Group 2
AGE(Yr) [†]	44.27	44.4
Sex(F\M) [‡]	20\10	18\12
ASA(III) [†]	21\9	23\7
WT(Kg) [†]	66.33	66.23
HT(Cm) [†]	161.73	163.2
PREOP HR(Mt) [†]	75.53	74.83
PREOP MAP(Mmhg) [†]	89.3	87.53
Hematocrit(%) [†]	34.13	34.23

Values as †-mean, ‡-number

The heart rate was comparatively less in Group 1 than in Group 2 during intraoperative period, but not able to find any statistical significance. [Figure 1]

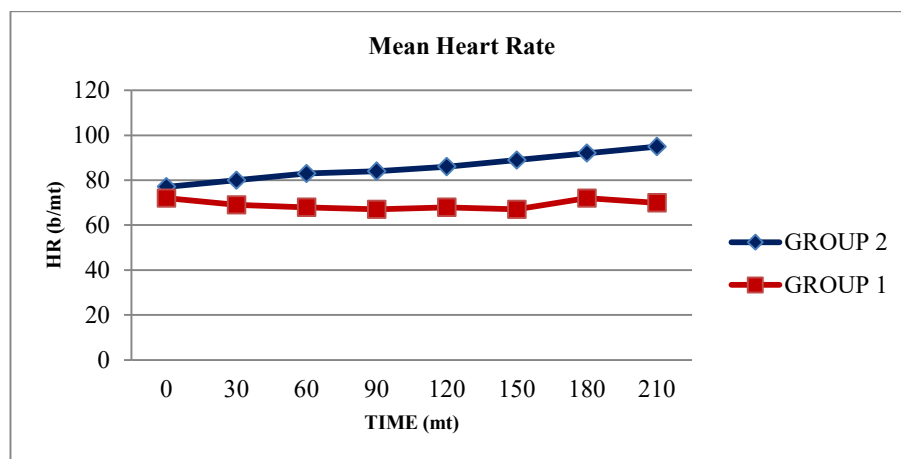


Figure 1: Mean Heart Rate at various time measurements during surgery

Though there was no significance, the MAP was comparatively low in clonidine group than placebo after induction and during intra operative period as well.[Figure 2] After recovery, in the immediate postoperative heart rate and mean blood pressure (MAP) remained significantly (*P* value 0.001*) less in clonidine group than placebo.[Table 2]

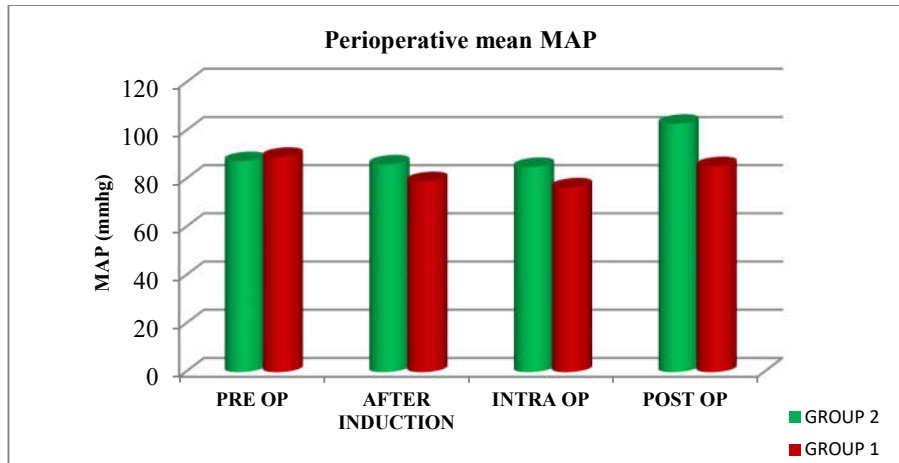


Figure 2 Perioperative mean MAP

Table 2: Heart rate and blood pressure after recovery - comparison

	Group 1	Group 2	P Value
Postop.HR(mt)	69.73±11.27	101.07±7.54	0.001*
Postop.MAP(mmHg)	85.43±6.51	103.03±4.08	0.001*

*P<0.05 considered statistically significant Values as mean±Standard deviation

The quality of surgical bleeding was assessed every thirty minutes with a five point bleeding score. The quality of surgical field was better in clonidine than placebo in all times of measurements and it was statistically significant at 150 minutes (P =0.003*).Number of patients in the clonidine group with surgical area bleeding score of 3 and 4 (bleeding compromises dissection) was less compare to placebo group. [Figure 3] There was no need for nitroglycerin as a rescue hypotensive agent to maintain controlled hypotension in either group.

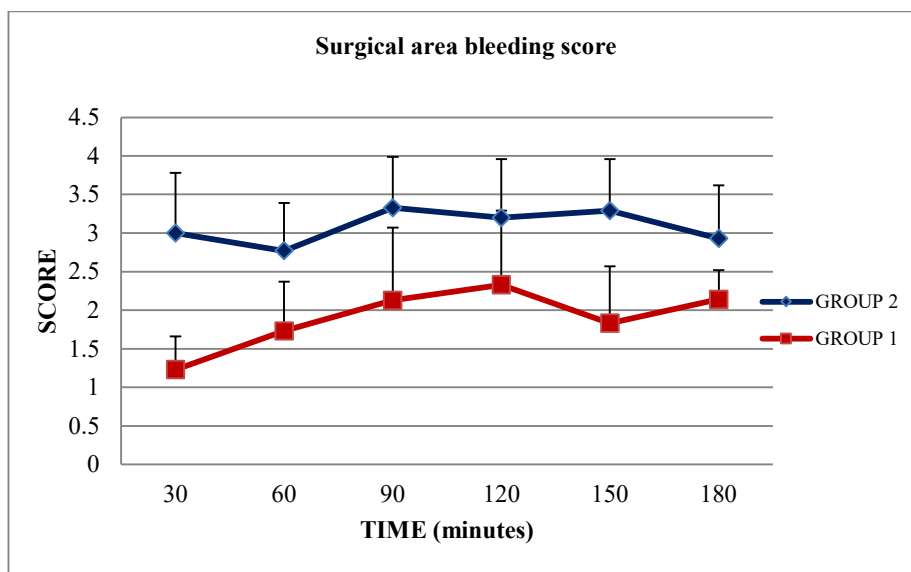


Figure 3: Surgical area bleeding score (mean + SD)

The analysis of estimated blood loss shows that clonidine group had significantly less intraoperative blood loss (390.8±99.99 mL; P<0.05*) compared to placebo group (741.13±79.90 mL). It shows approximately 47% reduction of

blood loss in clonidine group than placebo. The duration of surgery was significantly less in clonidine Group than placebo Group (160.67 ± 16.91 vs 205.9 ± 16.72 min, $P < 0.05^*$). [Table 3] No of patients received blood transfusion was higher in placebo when compare to clonidine. In placebo group 12 patients received blood transfusion, in that 5 patients were transfused with 2 units of blood. In clonidine group only 3 patients received blood transfusion.

Table 3: Amount of blood loss and duration of surgery - comparison

	Group 1	Group 2	P Value
Blood loss(ml)	390.8±99.99	741.13±79.90	0.001*
Duration(mt)	160.67±16.91	205.9±16.72	0.001*

* $P < 0.05$ considered statistically significant Values as mean±Standard deviation

In clonidine group, three patients were treated with inj.atropine 0.5mg for severe bradycardia otherwise intraoperative period was hemodynamically stable in all patients.

Discussion

Spine surgeries always associated with major blood loss, necessitates blood transfusion[8,9]. Now a days, avoiding blood transfusion even in major surgical procedures become important to decrease perioperative morbidity and mortality caused by transfusion related adverse events (like transfusion reaction, transmission of infection, TRALI [Transfusion Related Acute Lung Injury], risk of immunosuppression and the cost of hospitalization) [10,11]. Blood transfusion can be limited by decreasing intra operative blood loss, also improves quality of surgical field in turn increases surgeon satisfaction, decreases duration of surgery and neurological complications as well.

Controlled hypotension is the widely accepted technique to reduce intraoperative blood loss in spine surgeries[12]. Malcom-smith study found upto 55% reduction in the blood loss by induced hypotension method [13].

Recently, the centrally acting antihypertensive agent clonidine has gained considerable interest as an adjuvant in anesthesia. Many previous studies compared the effect of oral clonidine to produce blood less surgical field by its hypotensive action [14-16]. But study on intravenous clonidine was few and they analysed the effect of clonidine on reduction of hemodynamic stress response to laryngoscopy, maintaining controlled hypotension, hemodynamic stability intraoperatively, sedation, analgesia and postoperative shivering [17-22].

Previous studies with oral clonidine premedication shows significant reduction in the requirement of blood transfusion by achieving moderate hypotensive anesthesia [14]. In our study, the effect of intravenous clonidine was compared to placebo for bloodless surgical field alongwith sevoflurane and fentanyl combination. All patients were operated at single level spinal segment for degenerative spine disorders by the same surgical team, and prone positioning done in the same way by the same team. There was no significant difference in weight & height between the two groups. This way, the other factors (1. Position based increased abdominal pressure causing venous congestion at surgical area. 2. No of segments, 3. Weight, 4. Pathology of disease) which affects surgical area bleeding was minimized.

The MAP was comparatively low in clonidine group than placebo after induction and during intra operative & immediate post-operative period as well. Also, mean intraoperative estimated blood loss & duration of surgery were significantly less in the clonidine group than control group. Around 47% reduction in estimated blood loss was achieved with clonidine compare to placebo.

In our study even with moderate hypotension which is statistically not significant, we found significant amount of reduction in estimated blood loss and the better quality of surgical field with clonidine compare to placebo. The quality of surgical field with bleeding score 3 & 4 were less with clonidine compare to

placebo. This well correlated with the findings of Anvari et al[14] and Jabalameli et al[16] studies.

Kulka et al[17], study on hemodynamic stability with various doses of intravenous clonidine found 4µg/kg is optimal dose to get better hemodynamic stability than 2µg/kg. And a higher dose at 6µg/kg does not have any enhanced effect on catecholamine release or hemodynamic variables.

Altan et al[20] and Ray et al[22] studies found significant incidence of bradycardia and hypotension requires treatment which was not there in our study. Altan et al used intravenous clonidine 3 µg/kg 15 minutes before induction followed by 2 µg/kg/h continuous infusion during surgery. Ray et al administered clonidine 3 µg/kg intravenously 15 minutes before induction and continuous infusion with 1 µg/kg/hour intraoperatively. They observed significant incidences of bradycardia and hypotension in their study. Sahajananda & Rao [19] and Samantaray et al[21] studied the effect of intravenous clonidine at 3µg/kg observed no significant events like bradycardia and hypotension requires vasopressor, correlates better with our observation.

Conclusion

Even with moderate hypotension, clonidine in a dose of 3µg/kg, effectively decreases surgical site bleeding and gives bloodless surgical field. So the present study concludes that intravenous clonidine premedication at 3µg/kg found clinically safe & effective in controlling blood loss and improves quality of surgical field and decreases need for blood transfusion in single level posterior lumbar fusion surgeries as a sole hypotensive agent.

Funding: Nil

Conflict of interest: None.

Permission of IRB: Yes

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How to cite this article?

Suresh Rajkumar, Senthil M, Ezhilrajan V. The efficacy of intravenous clonidine premedication to reduce surgical area bleeding in posterior lumbar spine fusion surgery. *Int J Med Res Rev* 2016;4(3):361-367. doi: 10.17511/ijmrr.2016.i03.13
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