

Effects of preoperative β -blocker on blood loss and blood transfusion during spinal surgeries with sodium nitroprusside–controlled hypotension

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ABSTRACT

Background: The present study sought to determine whether premedication with oral β -blocker before hypotensive anesthesia with sodium nitroprusside could improve the quality of surgical field, decrease the blood loss, and decrease the need for homologous blood transfusion and duration of surgery. **Methods:** Eighty patients scheduled for spinal fixation surgery were included in a prospective, randomized, double-blinded study. Patients were classified into two groups: Group I received oral atenolol 50 mg twice one day before surgery; and Group II received placebo tablets identical in appearance to atenolol tablets for the same period and interval. All patients in both the groups received intraoperative sodium nitroprusside (SNP) as a hypotensive agent. Hemodynamic variables, amount of sodium nitroprusside used, quality of surgical field, and the amount of homologous blood transfusion and blood loss were compared between groups. **Results:** Heart rate and amount of SNP used were significantly less ($P < 0.0001$) in the atenolol group, but no significant difference was found in intraoperative mean arterial blood pressure (MABP) between the two groups. The time of surgeries was significantly shorter in Group I than in Group II (185 ± 15.21 vs 225 ± 12.61 min), $P < 0.0001$. The quality of surgical field was better in Group I than in Group II in all times of measurements, $P < 0.0001$. The amount of blood loss and the amount of packed red blood cells transfused were significantly less in Group I than in Group II, $P < 0.0001$. No clinically significant complications were observed in either group. **Conclusion:** Premedication with oral atenolol 50 mg twice/day for one day before hypotensive anesthesia with SNP during spinal surgeries seems to be clinically safe and effective to reduce heart rate, amount of SNP used, amount of blood loss, and amount of blood transfused with better quality of surgical field.

Key words: β -Blocker, controlled hypotension, preoperative, sodium nitroprusside

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INTRODUCTION

Spinal surgeries are associated with significant blood loss, which vary from 10 to 30 mL/kg and its volume depends on the number of spinal levels fused; body weight^[1]; surgery for tumors^[2]; and raised intra-abdominal pressure in the prone position. This loss results from decorticated bone and disruption of rich vascular networks.^[3]

Blood loss will increase the time of surgery, time of anesthesia, and the need for homologous blood transfusion, which increase the patient morbidity and mortality.^[4,5]

Hypotensive anesthesia was used since long time to decrease the intraoperative blood loss and homologous blood transfusion by reducing the MABP. Various drugs have been used to facilitate the induction of controlled hypotension.^[6,7]

However, induction of hypotension with sodium nitroprusside (SNP) had not been expected to improve the quality of surgical field because of reflex tachycardia, increased cardiac output, increased blood flow to the mucous membrane, and endogenous catecholamine have little effect on blood vessel of mucous membrane in presence of SNP.^[7] We hypothesized that β -blocker

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through its negative inotropic^[8] and chronotropic^[9] effects will prevent some of the adverse effects of SNP.

Accordingly, we designed this study to determine whether preoperative oral β -blocker (atenolol) combined with intraoperative SNP will improve quality of surgical field, minimize blood loss, decrease the need for homologous blood transfusion and decrease the duration of surgery.

METHODS

This study was carried out on 80 patients ASA I and II scheduled for spinal surgeries. Written informed consent had been taken from the patients after approval of institutional ethical committee.

Uncontrolled hypertension, patients receiving anticoagulant or drugs that impair coagulation as aspirin or NSAID, patients with liver, renal disease, bleeding disorder, or heart block, asthmatic patients, and those using β -blockers or calcium channel blockers were excluded from the study.

The patients were classified into two groups: Group I: Patients received oral atenolol 50 mg twice one day before surgery. Group II: Patients received placebo tablets identical in appearance to atenolol tablets for the same period and interval.

The randomization was performed using sealed envelopes indicating the group of the assignment at the time of preoperative assessment. A blinded anesthesiologist who did not participate in the study or data collection, read the number contained in the envelope and made group assignments.

A blinded chief nurse who did not participate in the study confirmed that each patient ingested the tablets as scheduled. Patients were monitored for the side effects of atenolol, including arrhythmia, confusion, chest pain, tingling, or numbness in the hands or feet, and signs of an allergic reaction.

Patients were premedicated with 0.05 mg/kg midazolam intravenously 15 min before entering the operating room. Anesthesia was induced with fentanyl 2 μ g/kg, propofol 2 mg/kg, and vecuronium 0.1 mg/kg to facilitate endotracheal intubation. We used an armored endotracheal tube to minimize the risk of kinking and to ensure that the tube is well secured before and after turning the patient. Central venous and radial artery catheter was inserted and Foley catheter was used to decompress the urinary bladder.

Patients were placed in prone position and precautions were taken to avoid abdominal compression. Anesthesia

was maintained with isoflurane 1.5%, and top up dose of vecuronium was 0.01 mg/kg every 30 min. Signs of awareness (eg, increase in arterial pressure greater than the targeted MAP, tearing, or sweating) were managed with additional boluses of 1 μ g/kg fentanyl. Ventilator settings were adjusted to maintain endtidal CO₂ around 35 mmHg.

All patients in both the groups received intraoperative SNP as hypotensive agent, SNP was infused 1–2 μ g/kg/min by infusion pump (injectomat MC Agilia, Fresenius Kabi AG, Homburg - Germany) to maintain MABP between 55 and 60 mmHg. SNP solution was prepared by the addition of 25 mg to 500 mL of 5% dextrose. The infusion was begun at a rate of 1 μ g/kg/min and then was adjusted to maintain the MABP to target level before skin incision and maintain it throughout the surgery in both the groups.

During intraoperative period, patients in both groups received Ringer's acetate infusion at a rate of 10 mL/kg/h.

If the heart rate decreased to less than 50 beats/min, 0.5 mg of atropine was given and may be repeated and if bradycardia persisted, epinephrine in dose 0.01 mg/kg (1/10000) was given.

In case of decreasing MABP less than 50 mmHg, concentration of inhalational anesthetics and infusion rate of nitroprusside was decreased and if there was no response, 5 mg of ephedrine was given and repeated if needed and the patient was excluded from the study.

Measurements

During maintenance of anesthesia, invasive blood pressure, electrocardiogram, heart rate, pulse oximetry, capnography, CVP central venous pressure, and urine output were monitored before induction of anesthesia as a baseline, after induction of anesthesia, every 30 min during surgery and then immediately after recovery.

The surgeon estimated the quality of surgical field every 30 min during surgical procedure with a predefined scale adapted from that of Dolman *et al.*^[10] Surgeons were all equally familiar and experts in these types of surgeries for at least 20 years.

- 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.

Intraoperative blood loss was estimated by the assessment of the suction bottle, sponges, surgical drapes, and gowns. Arterial blood was sampled every 30 min, and when

clinically indicated, for measurement of hematocrit (Hct). Fraction of inspired oxygen was increased from 0.5 to 1.0 when the transfusion trigger was reached, blood was given only if Hct was less than 25% at any time during surgery and the target was to achieve Hct=25%. Quick Formula had been used to determine the volume of red cells for transfusion, Transfusion volume=[Total blood volume \times (Hct goal – Hct measured)]/Hct of donor unit.^[11]

At the end of operation, and before wound closure in both groups, SNP was stopped to allow rise in blood pressure for effective hemostasis after skin closure, inhalational anesthetics were closed and the patient allowed to breathe 100% oxygen. Residual nondepolarizing muscle relaxant was reversed with prostigmine 0.05 mg/kg and atropine 0.02 mg/kg given intravenously, extubation was done and the patient was admitted to the recovery room.

Statistical analysis

The sample size was calculated using the following assumption: the surgical area bleeding score was the main response variable, nQuery advisor version 5 was used for sample size calculation.

Power analysis identified 35 patients per group, required to detect 15% difference between groups with a power 80% and a significant level of 0.05. However, to enable detection of potential variations between the two groups and avoid potential errors, 40 patients were included in each group.

Comparison of demographic data, Hct, amount of blood loss and volume of packed red cell transfused between groups was done by Student's *t* test. Fisher exact test was used when appropriate. Two-way analysis of variance with correction for repeated measurements was used for heart rate and blood pressure comparison. Mann-Whitney *U* test was used for nonparametric measurements including quality of surgical field. $P < 0.05$ was considered significant.

RESULTS

Eighty patients, scheduled for spinal fixation surgeries were enrolled in the study. Demographic data, type of operation and duration of surgeries are shown in Table 1. There was no significant difference between groups with regard to the demographic data and type of operation.

The duration of surgeries was significantly shorter in Group I than in Group II. (185 ± 15.21 vs 225 ± 12.61 min), $P < 0.0001$. The quality of surgical field was better in Group I than in Group II in all times of measurements; P value was < 0.0001 [Figure 1].

Hemodynamic changes

The heart rate was significantly less in Group I than in Group II throughout the study period $P < 0.0001$ [Figure 2]. Preoperatively, MABP was significantly decreased in Group I than in Group II. The changes in MABP was comparable between both groups after SNP infusion $P = 0.15$. Meanwhile, after recovery the blood pressure remained significantly decreased in Group I than in Group II [Table 2]. The dose of nitroprusside used was less in Group I than in Group II (1.45 ± 0.45 vs 2.54 ± 1.65 $\mu\text{g}/\text{kg}/\text{min}$), $P = 0.0001$.

Preoperative Hct was comparable in both groups, $P > 0.05$. The lowest intraoperative Hct was significantly low in Group II versus Group I, $P < 0.0001$. The amount of blood loss was significantly less in Group I than in Group II,

Table 1: Demographic data, duration of surgeries, and type of operation in both groups

	Group I N=40	Group II N=40	P value
Sex M/F	24/16	28/12	
Height (cm)	165 \pm 12.09	162 \pm 10.06	
Weight (kg)	85.15 \pm 4.15	86.7 \pm 5.07	
Age (yr)	37.5 \pm 8.5	36.4 \pm 9.3	
Duration of surgeries (min)	185 \pm 15.21	225 \pm 12.61	<0.0001*
Type of operation			
Fracture lumbar spine	15	16	
Fracture dorsal spine	4	5	
Scoliosis	6	3	
Lumbar spondylolisthesis	15	16	

* $P < 0.0001$

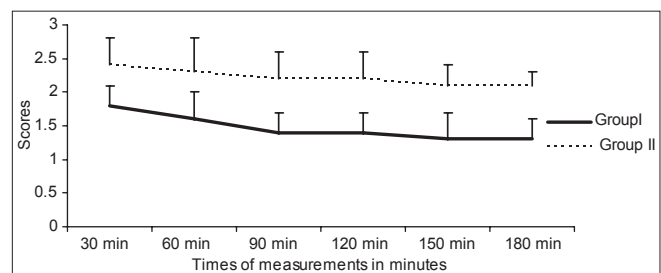


Figure 1: Surgical area bleeding score for the studied groups (mean, standard deviation)

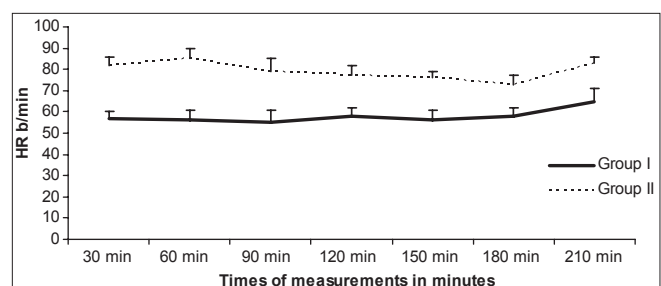


Figure 2: Heart rate in the studied groups (mean, standard deviation)

$P < 0.0001$. The amount of packed red blood cell transfused was significantly less in Group I than in Group II, $P < 0.0001$ [Table 3]. Number of patients, who did not receive RBCs transfusion in both groups was 10 and 2 respectively, $P = 0.025$.

Intraoperative urine output was comparable in both the groups (733 ± 178 vs 665 ± 142 , respectively), $P = 0.06$.

DISCUSSION

Our study showed that heart rate and the amount of SNP used, duration of surgeries, amount of blood loss, and amount of packed red blood cell transfused were significantly less in the atenolol group. Quality of surgical field was better in the atenolol group.

Operative bleeding resulting from cut vessels may be arterial, dependent on the MABP; capillary, which is dependent on blood flow in the capillary bed; or venous, dependent on venous return and venous tone.^[12]

Anesthetic agents alone can affect the amount of blood loss through their pharmacologic effects on the degree of vasodilation and heart rate. Inhalational agents have a vasodilatory effect in a concentration-dependent manner.^[13,14] However, the extent of reflex tachycardia is quite variable. Regarding the apparent reflex tachycardia in isoflurane, sevoflurane is considered as more beneficial.^[14] However, in this study we used isoflurane to clarify the potential benefits of beta-blockers in reducing heart rate and lack of availability of sevoflurane in our hospital.

Table 2: Mean arterial blood pressure changes in both groups

	Group I	Group II	P value
Preoperative	75.4 \pm 5.44	88.4 \pm 5.74	<0.0001*
After induction	80.75 \pm 6.09	92.55 \pm 6.29	<0.0001*
During surgery	59.20 \pm 2.01	58.50 \pm 2.31	0.15
After recovery	80.05 \pm 5.42	88.65 \pm 4.95	<0.0001*

* $P < 0.05$ was considered significant

Table 3: Preoperative Hct, lowest intraoperative Hct, amount of blood loss, and the amount of packed red blood cell transfused in both groups

	Group I	Group II	P value
Preoperative Hct	35.4 \pm 3.73	36.2 \pm 3.12	>0.05
Lowest intraoperative Hct	27.36 \pm 4.64	23.72 \pm 3.32	<0.0001*
Amount of blood loss	527.5 \pm 163.4	901.0 \pm 149.1	<0.0001*
Amount of packed red blood cell transfused	87.5	162.5	<0.0001*

* $P < 0.05$ was considered significant

SNP is one of the most commonly used agents for controlled hypotension. It is a direct-acting, nonselective peripheral vasodilator that primarily dilates resistance vessels leading to venous pooling and decrease SVR systemic vascular resistance. Peripheral vasodilation results in baroreceptor-mediated sympathetic responses with tachycardia and increased myocardial contractility. The renin-angiotensin system and sympathetic nervous system are also activated. These changes increase cardiac output, which may offset the initial decrease in MABP. Plasma catecholamine and renin activity may remain elevated after discontinuation of nitroprusside, resulting in rebound hypertension.^[15]

So the combination of β -blocker and nitroprusside to induce controlled hypotensive anesthesia for spinal surgeries will improve the quality of surgical field, reduce adverse effects of nitroprusside, and decrease the amount of nitroprusside used through negative inotropic and chronotropic effect of β -blocker. Also, this combination will prevent the postoperative rebound hypertension after discontinuation of SNP.

The target MABP was achieved easily and rapidly with low dose in patients who received preoperative atenolol even so the quality of surgical field was better at high level of MABP than in the patients in control group. Also, atenolol group showed less intraoperative blood loss and less amount of blood transfused than the other group.

Our study was in agreement with the study by Apipan *et al.*,^[16] which used oral propranolol premedication during hypotensive anesthesia with nitroprusside in orognathic surgery and concluded that premedication with oral propranolol is safe and effective to reduce reflex tachycardia and the amount of SNP used.

The effect of oral β -blocker premedication was previously studied by Nair *et al.*,^[17] who concluded that optimum conditions were present in the patients received β -blocker in comparison to placebo. However, the crucial finding in Nair's study was the significant correlation between the surgical grade and heart rate without any correlation with the MABP.

Also Marshall *et al.*^[18] examined the effects of controlled hypotension induced with SNP with or without propranolol on cardiovascular, pulmonary, and renin-angiotensin system, and concluded that propranolol, when given during SNP hypotension, exhibits an early cardiovascular response manifested as a decrease in cardiac output and heart rate and a delayed action on the kidney resulting in an inhibition of renin release and decrease the amount of SNP.

This study had several limitations including lack of control group who were given placebo because of the proven benefit of controlled hypotension. These patients had no comorbid illness. The quality of the operative field was subjectively evaluated by surgeons, which may predispose to inaccuracy in collecting data. This study did not include measurements for safety on functions of different body organs.

CONCLUSION

Premedication with oral atenolol 50 mg twice/day for one day before hypotensive anesthesia with SNP during spinal surgeries seems to be clinically safe and effective to reduce heart rate, the amount of SNP used, amount of blood loss, and amount of blood transfused with better quality of surgical field.

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