

Is a combination of Isoflurane with nitroglycerine better than halothane with nitroglycerine for controlled hypotension in spine surgery: A comparative clinical evaluation?

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Citation

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Abstract

Methods and techniques for producing deliberate hypotension has been changing continuously and evolving, not only as the result of the discovery of newer agents and techniques but also from an improved understanding of the underlying physiological changes. This study was conducted at Himalayan Institute Of Medical Sciences in 90 patients of either sex undergoing spinal surgery in the age group 21-70years of ASA grade I,II. They were divided randomly into three groups of 30 patients each group I (Nitroglycerine: NTG) Group II (halothane +NTG) and Group III (Isoflurane +NTG). Various hemodynamic, physiological parameters and were recorded. Heart rate was maximally increased ($p < 0.01$) at 15 min after starting NTG (79.5.11 to 92.9.6.35 beats /min) in group I. The use of combinations agents was hemodynamically more stable. There was significant decrease in rate pressure product in all the three groups. The order of time taken to achieve desired levels of Systolic blood pressure was group II > Group III > Group I. The order of time taken to achieve near normotensive levels was group II > Group III > Group I. Thus we can conclude that better cardiovascular and hemodynamic stability can achieve the best outcome for the patient, using deliberate hypotensive technique with NTG and isoflurane combination.

INTRODUCTION

Virtually all surgeries involve cutting of the blood vessels which will obviously result in bleeding. Frequently bleeding is so excessive as to endanger the life of the patient. A more complex problem is the persistent ooze that makes certain operations difficult or impossible. ¹

Deliberate hypotension is an attempt to produce a controlled and safe reduction in the intravascular pressure, obtaining favorable outcome of the surgery. By enhancing the visualization of the surgical field, hypotension allows accurate delineation of lesions thereby causing fewer traumas to the delicate structures. With its aid intricate operations may be performed more easily, more exactly and therefore more successfully. ^{2,3}

The control of bleeding and the maintenance of an adequate circulating blood volume are fundamental tenets of sound surgical practices, but such control is not always easy. The use of circulatory adjustments to achieve a desirable hemodynamic state is a cornerstone of perioperative

anaesthetic management. ^{4,5,6} These maneuvers are mostly accomplished by physiologic and pharmacological manipulations and thus are within the purview of the anesthesiologists.

Deliberate hypotension is defined as the intentional reduction of the systemic perfusion pressure. Deliberate hypotension is defined as reduction in systolic blood pressure (SBP) to 80-90mm Hg (30% decrease in the SBP from the baseline pressure) or a decrease in the mean arterial pressure (MAP) to 50-65 mm Hg in normotensive patients. ⁷

Hypotension is broadly achievable by vasodilatation and /or reduced myocardial contractility ^{8,9,10}. Various inhalational agents (Halothane, isoflurane, sevoflurane,) ^{11,12} and intravenous agents (pentamethonium iodide, nitroglycerine, labetalol, esmolol, adenosine) ^{13,14,15,16,17,18} are usually used to achieve this hypotension. Best attempt is made to maintain adequate organ perfusion at low perfusion pressure (During hypotensive state).

This study considers some of the anaesthetic choices and

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ideas behind attempts for better cardiovascular and hemodynamic stability to achieve the best outcome for the patient, using deliberate hypotensive technique.

AIM

The aim of this study was to study hemodynamic changes by using various drugs and combinations used for producing deliberate hypotension. To find out the safer dose limits in order to achieve target safe hypotension. To study side effects and complications of the drugs used for hypotension. To conclude upon merits and demerits of deliberate hypotension.

MATERIAL & METHODS

This study was conducted in Department of Anesthesiology and Intensive care, Himalayan Institute of Medical Sciences, Swami Rama Nagar, Dehradun. After obtaining approval from hospital Ethics Committee and written informed consent, 90 controlled hypertensive patients in the age group 20-70 years of either sex belonging to ASA grade I,II, undergoing elective spinal surgical procedures under general anaesthesia with deliberate hypotension were randomly allocated (by opening a sealed envelope) to three groups. Group I (n=30):- patients given Nitroglycerine (NTG), Group II (n=30) patients given halothane +NTG, Group III (n=30) Isoflurane+ NTG.

Exclusion criteria were history of difficult airway management, ASA grade III,IV, diabetes mellitus, pulmonary disease, uncontrolled hypertension, ischemic heart disease and gastro-esophageal reflux disease. After proper history and physical examination, basic routine investigations were advised. Special investigations were advised in specific patients where ever it was required to rule out systemic illness. Mallampatti score, thyromental and sternomental distances were noted. All the patients were kept fasting for at least eight hours prior to surgery. All the patients were given 10 mg tab diazepam H.S. and 5 mg with a sip of water two hours prior to surgery.

In all the groups patients received injection glycopyrrolate 0.2mg intramuscular at least 30 minutes prior to surgery to counteract the vagomimetic effect of propofol and fentanyl. Patients were placed in supine position with the head on a standard firm pillow 7 cm in height. All the monitors were attached. Under all aseptic precautions a 45 cm central venous catheter was inserted via the right antecubital vein into the right atrium. Placement was confirmed by fluoroscopy. Fluid replacement was done at 6ml/kg/hr. All

the patients were catheterized with Foley's catheter for measuring urine output.

Oxygen was administered via a face mask for 5 minutes. Anaesthesia was induced 45 seconds later with i.v inj fentanyl 2 µg/kg, inj propofol 2.5 mg/kg followed by i.v. inj rocuronium 0.6-0.9mg/kg body weight. Mask ventilation with Bain's circuit was done for 60 -90 seconds and the trachea was intubated using Macintosh laryngoscopy and endotracheal cuffed tube. The lungs were ventilated to maintain normocapnia. As surgery was to be performed in prone position firm supports under chest and pelvis were kept so that the abdominal movements and the venous return was not hampered. Compression of the abdomen by faulty positioning would result in the increase in central venous pressure (CVP) and engorged epidural veins. The eyes were closed and covered and arms were padded. The selected hypotensive agent was started after changing the patient to prone position.

Anaesthesia was maintained using 65% nitrous oxide in oxygen via Bains circuit with a fresh gas flow of 100ml/kg/min with a ventilatory frequency of 12-15 bpm and i.v. inj rocuronium 0.15 mg/kg.

In NTG group the infusion was started with 3µg/kg/min and titrated to achieve and maintain the desired hypotension. In group II, III halothane and isoflurane was started at 0.5 vol % .It was increased to 1 vol% by 1 min and was kept constant throughout the duration of hypotension. In these two groups the infusion rate of NTG was titrated to achieve and maintain the desired hypotension, NTG infusion was started with 2µg/kg/min.

Monitoring of following parameters was done: NIBP, HR, SpO₂, ETCO₂, ECG, CVP, Temperature, urine output, was done using Lunar L & T Medical multichannel monitor.

At least three measurements of arterial blood pressure, heart rate, and peripheral oxygen saturation were obtained and the mean was taken to determine the baseline (B1). A second investigator that was not aware of the patient group recorded these measurements. Values were recorded at the time of induction (A1), at the start of hypotensive agent (A5) and then at 15,30,45,60 minutes after the start of hypotensive agent (H15, H30, H45, H60), at hypotensive agent discontinuation (Hd) and after extubation (Ae).

At the end of surgery patients were reversed with IV neostigmine 0.05mg/kg and atropine 1.2 mg. Fluid input

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during surgery period was determined by the anesthetist based on preoperative fasting, blood loss and clinical criteria (arterial pressure, heart rate and observation of the patient).

Data analyzed with paired t test. $p < 0.05$ was considered significant. The data was analysed using ANOVA/MANOVA to find out overall significance in between groups and over period of time.

DISCUSSION

Figure 1

Table 1: Demographic data of all patients

Patient characteristics	GROUP I (n=30)	GROUP II (n=30)	GROUP III (n=30)
Patient Age (in years)	22-66	21-70	22-68
Mean ± SD	42.20 ± 11.23	44.9 ± 15.73	41.6 ± 13.12
Male: Female	20 (66.67%):10(33.3%)	18(60%):12(40%)	17(56.6%):13(43.3%)
MP Grade I:II	18(60%):12(40%)	16 (53.3%):14(46.7%)	15(50%):15(50%)
ASA Grade I:II	14(46.7%): 16(53.3%)	13 (43.3%): 17(56.6%)	12(40%): 18(60%)

There was statistically no significant difference in the patient characteristics between the groups (table 1). The mean duration of surgery was significantly reduced in all the three groups. There was no significant difference between the duration of hypotension in all the three groups ($p > 0.05$) (table 2)

Figure 2

Table 2: Operative details of all groups

Patient characteristics	GROUP I (n=30)	GROUP II (n=30)	GROUP III (n=30)
Duration of surgery	135-240	110-140	105-205
Mean ± SD	178.5 ± 28.75	170.75 ± 11.23	177.45 ± 33.73
Duration of hypotension	102-207min	84-207	72-174
Mean ± SD	143.55 ± 29.64	135.30 ± 37.66	118.05 ± 31.57

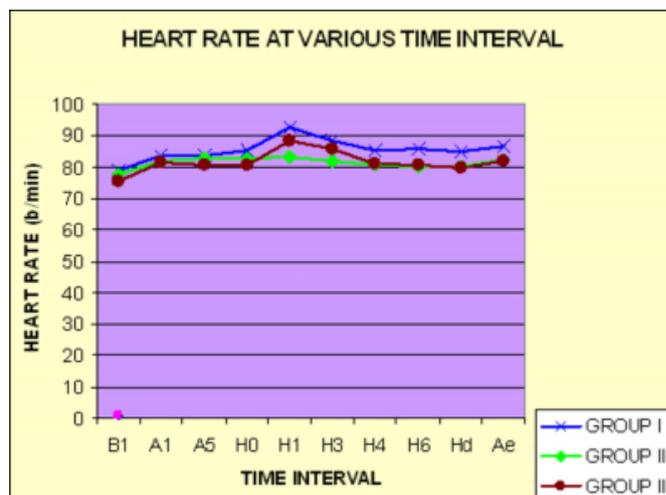
Heart rate was compared in all the three groups .In group I there was a significant increase ($p < 0.05$) in heart rate seen from the baseline after induction. There was a highly significant increase in heart rate at 15, 30 minutes($p < 0.001$) after the start of the hypotensive agent and highly significant increase ($p < 0.01$) in heart rate till the end of the surgery when compared with the baseline values. On comparing intra group we observed that HR had decreased significantly in group II as compared to group I. at 15, 30 min.

In group II, III there was a significant increase in heart rate ($p < 0.05$) after induction, at 5min after induction at the start of hypotensive agent. There was a highly significant increase

in heart rate ($p < 0.001$) at 15 and 30 min after the start of hypotensive agent in group III but there was no significant alterations in group II at other time intervals when compared to baseline values.

Figure 3

Figure 1: Heart rate at various time interval of different groups.



B1:Baseline, A1: at the time of induction, A5 :at the start of hypotensive agent

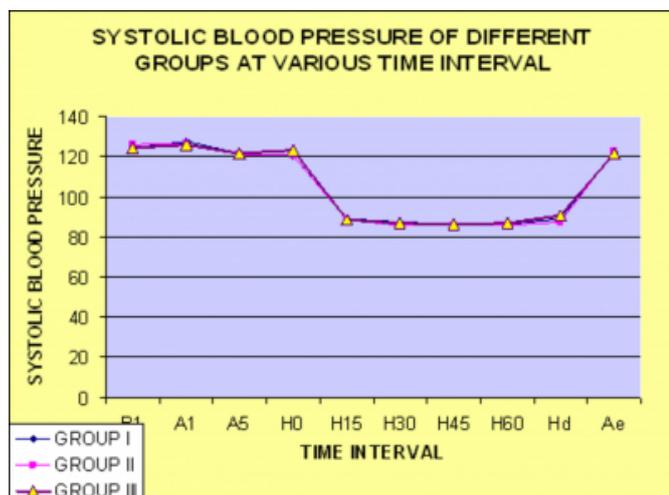
H15: 15 minutes after the start of hypotensive agent , H30: 30min after start of hypotensive agent, H45: 45min after start hypotensive agent H60: 60min after start hypotensive agent Hd: hypotensive agent discontinuation , Ae :after extubation

The SBP was well maintained in between 80-90mm Hg in groups I,II,III during the hypotensive period. There was no significant in various groups during the course of hypotension. There was no incidence of rebound hypertension seen in any of the hypotensive group.

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Figure 4

Figure 2: Systolic blood pressure at various time interval of different groups.



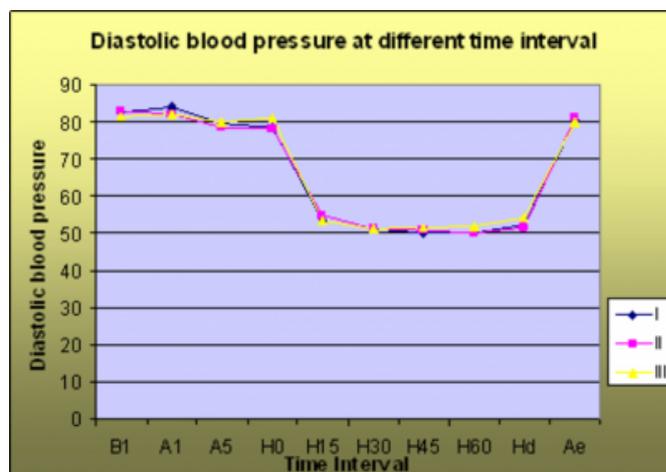
B1: Baseline, A1: at the time of induction, A5 :at the start of hypotensive agent

H15: 15 minutes after the start of hypotensive agent , H30: 30min after start of hypotensive agent, H45: 45min after start hypotensive agent H60: 60min after start hypotensive agent Hd: hypotensive agent discontinuation , Ae :after extubation

There was statistically no significant difference ($p > 0.05$) in diastolic blood pressure before induction in all the groups. Average 33-40% reduction in DBP was seen from the baseline values in all the hypotensive groups. When compared to baseline in group I, II, III DBP at 15, 30, 45, 60min till the drug discontinuation the variation was highly significant due to deliberate hypotension.

Figure 5

Figure 3: Diastolic blood pressure at various time interval of different groups.



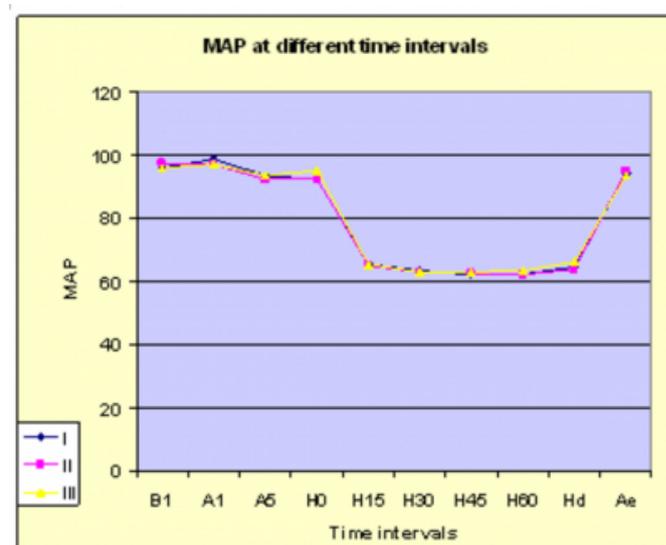
B1: Baseline, A1: at the time of induction, A5 :at the start of hypotensive agent

H15: 15 minutes after the start of hypotensive agent , H30: 30min after start of hypotensive agent, H45: 45min after start hypotensive agent H60: 60min after start hypotensive agent Hd: hypotensive agent discontinuation , Ae :after extubation

Mean arterial pressure (MAP) decreased from 31-35% in all the three groups. There was no significant difference in MAP in all the three groups during the course of hypotension.

Figure 6

Figure 4: Mean arterial blood pressure at various time interval of different groups.



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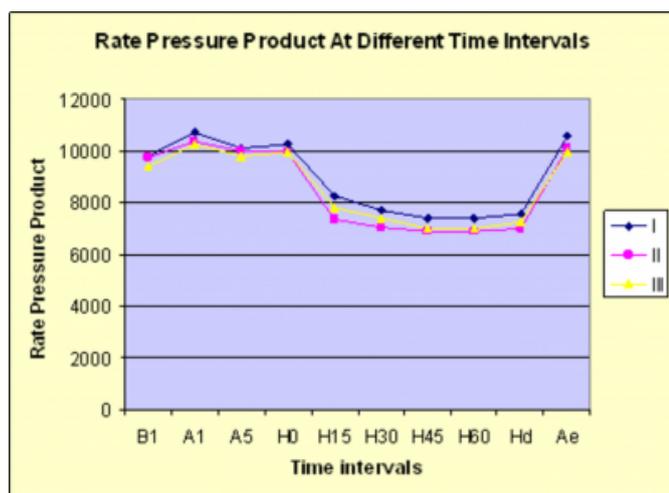
B1:Baseline, A1: at the time of induction, A5 :at the start of hypotensive agent

H15: 15 minutes after the start of hypotensive agent , H30: 30min after start of hypotensive agent, H45: 45min after start hypotensive agent H60: 60min after start hypotensive agent Hd: hypotensive agent discontinuation , Ae :after extubation

The initial rate pressure product (RPP) is deduced by multiplying systolic blood pressure and heart rate (SBP \times HR). During induction RPP increased highly significantly in group I,II and significant in group III. After the start of the hypotensive agent the decrease in the hypotensive groups was highly significant ($p<0.001$) at 15, 30, 45, 60 min time interval and at hypotensive drug discontinuation. But there was no significant difference in between the hypotensive groups.

Figure 7

Figure 5: Rate pressure product at various time interval of different groups.



B1:Baseline, A1: at the time of induction, A5 :at the start of hypotensive agent

H15: 15 minutes after the start of hypotensive agent , H30: 30min after start of hypotensive agent, H45: 45min after start hypotensive agent H60: 60min after start hypotensive agent Hd: hypotensive agent discontinuation , Ae :after extubation

The CVP increased from the baseline significantly after 5min of induction then remained significantly raised The mean urine output in group I,II,III was 1.11 \pm 0.22ml/kg/hr, 1.0 \pm 0.26 and 1.130.16 ml/kg/hr respectively.

There was no significant difference in temperature, end tidal carbon dioxide, SpO₂ and ECG changes in all the three groups.

Majority of spinal surgical procedures performed in the study were laminectomies, dissectomies or both for prolapsed intervertebral disc of the lumbar area. Others were decompression surgeries for the lumbar canal stenosis or tumors and surgeries involving fixation of the spine. (13.33%).

The time taken to achieve desired SBP was less in group I and significant ($p<0.05$) as compared to group II, III. In group III the time taken to achieve normotensive level from hypotensive levels was less than all the other groups.

Figure 8

Table 3: Operative details of all groups

Patient characteristics	GROUP I (n=30)	GROUP II (n=30)	GROUP III (n=30)
Mean time taken to achieve desired SBP from normotensive levels Mean \pm SD	3.8 \pm 1.61	6.3 \pm 1.66	6.15 \pm 2.06
Mean time taken to achieve the normotensive levels from hypotensive levels Mean \pm SD	8.20 \pm 2.07	8.75 \pm 2.07	7.5 \pm 1.82
Maximum dose required to achieve the desired SBP Mean \pm SD μ g/kg/min	5.72 \pm 1.62	3.65 \pm 1.14	4.65 \pm 1.09
Minimum dose to maintain the desired SBP (Mean \pm SD) μ g/kg/min	2.38 \pm 1.13	1.55 \pm 0.90	1.58 \pm 0.84
Maximum dose to maintain the desired SBP (Mean \pm SD) μ g/kg/min	4.05 \pm 1.54	2.62 \pm 1.01	2.90 \pm 0.95

No major complications were observed in this study.

DISCUSSION

Blood loss during spinal surgery has been a continuing problem. Spinal surgery may be associated with bleeding that cannot be adequately controlled. Exposed cancellous bone structures, friable epidural veins and vessels in the subcutaneous tissues and the paraspinous muscles can all be the sources of continued blood loss.

This prospective randomized double blind study was conducted in the department of Anaesthesiology, Intensive care and pain management, Himalayan Institute of Medical

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Sciences. The study was undertaken on 90 patients of age group 21-70 years of ASA grade I, II of either sex undergoing spinal surgery under general anaesthesia after taking consent from the patient.

In a study on deliberate hypotension in back surgery Sleath et al ¹⁹ had a male preponderance. In our study too there was a male preponderance 55(60.1%) and female 35 (39.9%). This male preponderance can be attributed to the fact that larger population in our state is living mainly in hilly areas. Men of this region are devoted to the farming activities and are laborers lifting heavy weights, hence many workmen in this area engage in activity that involves strain or trauma of lumbar spine.

The age group in this study ranged from 21-70 mainly being in the age group 21-50 years (67.5%). Age group of 21-50 years is the working men age group that is why we can attribute more of spinal problems to this age group.

In a study done by Beaussier et al ²⁰ maintained the hypotensive levels i.e. SBP between 80-100 mm Hg in the study period. In this study SBP was reduced to 25-30% of the preinduction values which was correlating with the observations of Sleath et al ¹⁹ who also decreased the SBP to 25%. More reduction in SBP than this level is not safe as it alters the cerebral and renal autoregulation. Another reason for not reducing the SBP further to more than 20-30mm Hg in this study is because Mandel et al ²¹ in their observation reported that reduction in SBP greater than 20mm Hg was not associated with greater reduction in blood loss.

In this study NTG caused significant increase in heart rate from baseline 79 ± 5.11 beats/min to 92.90 ± 6.35 and 88.35 ± 4.71 at 15 and 30 min respectively after the start of NTG infusion. At the other time intervals during hypotension the heart rate was increased but nearer to the baseline values. This is in accordance with the studies of Shirashi et al ²² and Fahmy et al ²³ except a study by Tannieres et al ²⁴ which demonstrated that there is no modification in heart rate though there was a decrease in MAP by 34%.

Shirasishi et al ²² used NTG infusion along with halothane in small concentration for maintenance of anaesthesia. In their study the heart rate increased from baseline 88.3 ± 14 to 96.8 ± 16.4 beats per min after the start of drug. In this study increase in heart rate ($p < 0.05$) in this combination group was from 77.55 ± 4.76 baseline 83.15 ± 4.13 beats /min after 15

minutes of the start of hypotensive agents in which the halothane was kept constant at 1 volume % and the NTG dose was varied to achieve and maintain the desired SBP.

In their study Shirashi et al ²² used the dose of NTG $5 \mu\text{g}/\text{kg}/\text{min}$ in our study the maximum dose of NTG required was $3.65 \mu\text{g}/\text{kg}/\text{min}$. This may be responsible for more increase in heart rate in the study done by Shirashi et al ²². Concentration of halothane was low in their study than in our study so more effect of NTG and therefore more tachycardia.

In our study the isoflurane was kept constant at 1% and the NTG was titrated to achieve the desired SBP. The heart rate increased from baseline 75.7 ± 5.51 baseline to 88.3 ± 6.09 beats /min group III. The reason for this tachycardia might be due to that NTG causes reflex tachycardia during the early phase of hypotension and isoflurane causes little or no effect on heart rate when used in the concentration of 1 volume %.

Fahmy et al ²³ in his study employed RPP which is an indirect index of myocardial oxygen consumption to evaluate relative changes in myocardial oxygen consumption. In his study the RPP decreased significantly with both NTG and Sodium nitroprusside these drugs decrease preload and afterload, leading to decrease in left ventricular work and myocardial oxygen consumption. NTG has been shown to increase coronary blood flow in normal man.

In the group III we observed a decrease in CVP as with NTG systemic vascular resistance decreases therefore, there is a decrease in the CVP though not significant. In group II, III there was more stability as the dose required in combination was less than when each agent was used alone and therefore less of hemodynamic derangement and less of individual toxicity. No significant alteration in urine output, ECG, SpO₂ was observed in all the three groups. In this study nasopharyngeal temperature was recorded during the surgical procedure. It was in the range of 35-37.2° C. There was no significant difference within and the control Group. The decrease in temperature can be explained as the core temperature (central body temperature) usually drops 1-2° C during the first hour of anaesthesia and nasopharyngeal temperature accurately measures core temperature. ^{25,26}

The order of the time taken to achieve desired levels of SBP in various groups: group II > Group III > Group I. In our study

the time required by NTG to achieve desired SBP was 3.8 ± 1.61 min correlating well with the studies of Tannieres et al²⁴ (3-4 min) and Shenoy et al²⁷ (2-5) min. Murat et al²⁸ in his study reported that the hypotension was effective in less than 15 min with isoflurane and NTG combination in all cases. In our study for the same combination, the time taken to achieve the target SBP 6.3 ± 1.66 min. The pattern of study was different that Murat et al²⁸ kept NTG constant and varied isoflurane concentrations for achieving the desired blood pressure.

The dose required to maintain the blood pressure at the desired level ranged from average of 2.38 to 4.05 $\mu\text{g}/\text{kg}/\text{min}$ which is quite similar to the doses used by Fahmy²³ and Shiraishi et al²². In group II and III the dose requirement of NTG were decreased as anticipated due to the combined effect of both the agents. The halothane and isoflurane was kept constant in these groups at 1%. Recovery time was taken maximum by group II.

Because of the intense surgical interest and demand we have attempted to provide anaesthesia that with minimum hazard to the patient would provide maximum visibility, relaxed musculature, and minimal blood loss, for rapid and quiet recovery.

CONCLUSION

Hemodynamic can be more stable than by the use of combination of halothane /isoflurane with NTG to produce deliberate hypotension. With combination agents used, the dose required for each agent was reduced. Hence reduction of the concentration of volatile anaesthetic agent required reduced their side effects like bradycardia, delayed recovery, postoperative shivering etc. and also proved to be cost effective (as the inhalational agents are costlier).

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