



## Study of four combinations of anesthetic drugs for assessing the intraocular pressure changes during gynaecological laparoscopic procedures

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### ABSTRACT

During Laparoscopic surgery, pneumoperitoneum (PNO) and trendelenburg position increase the intraocular pressure (IOP) leading to decrease in perfusion of retina and at times the significant risk of ischemic retinopathy. Our aim of the study is to find out the suitable combination of induction and maintenance agent for combating the increase in IOP by PNO, lithotomy and trendelenburg position, and to study the changes in IOP at different time points and positions in gynaecological laparoscopic procedures. 100 female patients of ASA grade I and II were divided arbitrarily in four groups each comprising 25 patients. In group A and B induction was done with propofol 2.5 mg/kg given IV and in group C and D induction was done with thiopentone 5 mg/kg given IV. Atracurium 0.5 mg/kg IV was used as neuromuscular blocking agent (NMBA). Laryngeal mask airway (LMA) was inserted in all the cases and patients were ventilated with Bain's circuit. Maintenance of anesthesia was done with total intra venous anesthesia (TIVA) with propofol and 100% oxygen in group A and C. In group B and D maintenance was done with 1% isoflurane with oxygen (O<sub>2</sub>) and nitrous oxide (N<sub>2</sub>O) in the ratio of 40:60. Changes in IOP, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) were measured. Baseline readings were taken initially and then 2 min after premedication, 1 min after LMA insertion, 1 min after PNO with lithotomy position, 5 min after 20° head down tilt and PNO in situ and 2 min after exsufflation of PNO with supine horizontal position. To mitigate increase in IOP during gynaecological laparoscopic surgeries, propofol, and propofol TIVA (Group A) proved to be the best option. Propofol and isoflurane (Group B) thiopentone and propofol TIVA (Group C) were not as effective as group A. However, induction with thiopentone and maintenance with isoflurane (Group D) were not effective at all.

**KEYWORDS :** Gynaecological laparoscopy, Intra-ocular pressure, position,

### INTRODUCTION

In most of the Laparoscopic surgery, carbon dioxide (CO<sub>2</sub>) pneumoperitoneum results in ventilatory and respiratory changes which decrease thoracopulmonary compliance. Peritoneal insufflation induces alteration of hemodynamics characterized by decrease in cardiac output, elevation of arterial pressure, and increase in systemic and pulmonary vascular resistance. Heart rate remains unchanged or increases only slightly. PNO and trendelenburg position increase the intraocular pressure (IOP) leading to decrease in perfusion of retina and at times the significant risk of ischemic retinopathy. Increase in IOP, in patients with ocular hypertension has raised concern that laparoscopic surgery may aggravate IOP in susceptible patients. IOP is affected by the various factors. Hypoventilation, hypercapnia, the increase in central venous pressure (CVP), light planes of anesthesia, laryngoscopy and intubation, drugs like atropine, depolarizing muscle relaxants like, succinylcholine, ketamine, trendelenburg position and large volume of fluid of peribulbar block are responsible for increase in IOP. Reduction in IOP is induced by 15° head up tilt, hyperventilation, thiopentone, fentanyl, propofol, inhalation agents like, nitrous oxide (N<sub>2</sub>O), halothane, Isoflurane, non-depolarizing muscle relaxants, small taming dose of succinylcholine, alfentanil, lignocaine, topical application of pilocarpine, timolol, and acetazolamide etc. Propofol total intra venous anaesthesia (TIVA) prevents the increase in IOP with PNO and head down position in laparoscopic surgeries. The mechanism of this propofol taming effect on IOP during laparoscopic surgery may be attributable to the effect of propofol on arginine vasopressin (AVP) which is markedly increased during laparoscopy especially post-insufflation and trendelenburg position. AVP and its synthetic derivative desmopressin produce a dose dependent increase in IOP. Propofol inhibits the somatodendritic AVP release from the supraoptic nucleus and may therefore prevent the increase of IOP associated with PNO and the trendelenburg position. Our present

aim is to find out the suitable combination of induction and maintenance agent for combating the increase in IOP by PNO and trendelenburg position and to study changes in IOP at different time points and positions with different combinations of drugs in gynaecological laparoscopic procedures.

### MATERIALS AND METHODS

100 female patients of ASA grade I and II with age between 20 and 45 years and weight between 40 to 70 kg were selected for the study that were scheduled for diagnostic and therapeutic gynaecological laparoscopic surgery requiring general anesthesia at RIMS, RAIPUR, CHHATTISGARH.

Pre-anesthetic check-up was done a day before surgery and informed written consent was taken. The patients with compromised cardiac, renal or pulmonary status on medications, patients suffering from acute or chronic disorders of eye, any coagulopathy, diabetes, hypertensive, and coronary artery disease, patients unwilling to participate in the study, anemic (Hb < 10gm), and obese patients (>70 Kg) were excluded from the study. The patients were divided arbitrarily in four groups each comprising 30 patients. Patients were kept fasting after 10 pm on night before surgery. In operation theatre proparacaine 0.5% eye drop (one drop in each eye) was instilled. After 1 min, base line IOP was measured with Schiotz tonometer in supine position. Normal saline was instilled in both eyes. Base line vitals, e.g. HR, SBP, DBP, MBP, and arterial saturation of O<sub>2</sub> (SpO<sub>2</sub>) were noted. After getting an IV access, an infusion of ringer lactate, at the rate of 4 ml/Kg/h. was started. The patients were premedicated with inj. glycopyrrolate 0.2 mg, inj. ranitidine 150 mg, inj. midazolam 2 mg, and inj. ondansetron 4 mg and inj. fentanyl 2 mg/Kg body weight given intravenously. After 2 min of premedication, IOP and vitals were noted. Patients were preoxygenated for 2 min with 100% oxygen and induction agent

was given according to the group. Induction of anesthesia was done as follows: Group A – Induction with propofol 2.5 mg/kg and atracurium 0.5 mg/kg, Group B – Induction with propofol 2.5 mg/kg and atracurium 0.5 mg/kg, Group C – Induction with thiopentone 5 mg/kg and atracurium 0.5 mg/kg, Group D – Induction with thiopentone 5 mg/kg and atracurium 0.5 mg/kg. Patients were ventilated with 100% O<sub>2</sub> and LMA was inserted and bilateral expansion of chest was observed and LMA fixed. After 1 min of LMA insertion IOP was measured in supine horizontal position before PNO and vitals were measured. Patients were ventilated with Bain's circuit. Maintenance of anesthesia was done as follows: In group A – Maintenance of anesthesia was done with propofol TIVA. Propofol infusion was started at the rate of 10 mg/kg/h for first 15 min, then it was reduced to 8 mg/kg/h for next 15 min and for the rest of the time infusion was given at the rate of 6 mg/kg/h. Inj. atracurium was repeated in a dose of 5 mg whenever required. Patients were ventilated with 100% O<sub>2</sub>. In group B – Maintenance of anesthesia was done with 1% isoflurane with O<sub>2</sub> and N<sub>2</sub>O in the ratio of 40:60. Inj. atracurium was repeated in a dose of 5 mg as and when required. In group C – Maintenance of anesthesia was done with propofol TIVA. Propofol infusion was started at the rate of 10 mg/kg/h for first 15 min, then it was reduced to 8 mg/kg/h for next 15 min and for the rest of the time the infusion was given at the rate of 6 mg/kg/h. Inj. atracurium was repeated in a dose of 5 mg whenever required. The patients were ventilated with 100% oxygen. In group D – Maintenance of anesthesia was done with 1% isoflurane along with O<sub>2</sub> and N<sub>2</sub>O in the ratio of 40:60. Inj. atracurium was repeated in a dose of 5 mg as and when required. Infusion rate of propofol and concentration of isoflurane was decreased if SBP fell >20% of the base line values and the infusion rate of propofol and concentration of isoflurane was increased if SBP increased >20% of the base line value. Patients were put in lithotomy position and PNO was created by intraperitoneal insufflation of CO<sub>2</sub> with patients in supine position. Throughout the surgery intraperitoneal pressure was maintained at 12 mmHg by a CO<sub>2</sub> insufflator. Expired concentration of CO<sub>2</sub> (EtCO<sub>2</sub>) was kept between 30 and 35 mmHg. After 1 min of establishment of PNO, IOP was measured in lithotomy position along with vitals. After that, the patients were positioned to 20° head down tilt position (trendelenburg). After 5 min of head down position and PNO *in situ*, IOP was measured along with vitals. At the conclusion of the procedure and after the laparoscope was taken out, infusion of propofol was stopped in group A and Group C and isoflurane was stopped in group B and D. The patients were returned to horizontal position and PNO was evacuated. After 2 min of evacuation of PNO, IOP was measured in supine horizontal position along with vitals. Ciprofloxacin 0.3% eye ointment was put in both the eyes. The patients were reversed with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 8 µg/kg given IV. LMA was removed when patient had good spontaneous efforts, adequate tidal volume on spontaneous respiration and adequate muscle power. Consciousness and orientation were checked. Vitals were recorded at the time of shifting. Scaled readings noted with Schiotz Tonometer were converted to pressure in mmHg (intra ocular pressure) with the help of Schiotz tonometer chart. At the end of the study the data were compiled systematically and analyzed using statistical package for social sciences (SPSS) version 15 for Windows. Chi-square test was used to compare the proportional data. Mean differences were compared using students t-test and a  $P < 0.05$  showed a significant intergroup difference.

## RESULTS

This study comprised 100 patients between the ages of 20 and 45 years weighing between 45 and 60 kg. Each group received specific combination of induction and maintenance agent. Comparison was done with regard to changes in IOP, HR, SBP, DBP, and MBP. Baseline readings were taken initially and then 2 min after premedication, 1 min after LMA insertion, 1 min after PNO with lithotomy position, 5 min after 20° head down tilt, and PNO *in situ*, and 2 min after exsufflation of PNO with supine horizontal position. There was no significant difference in patient characteristics with respect to age, weight, baseline reading of HR, SBP, DBP, and MBP and IOP in all the four groups. SpO<sub>2</sub> was within 95-99% in all the groups, all the time.

EtCO<sub>2</sub> was maintained within the range of 30-35 mmHg in all the cases. We noticed that, as compared to baseline readings, a significant fall in IOP ( $P < 0.05$ ) was observed in all the four groups as a result of premedication. In all the four groups LMA was inserted after induction with propofol (in group A and B) or thiopentone (in group C and D) and atracurium used as a NMBA. We noticed, after induction with propofol IOP decreased by almost 50% (in group A and B) while it decreased by almost 25% after thiopentone induction (in group C and D). IOP increased in all the four groups after PNO and lithotomy position. It further increased after 20° head down position. We noticed that, with propofol TIVA the IOP increase was less therefore curve of the graph was less steep and parallel in group A and C while maintenance with 1% isoflurane could not combat increase in IOP during PNO, lithotomy and 20° head down position therefore, curve of the graph was more steep and almost parallel in group B and D. After exsufflation and return to horizontal position IOP decreased in all the groups but it was above baseline in group D while it was near baseline in group B and C and below baseline in group A. There was a significant fall in the heart rate after premedication in all the groups. In group A and B, HR decreased further at 1 min after LMA insertion, due to propofol induction. In group C and D, HR increased at 1 min after LMA insertion where thiopentone was used as induction agents. In group A and C where propofol TIVA was used as maintenance agent HR remained stable during PNO and 20° head down position. In group B and D where 1% isoflurane was used as maintenance agent HR showed an increasing trend during PNO and 20° head down position. After premedication SBP, DBP, and MBP decreased in all the four groups and reached 93% of baseline value. SBP, DBP, and MBP decreased further at 1 min after LMA insertion ( $P < 0.05$ ). SBP, DBP, and MBP increased at 1 min after PNO and lithotomy position and 5 min after 20° head down tilt and PNO *in situ*. After 2 min of exsufflation of PNO and return to supine horizontal position, SBP, DBP, and MBP decreased in all the four groups, to non-significant level as compared to baseline level. Graph and tables of observations are given in the last.

## DISCUSSION

Our study was undertaken to study the changes in IOP at different time points and positions with different combinations of anesthetic drugs. The aim was to find out an appropriate combination to combat an increase in IOP in gynaecological laparoscopic surgeries. Since all the four groups received the same premedication, it can be presumed that it did not influence the results of our comparison. Out of all the drugs used in premedication, fentanyl contributed mainly for fall in IOP. Fall in IOP after premedication can be mainly attributed to fentanyl as midazolam does not have significant effect on IOP. Since IOP increase is more with endotracheal intubation, we used LMA instead of endotracheal tube. In all the four groups LMA was inserted after induction with propofol (in group A and B) or thiopentone (in group C and D) and atracurium used as a NMBA. IOP changes 1 min after LMA insertion were due to persistent effect of induction agents as atracurium and LMA insertion do not affect IOP significantly. After induction with propofol IOP decreased by almost 50% while it decreased by almost 25% only after thiopentone induction. IOP increased in all the four groups after PNO and lithotomy and 20° head down position. With propofol TIVA the IOP increase was less as compared to 1% isoflurane maintenance. This single observation endorses the hypothesis that the administration of propofol in any form (induction or TIVA) is better than 1% isoflurane in controlling the rise in IOP. This clearly indicates that propofol induction and maintenance with propofol TIVA was the best option as regards the decrease in IOP (group A) and induction with thiopentone and maintenance with 1% isoflurane could not decrease IOP (group D). Propofol decreased IOP more as compared to thiopentone. The administration of succinylcholine increased IOP in all the patients, more so in those given thiopentone. 1% isoflurane could not combat IOP even after propofol induction as the effect of latter was short lived. IOP decreased significantly after induction of anesthesia in both the groups and remained so throughout the procedure in propofol group. However, in isoflurane group IOP increased significantly above pre-induction level after PNO and head down position. After premedication SBP, DBP, and MBP

decreased in all the four groups and reached 93% of baseline value due to midazolam (2 mg) and fentanyl (2 µg/kg). SBP, DBP, and MBP decreased further at 1 min after LMA insertion ( $P < 0.05$ ) with propofol atracurium induction. This was due to the effect of propofol which reduces stroke volume, cardiac index, and systemic vascular resistance. SBP, DBP, and MBP increased at 1 min after PNO and lithotomy position and 5 min after 20° head down tilt and PNO *in situ*. Falabelle *et al.*, studied hemodynamic changes associated with PNO and trendelenburg position during GA. They concluded that PNO and trendelenburg position significantly increase MAP and systemic vascular resistance. Awad *et al.* measured IOP in patients undergoing robot assisted prostatectomy. They found that surgical duration (in minutes) and EtCo<sub>2</sub> were the only significant variables predicting changes in IOP during stable and prolonged trendelenburg positioning. On an average, IOP increased 0.21 mmHg per mmHg increase in EtCo<sub>2</sub> after adjusting for time. EtCo<sub>2</sub> was kept constant between 30-35 mmHg throughout the procedure, so that EtCo<sub>2</sub> changes may not show any variation on our results.

### CONCLUSION

We conclude that to mitigate increase in IOP during gynaecological laparoscopic surgeries with a combination of propofol and propofol TIVA (Group A) proved to be very satisfactory and superior to all combination of drugs. Propofol and isoflurane (Group B) thiopentone and propofol TIVA (Group C) were not as effective as group I in controlling an increase in IOP. However, induction with thiopentone and maintenance with isoflurane (Group D) did not prove to be satisfactory out of all four groups.

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