A Comparison of Hemodynamic Response To Induction With Propofol And Etomidate In Elective Surgery– A Study Protocol

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Abstract:

Background: Intravenous induction is a crucial part of anaesthesia. Laryngoscopy and intubation are noxious stimuli. Adverse cardiovascular events, arrhythmias, hemodynamic imbalance are alarming effects after intravenous injection of inducing agents in patients. Thus, the need to use a safer induction agent with lesser side effects.

Objectives: This observational, cross sectional study is protocolised to compare hemodynamic response to induction with propofol and etomidate in patient posted for elective surgery.

Methodology: Following approval from institutional ethics committee hundred & twenty (120) ASA I and II class patients of age group 20 to 60 years of either gender posted for elective surgical procedures requiring general anaesthesia will be enlisted for the study. Subjects will be randomly allocated into two groups of sixty (60) each, one group of subjects receiving propofol injection (2mg/kg) and the other injection etomidate (0.3 mg/kg) as inducing agent. Vitals will be recorded at six different intervals. Adverse effects like pain on injection, apnoea, myoclonus will be carefully observed and noted.

Results: Both groups have similar demographic variables. It has been hypothesised that minimal changes in HR and MAP is noticed in patients induced with etomidate. Propofol group is expected to show greater incidence of pain on injection whereas etomidate grup is expected to show higher incidence of myoclonus.

Conclusion: Etomidate is a better inducing agent than propofol with regard to their hemodynamic stability with lesser pain on injection.

Keywords: general anaesthesia, balanced anaesthesia, induction agents, propofol, etomidate, hemodynamic response, sympathetic response, myoclonus, injection pain, laryngoscopy.

Background and Rationale:

Traditionally patients were made unconscious by administering gases for inhalation. This allowed patient to undergo surgery and other procedures. The technical difficulties associated with administration of these gases lead to many deaths during anaesthesia. These lead to development of many new apparatus for delivering these gases.as a result of complexity of the apparatuses balanced anaesthesia was not produced by inhaled gases[1-4].

Intravenous induction agents are drugs that are given in appropriate doses to cause rapid loss of consciousness and are given prior to other drugs that are used to maintain anaesthesia [5].

The ideal induction agent used for general anaesthesia should display good haemodynamic stability, minimal side effects on respiratory system, minimal stress response on intubation and rapid clearance. Over the years, a continuous search for a safer and better intravenous induction agent has been conducted. Presently etomidate and propofol are rapid acting, safe and popular intravenous induction agents, however there are different induction characteristics of these two drugs.

By the 1970's a new intravenous induction agent, propofol was formulated and applied into anaesthesia practice by 1977[6]. Effects noted that Propofol provides swift onset of action, rapid recovery and efficacious suppression of pharyngeal and laryngeal reflexes, adequate depth of anesthesia during intubation and antiemesis[7, 8, 9, 10]. A major disadvantage noted with use of propofol is drastic fall in blood pressure which occurs due to vasodilatation[11]. The earlier preparation of propofol was insoluble with water and therefore was initially formulated with cremophor EL. As a result of anaphylactoid adverse effects associated with cremophor EL, a reformulated preparation of the drug was done using soya been oil emulsion and reintroduced in 1986.
Etomidate, an intravenous induction agent was first formulated in the year 1964 and applied into anaesthesia practice by 1972. With use of etomidate, faster onset of action along with rapid recovery and associated hemodynamic stableness with smallest respiratory depression was noted. These beneficial properties lead to wide spread use of etomidate[11,12,13,14,15]. Use of etomidate declined following numerous reports of adrenocortical suppression and other inconsequential adverse effects such as pain during injection, myoclonic movements, and nausea & vomiting post-operatively)[16]. In recent times, with lack of new reports of adrenocortical suppression and established beneficial effect on hemodynamics of etomidate, has renewed interest to use etomidate for intravenous induction of general anaesthesia[17]. The drug has been reformulated using lipid emulsion and was applied into clinical practice in 2007 in India.

With this study, we wish to compare and evaluate effects of propofol vs etomidate by comparison of parameters such as changes in systolic blood pressure, diastolic blood pressure, mean arterial pressure during induction as primary outcome and effects such as pain on injection, myoclonus, postoperative nausea and vomiting , in turn this will help us choose a safer intravenous induction agent.

Objectives:

Primary objective: To study and compare the haemodynamic response to induction with propofol vs etomidate in adult patients scheduled for elective surgery. The various parameters being:

Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressures (MAP).

Secondary Objective: To calculate rate pressure product and study any untoward effects of either of the drugs perioperatively such as pain on injection, myoclonus, nausea and vomiting or any other adverse effect.

Methods:

Study design: This is an observational cross-sectional study

Setting: Present study will be chaperoned in Jawaharlal Institute of Medical Sciences, Sawangi (Meghe) Wardha in accordance with the guidelines of the institutional ethical review board to to be conducted over a three-year period From May 2018 - May 2021.

Participants: Patients will be divided into two groups of 60 each and randomization will be based on computer generated random numbers. **Group E** receive etomidate - 0.3 mg/Kg for induction of anaesthesia. **Group P** receive propofol- 2 mg/Kg for induction of anaesthesia

INCLUSION CRITERIA: ASA classes I and II. Age between 20-60 years. Patients undergoing elective surgical procedures requiring general anaesthesia

EXCLUSION CRITERIA: Patients refusal, Patients belonging to ASA class III and above. Age less than 20 years and age more than 60 years. Patients undergoing emergency surgeries. Patients having co morbid conditions including epilepsy, significant Cardiac, Respiratory, hepatic or renal dysfunction, Obstetric, paediatric and obese patients. Anticipated difficult airway. Presence of primary and secondary steroid deficiency or on any steroid medication. Patients with shock. Drug allergies.

Variables: consist of following parameters which will be recorded, which are Heart rate (HR) where HR<50 is defined as bradycardia and HR> 100 as tachycardia, Systolic blood pressure (SBP)/ Diastolic blood pressure (DBP) where blood pressure < 90/60 mm Hg is defined as hypotension and blood pressure > 130/ 85 is defined as hypertension, Mean arterial pressures (MAP) , End tidal CO_2 (range of 35 to 45 mm Hg as standard), SpO_2 (percentage saturation of oxygen) where SpO_2 < 92% is defined as hypoxia.

Study size: was derived from the formula given below

$n = [\sigma^2 * 2(Z_\alpha + Z_{1-\beta})^2] / \Delta^2$

where n: sample size, σ: standard deviation from previous studies (during laryngoscopy = 11 mm Hg), Zα: 1.96 (from Z table) at type 1 error at 5 % level of significance. $Z_{1-\beta}$: This depends on power, for 80% power, this is 0.84. Δ: difference between the mean /expected values. We are expecting 16mm Hg mean change during laryngoscopy in our study.

Thus $n = [2(11)^2 (1.96 + 0.84)^2] \div (16)^2 = 58$. Using the formula above we arrive at n = 58.

Considering dropouts during the study the sample size is rounded of to 60 in each group.

Anaesthesia protocol:

After shifting patient into the operation theatre routine ASA standard monitors will attached. Pre oxygenation will be done with 100% oxygen by mask for 3 minutes prior to intubation. The above parameters will be recorded again and noted as at Level 0- and considered for comparison with subsequent recordings. Patient will then be induced in Group E with Inj. Etomidate 0.3mg/ kg and in Group P with Inj. Propofol 2mg/kg according to randomization. Anesthesia will be induced using

intravenous etomidate and propofol Muscle relaxation will be achieved with Inj. Vecuronium bromide (0.1mg/kg. body wt Nitrous oxide, oxygen will be used for mask ventilation in both study groups.

IPPV will be administered using 100% Oxygen for mask ventilation. Laryngoscopy followed by intubation will be done using a standard Macintosh Blade by an experienced anaesthesiologist with more than 3 years of experience. Oral Intubation will be effected with appropriately sized disposable, high-volume low pressure cuffed endotracheal tube within 15-20 seconds (not more than 30 Sec). If more than 2 laryngoscopy attempts or duration >30 seconds will be required for laryngoscopy and intubation, the patient will be disqualified from the study. Post intubation respiration will be controlled with rate between 12 to 14 cycles per minute and tidal volume adjusted to maintain appropriate $EtCO_2$.

All ventilated Patients will be maintained with O2(50%), N20 (50%), Sevoflurane & Inj Vecuronium Bromide 0.1 mg/Kg Body wt.

Upon completion of surgery, anaesthesia will be reversed with Inj. Neostigmine 0.05mg/Kg body wt. and Inj. Glycopyrrolate 0.004mg/Kg Body wt.

Vital parameters will be noted before induction(baseline) (T0), At Time of induction(T1), 1 min post induction(T2), 3min post induction(T3), 1 min after laryngoscopy and intubation(T4), 3 min post intubation(T5) for each patient.

Statistical Analysis:

Will be performed with SPSS for windows (SPSS Inc, Chicago II, USA), version 16.0 for analysis of demographic data and comparison of groups. Descriptive data and comparison of groups x 2, will be compared by unpaired T test And Mann Whitney U- Test. For all the tests “p” value of < 0.05 will be considered as statistically significant. Intra group comparison will be done using chi squared test.

Expected Outcomes:

It is expected that patients receiving intravenous induction using etomidate will show lesser variation in hemodynamic parameters HR, SBD, DBP and MAP than the patients receiving injection propofol. Injection pain is expected to be more in patients receiving propofol for induction of anaesthesia. Incidence of myoclonus is greater in patients receiving etomidate for induction

Discussion:

In Mackenzie N, Grant IS, the study of propofol induction of anaesthesia in day care patients. During the study, it was found that, propofol caused more marked decrease in systolic arterial blood pressure in the 2 minutes after induction, with more than half of the patients a decrease of more than 20%. The mean decreases in the systolic blood pressure in the group which was induced with propofol was 30mmHg, compared to 18mmHg in other groups[10].

In 1991 Fairfield and colleagues observed the hemodynamic responses with propofol induction, noted that at 2 minutes, after induction there was drop in cardiac output, mean arterial pressure[18].

In 2008 Jack and colleagues conducted a study on 10 patients to know changes in the cardiovascular system after achieving constant effect site concentration of propofol, it was observed that there was a fall in heart rate by 21%, cardiac index by 14% mean arterial pressure by 28% due to vasodilatation[19].

In 1986 Dundee and colleagues conducted a study comparing the induction characteristics of 4 intravenous anaesthetic agents, showed that induction was successful with thiopentone 5mg/kg, etomidate 0.3mg/kg, propofol 2mg/kg, and methohexitone 1.5mg/kg. Propofol produced more hypotension than thiopentone. In propofol group mean blood pressure decreased by 15%, in thiopentone group decreased by 10%, in etomidate group decreased by 5%[12].

Bendel, Ruokonen et al, conducted a randomized double-blinded study comparing the hemodynamic response of propofol and etomidate in patients suffering from severe aortic stenosis. Sixty-six patients who had severe aortic stenosis were scheduled for elective aortic valve replacement, were induced with propofol or etomidate. A decrease in MAP was noted in all the patients. The decrease in MAP was to a greater degree in patients receiving propofol in comparison to those receiving induction with etomidate. Patients who were induced with propofol needed phenyl ephedrine more regularly than those patients who were induced with etomidate (20/30 vs. 8/30)[20]. Studies related to other aspects of general anaesthesia are available[21-23]. Tendulkat et al conducted prospective comparison of pressor and airway responses to iv esmolol and iv dexmedetomidine during emergence from general anaesthesia and extubation[24]. Charan et al conducted a prospective study of intraoperative comparison between general anaesthesia with conventional opioid and thoracic epidural anaesthesia for off pump coronary artery bypass surgery[25].

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Annexures:

Tables:

TABLE 1

PAIN ON INJECTION	**MYOCLONUS**	**GAG REFLEX**	**TEARS**	**COUGH**

TABLE 2 : MONITORING OF VITALS

INDUCTION	**HR**	**SYSTOLIC BP**	**DIASTOLIC BP**	**MAP**	**RPP**
Before induction(baseline) (T0)					
At Time of induction(T1)					
1 min post induction(T2)					
3min post induction(T3)					
1 min after laryngoscopy and intubation(T4)					
3 min post intubation(T5)					

TABLE 3 : RECOVERY TIME

	CONSCIOUSNESS	OBEYS COMMANDS	ORIENTATION	ABILITY TO SIT UNAIDED
RECOVERY TIME (MIN)				