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Comparision of Induction Characteristics and Hemodynamic Parameters of Propofol Versus Etomidate in Patients Undergoing Surgeries under General Anaesthesia, a Bispectral Index Guided Study

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Abstract:

Background and Objective: *- The aim of the study is to compare hemodynamic parameters and side effects of both drugs in order to choose a better induction agent.*

Materials and Methods: *- This is a randomised double-blind study conducted at Bangalore Medical College and Research Institute on 70 patients scheduled for elective surgeries under general anaesthesia from october 2013 to may 2015. 70 patients were randomly allocated into either group P (propofol group) and to group E (etomidate group) of 35 each. All patients premedicated with inj.midazolam 0.02mg/kg IV, inj. Fentanyl 2 microgm/kg IV. Group P received propofol infusion at 0.5 mg/kg/hr and group E at 0.05mg/kg/hr until Bispectral index value dropped to 50. Then patients were intubated with vecuronium 0.1mg/kg and anaesthesia maintained according to institutional protocol followed by extubation after adequate recovery. Hemodynamic parameters and side effects during induction were recorded between both groups until the infusion of study drug.*

Results: *- There was statistically significant fall in heart rate in propofol group (Group P) from the baseline starting from 3 minutes of induction upto 10 minutes with p value < 0.05 and systolic, diastolic and mean arterial pressure with p value <0.01.There was no significant change in heart rate and blood pressure in etomidate (Group E) starting from baseline. 32 patients (91.5%) in propofol group had pain compared to 9 patients (28.5%) in etomidate group with p value <0.001.*

Myoclonus was observed among 4 patients induced with propofol when compared to 27 patients induced with etomidate with p value <0.001. Incidence of nausea was 22.9% in propofol group compared to 71.4% in etomidate group and incidence of vomiting was 22.8% in propofol group compared to 77.1% in etomidate group both with p value <0.001.

Conclusion: *In conclusion, etomidate is better for its hemodynamic stability over propofol along with less incidence of pain on injection. Only drawback was incidence of myoclonus and post-operative nausea and vomiting.*

Keywords: ***Etomidate; propofol; bispectral index; fentanyl.***

Background

A successful general anaesthesia is defined as a reversible triad of hypnosis, analgesia and abolition of reflex activity.[1]

Propofol was introduced clinically by kay and rolly in 1977. As a new anaesthetic agent, it provides faster onset of action, anti-emesis, potent attenuation of pharyngeal, laryngeal, tracheal reflex and adequate depth of anaesthesia during intubation and a clear and smooth recovery. It is a commonly used Intravenous induction agent in recent years.[2,3,4]

However high doses can cause side effects like hypotension due to direct myocardial depression and decreased peripheral vasodilatation along with venodilatation, respiratory depression/ apnea. It also causes pain on injection when injected into smaller veins. Pain is due to concentration of free propofol in the aqueous phase of emulsion.[5]

DOI: 10.23958/ijirms/vol02-i11/02

Etomidate is a carboxylated imidazole drug used for induction of general anaesthesia and sedation introduced into clinical practice in 1972.

Preclinical experiments demonstrated that etomidate injection was associated with minimal hemodynamic changes or respiratory depression, features that were presumed to result in it's unusually safety profile.[6] However pain on injection and myoclonus are the most common side effects of this drug.[7]

Pain on injection, venous irritation and hemolysis have been abolished by a new fat emulsion of etomidate (medium chain triglyceride and soya bean named etomidate- lipuro , germany) but the new solvent has not reduced the incidence of myoclonus after etomidate injection.[7]

The effect of etomidate on cardiac output and myocardial oxygenation and its wide theraupetic index, which is approximately six fold better than thiopentone and propofol, have logically served to maintain niche use in patients of all age groups.

However in 1983, an increase in mortality of critically ill patients associated with the use of etomidate infusions for sedation in intensive care units was reported. It is attributed to etomidate induced inhibition of an enzyme 11 beta hydroxylase involved in steroidogenesis.

Most opinion at that time and currently with notable exceptions concluded that although etomidate by infusion for critically ill patients was detrimental, single bolus injection of etomidate in these and other groups were safe.[8]

Assessment of depth of anaesthesia is fundamental to anaesthetic practice.[9] The first commercial depth of general anaesthesia monitor BIS monitor was introduced in 1992 by aspect medical system.The Bispectral index is a dimensionless number from 0 (isoelectricity) to 100 (awake) measured from patients forehead . A reading from 40-60 indicates an adequate depth of hypnosis with reasonably rapid recovery of consciousness.[9,10]

In view of the above, we proposed to study the induction characteristics including the hemodynamic characteristics and side effects between propofol and etomidate in patients undergoing surgeries under general anaesthesia under Bispectral index guidance.

Methodology

Patients undergoing surgeries under general anaesthesia in victoria and bowring and lady curzon hospital of Bangalore Medical College and Research Institute were studied from October 2013 to may 2015 in a randomised double-blind study. Included patients in this study were patients with ASA status 1 & 2, aged between 18-50 yrs and patients who gave informed written consent. Exclusion criteria were patients with BMI >= 30 and with systemic illness.

After approval by Institutional Ethical Committee and obtaining informed written consent from the patients, 70 of them were randomised into 2 groups of 35 each by the computer generated random list (www.random.org)

Group P: Propofol group (n = 35)
Group E: Etomidate group (n = 35)

The sequence was delivered in a sealed envelope on the morning of surgery. The minimum sample has been calculated at 5% level of significance and power of study 95% to detect atleast 15% difference in mean arterial pressure between each group. Accordingly, total sample size is 62, that is 31 each in etomidate and propofol group. To increase the validity of study, we included 35 patients in each group with total sample size of 70. Demographic parameters were recorded through questionnaire

All patients were kept fasting overnight. Upon arrival in the operating room, 20-gauge intravenous catheter secured and Ringer's lactate infusion started. Monitors for pulse oximetry, electrocardiogram and non-invasive blood pressure were attached and baseline readings noted. Datex ohmeda BIS module, BIS sensor, composed of a self-adhering flexible band holding three electrodes was applied to the forehead and temple to measure the Bispectral index of patients.

Both groups premedicated with Inj. midaz 0.02 mg/kg, and Inj. Fentanyl 2 microgm/kg IV. Two minutes after fentanyl administration, infusion of anaesthetic agent was started. Propofol group received propofol at an infusion rate of 0.5mg/kg/min and etomidate group received etomidate at an infusion rate of 0.05mg/kg/min. As soon as BIS value reached 50, infusion was stopped.

Tracheal intubation was facilitated using vecuronium 0.1 mg/kg and anaesthesia was maintained as per institutional protocol. Residual neuromuscular blockade was reversed with neostigmine 0.05mg/kg and glycopyrolate 0.008mg/kg. Trachea was extubated after adequate recovery of muscle power and patients were monitored post operatively.

Heart rate (HR), Systolic blood pressure (SBP), diastolic blood pressure(DBP), mean arterial pressure (MAP), oxygen saturation(spo_2) Bispectral index number (BIS) were recorded every minute for 10 minutes. Adverse effects such as pain on injection, myoclonus and post operative nausea & vomiting if any was documented. During intubation, if there was any increase in BIS reading, infusion of induction agent was restarted, until no increase in BIS values were observed.

DOI: 10.23958/ijirms/vol02-i11/02

Statistical Analysis:

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Paired t test is applied to find intragroup significance of parameters from baseline.

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value: 0.01<P ≤ 0.05)
** Strongly significant (P value: P≤0.01)

Observations and Results

Both groups were comparable with regard to age (Figure 1) and gender (Figure 2) and Height (figure 3a), Weight (figure 3b)

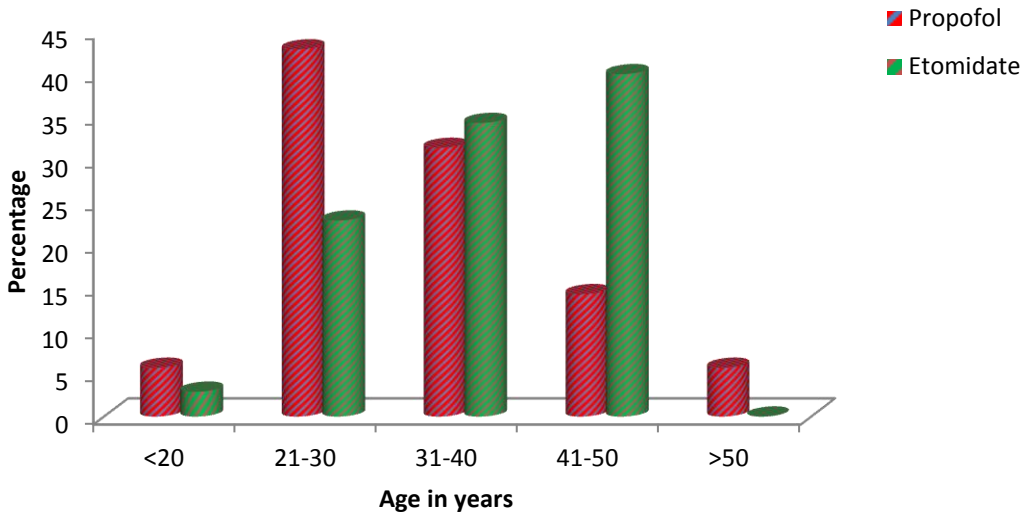

Figure 1: Age distribution of patients studied

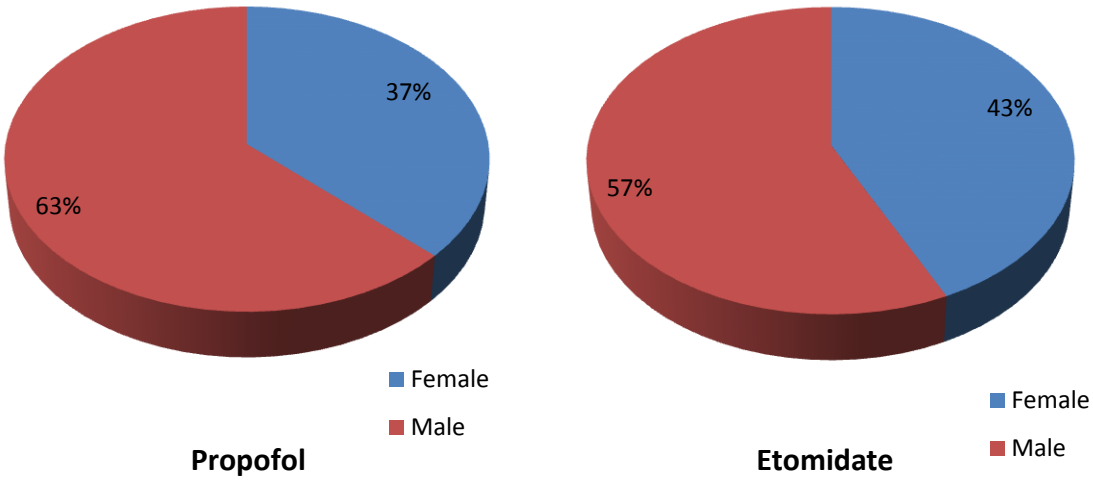

Figure 12: Gender distribution of patients studied

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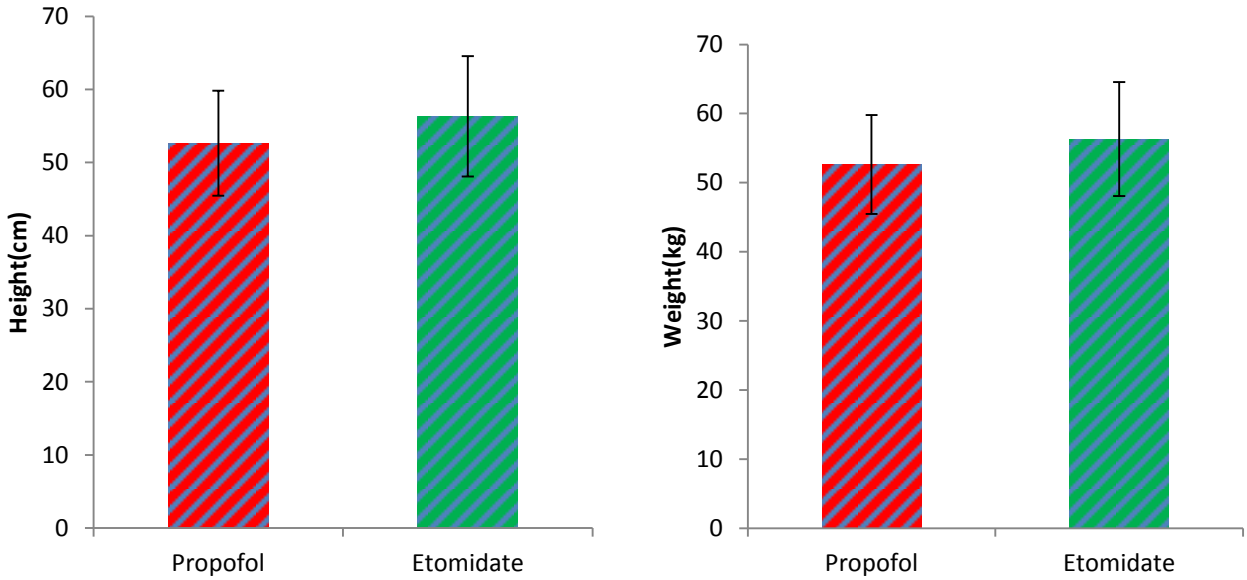

Figure 3: (a) and 3 (b): Height and Weight distribution of patients in both groups

In our study we found that there was statistically significant fall in heart rate in propofol group (Group P) from the baseline starting from 3 minutes of induction upto 10 minutes with p value < 0.05. There was no significant change in heart rate in etomidate (Group E) starting from baseline (fig 4). We also noted that there was a statistically significant decrease in systolic blood pressure, diastolic blood pressure and mean arterial blood pressures in propofol group on induction upto 10 minutes with p value <0.01 which responded to IV fluids infusion compared to increase in systolic blood pressure from 7th minute of induction till 10th minute in etomidate group which was clinically not significant and did not require any treatment (fig 5, 6, 7). There was also no statistically significant change in diastolic and mean arterial blood pressures from baseline in etomidate group indicating a stable hemodynamic profile of etomidate.

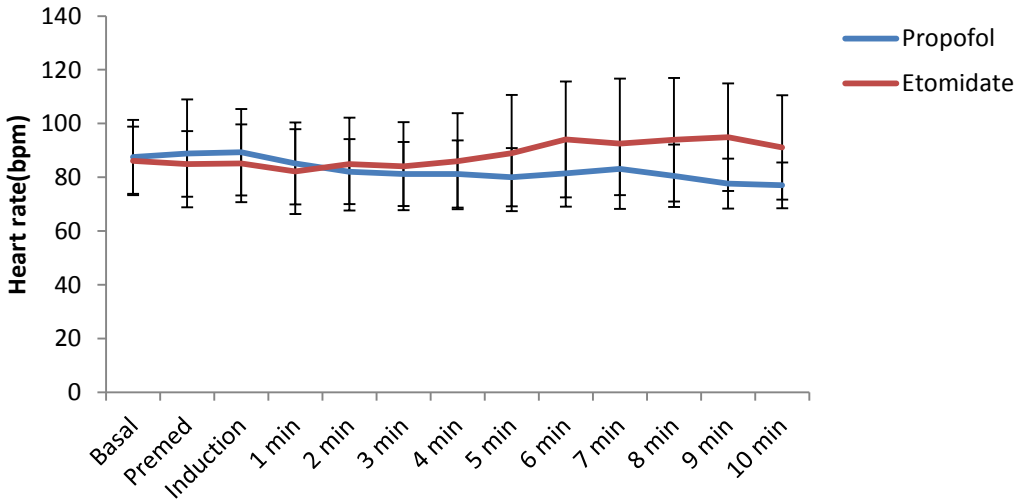

Figure 4: Comparison of Heart rate (bpm) in two groups studied

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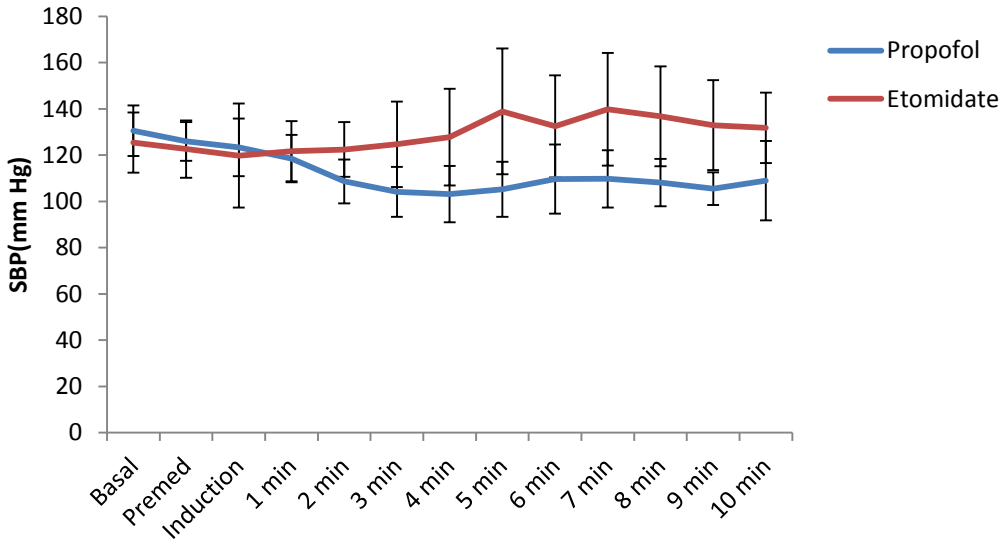

Figure 5: Comparison of systolic blood pressure - SBP (mm Hg) in two groups studied

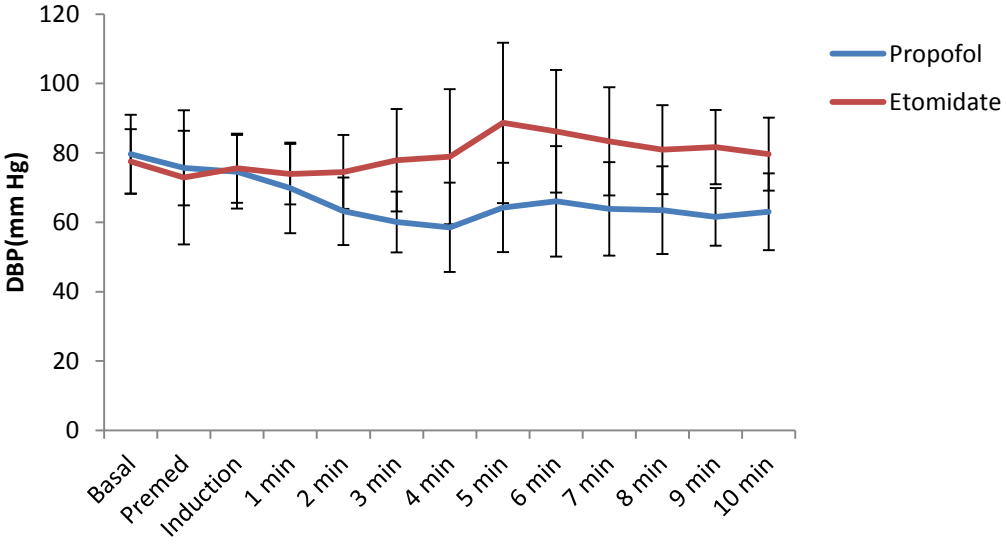

Figure 6: Comparison of diastolic blood pressure -DBP (mm Hg) in two groups studied

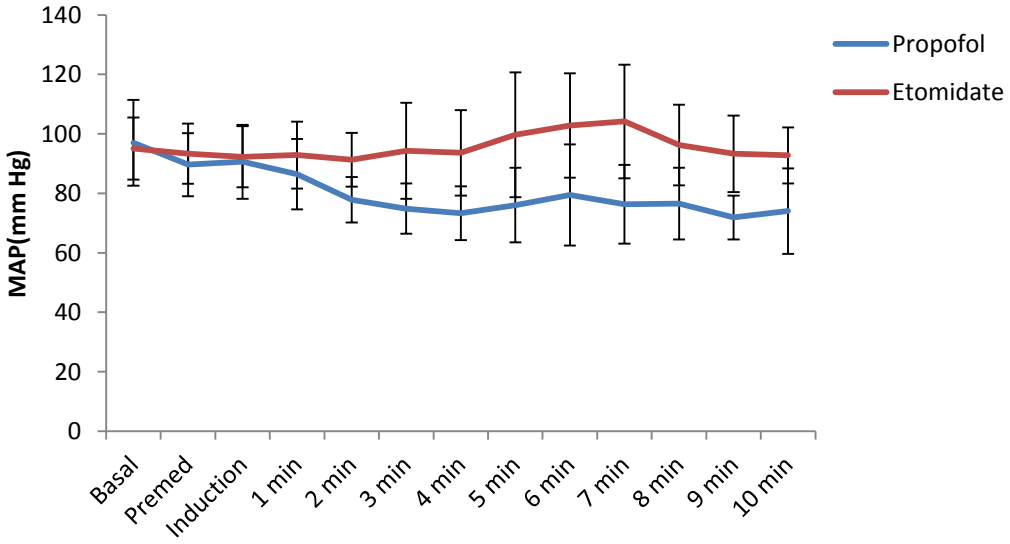

Figure 7: Comparison of mean arterial pressure- MAP (mm Hg) in two groups studied

DOI: 10.23958/ijirms/vol02-i11/02

When pain on injection was compared between the two groups 32 patients (91.5%) in propofol group had pain compared to 9 patients (28.5%) in etomidate group with p value <0.001 indicating that propofol induction caused significant increase in incidence of pain on injection (figure 8).

Myoclonus was observed among 4 patients induced with propofol when compared to 27 patients induced with etomidate which is statistically significant with p value <0.001 and the myoclonus observed with etomidate was transient and did not require any treatment (figure 9).

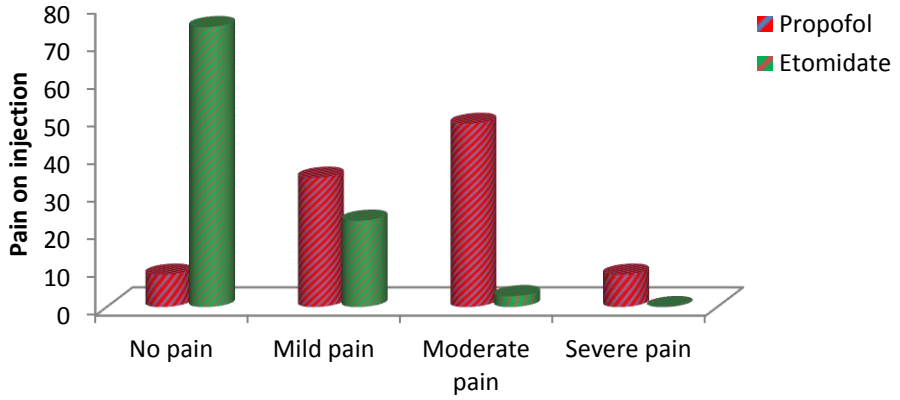

Figure 8: Pain on injection of patients studied

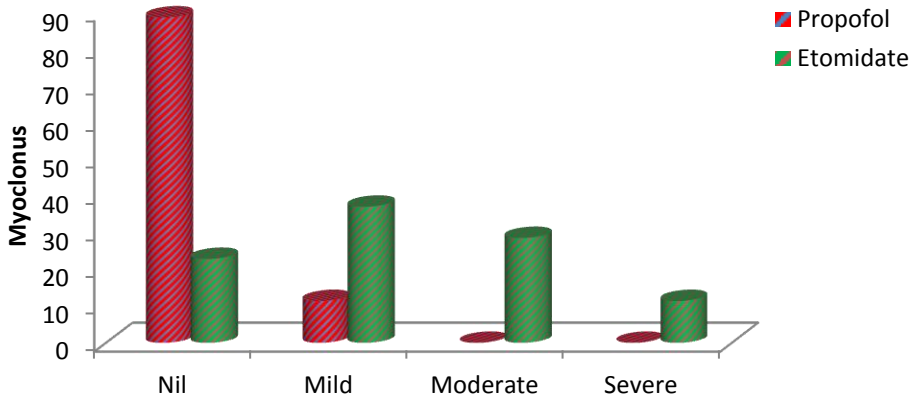

Figure 9: Myoclonus in two groups of patients studied

Incidence of nausea was 22.9% in propofol group compared to 71.4% in etomidate group (figure 10) and likewise incidence of vomiting was 22.8% in propofol group compared to 77.1% in etomidate group both with a p value <0.001 (figure 11) indicating that etomidate resulted in more incidence of nausea and vomiting compared to propofol which was treated with rescue antiemetics

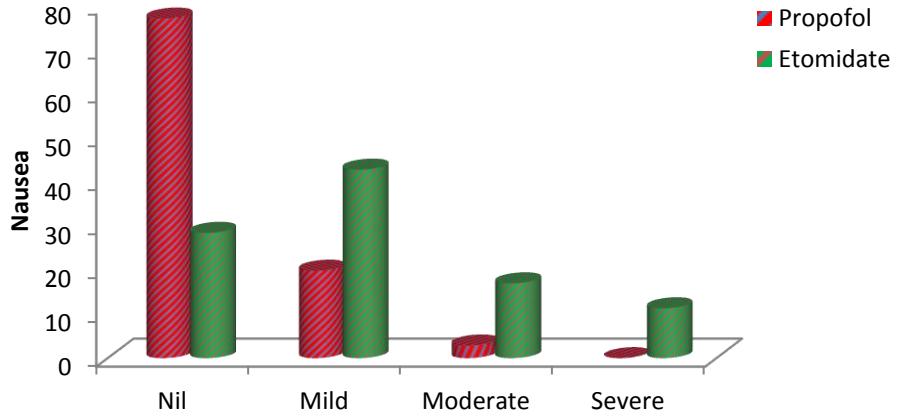

Figure 10: Nausea in two groups of patients studied

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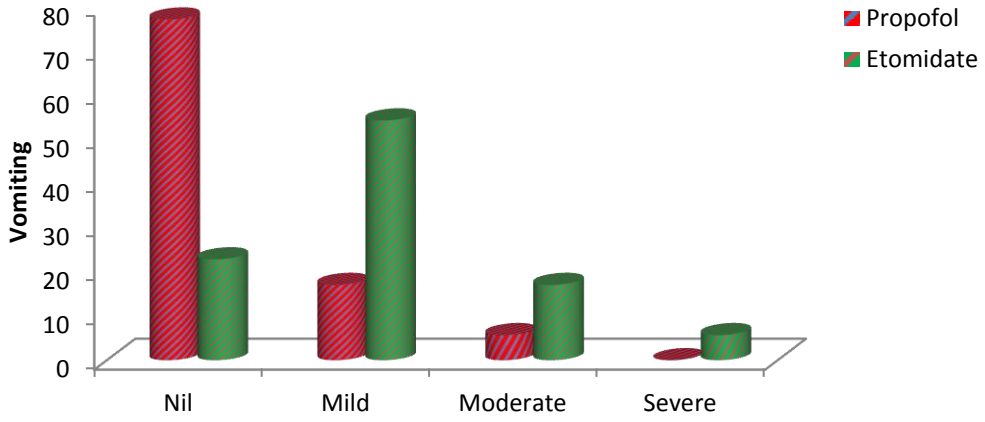

Figure 11: Vomiting in two groups of patients studied

Discussion

Propofol (2,6 di-iso prophylphenol) has got established as an excellent intravenous anaesthetic agent because of its faster onset and rapid recovery , better intubating conditions and minimal post-operative complications. Major disadvantage of induction with propofol is decrease in systemic blood pressure and pain during injection.[5]

Another inducing agent etomidate was introduced into clinical practice in 1972. It provides more cardiac stability with faster onset of action and rapid recovery. Major disadvantage was adrenal suppression and use of this drug was declined. A search through literature revealed that lack of evidence for adrenal suppression after single dose etomidate.[6] This rekindled interest in the drug.

Hence a constant search for ideal induction agent for general anaesthesia continued.

We conducted this study to compare the hemodynamic characteristics and side effects of both drugs during induction in order to choose a better induction agent for general anaesthesia.

Anil.K.Pandey[17] and colleagues concluded in their study that systolic blood pressure and diastolic blood pressure were significantly different between 2 groups at 5 minutes post induction and were statistically significantly lower in propofol group (SBP-p=0.005, DBP- p=0.0011) which is similar to findings in our study where both systolic blood pressure and diastolic blood pressures were lower in propofol group with significant p value of <0.01 indicating that etomidate is associated with more stable hemodynamics on induction of anesthesia.

Similarly **Moller petrun et al** [16] found in their study that the incidence of hypotension was higher in the propofol group than that in the etomidate group (8 vs 3; P=0.08) which was similar to our study with the p value of < 0.01.

Our study findings which indicated no significant change in heart rate and mean arterial blood pressure in etomidate group from baseline were consistent with the study conducted by **Supriya Agarwall et al**[21] in 2014, which showed that patients in etomidate group showed little change in mean arterial pressure (MAP) and heart rate (HR) compared to propofol ($p < 0.05$) from baseline value. Pain on injection was more in propofol group while myoclonus activity was higher in etomidate group.

In another study of **Bendel & Colleagues**[26] in patients with severe aortic stenosis, propofol is twice as likely to cause hypotension during induction than etomidate. MAP decreased in all patients ($P < 0.001$). MAP decreased to a greater extent in patients receiving propofol than in those receiving etomidate ($P = 0.006$) which is similar to finding in our study with p value <0.01.

A study by **Shagun Bhatia shah**[22] on comparision of hemodynamic effects of propofol versus etomidate reported that the percentage fall in SBP was 30% in propofol group compared to 17% in etomidate group and the fall in DBP was much sharper in Group-P (27%) as compared to Group-E (17%) respectively and the fall in MAP is much sharper for Group-P (24.3%) as compared with Group-E (15.87%) with p value <0.001 which is comparable with our study where fall in blood pressure in propofol group was statistically significant with p value <0.01 compared to etomidate group.

Ram Prasad Kaushal[19] and colleagues studied on Effect of etomidate and propofol induction on hemodynamic and endocrine response in patients undergoing coronary artery bypass grafting, mitral valve and aortic valve replacement surgery on cardiopulmonary bypass and showed that there was significant decrease in SBP (Group P 80.63±8.63 Vs Group E 98.5±14.73 P <0.001) DBP (Group P 59.7±7.28 Vs Group E 69.4±8.26 P= 0.007*) and MAP (Group P 67.97±5.79 Vs Group E 80.54±9.39 P<0.001*) after induction which is similar to our study with significant

DOI: 10.23958/ijirms/vol02-i11/02

decrease in SBP (Group P 108.06±10.23 Vs Group E 132.40±22.07 P<0.01) , DBP (Group P 64.26±12.8 Vs Group E 79.66±10.53 P<0.01), MAP (Group P 79.43±17.03 Vs Group E 93.63±14.4 ,P <0.01) indicating stable hemodynamics of etomidate.

M.St.Pierre et al[20] found that for etomidate Vs propofol 14.6% Vs 14.2% male and 26.8% Vs 27.5% female patients were nauseated during first two post-operative hours. The incidence of vomiting was higher in women receiving etomidate (20.8% Vs 10%). We also found that the incidence of vomiting is higher in etomidate group with a p value of <0.001.

A similar study conducted by **Fatma Saricoaglu et al**[7] reported incidence of pain on injection was 83.8% in propofol group and 63.2% in etomidate group but higher incidence of myoclonus in etomidate lipuro group(93.4%) than in propofol group(0%) p <0.000 and mean and systolic BP were significantly lower in propofol group from baseline than etomidate group as compared to our study where incidence of pain on injection with etomidate- lipuro compared with propofol was (25.8% Vs 91.5%) p value <0.001 and incidence of myoclonus was (77.1% Vs 11.4%) p value <0.001. Hence the results were similar to this study.

James.R.Miner et al[23] in their study concluded that 21 patients developed myoclonus in etomidate group as compared to only 2 patients in propofol group while in our study the incidence of myoclonus is 27 in etomidate group versus 4 in propofol group and hence their results were similar to our study.

In agreement with the present study which showed incidence of pain on injection with etomidate- lipuro compared with propofol was (25.8% Vs 91.5%) p value <0.001 and incidence of myoclonus was (77.1% Vs 11.4%) p value <0.001, **Y Nyman & co-workers**[18] also showed that etomidate-lipuro significantly reduced the incidence of pain on injection compared with propofol-lidocaine (5% Vs 47.5%) p <0.001 and also higher incidence of myoclonic activity was seen in etomidate lipuro group(85%) compared with propofol-lidocaine group (15%) p<0.001.

Pain on injection was observed more in the propofol group (91.5%) as compared to etomidate group (25.8%) in our study. These results were consistent with the study done by **Sowinski**[24]**et al.,** where pain on injection occurred in 4.5% patients in the etomidate group and in 27% patients in the propofol group, **Ayuso et al**[25] also observed that the incidence of pain on injection was 27% with the use of propofol-lipuro.

In our study, we observed that propofol caused significant hypotension at induction in comparison to etomidate. Hypotension occurs with propofol mainly due to reduction of sympathetic activity causing vasodilation or its direct effect on vascular smooth muscles. Sudden hypotension has deleterious effects on maintaining the circulation to vital organs in patients of coronary artery disease, valvular stenosis, uncontrolled hypertension and shock. In contrast hemodynamic stability observed with etomidate may be due to its unique lack of effect on the sympathetic nervous system and on baroreceptor functions.

Pain on injection was observed more with propofol than etomidate which can be minimized by using larger veins with rapid carrier infusion rates, wide bore IV cannula, by injecting lidocaine before or with propofol emulsion, or by injecting a synthetic opoid before propofol, formulation in medium chain rather than long chain triglycerides also reduce pain.[5]

The negative characteristics noted with etomidate was high incidence of myoclonic jerks and post-operative nausea and vomiting. Prior administration of opoid fentanyl 1-2 mcg/kg, etomidate 0.03-0.075mg/kg IV, dexmedetomidine 0.5-1 microgm/kg , magnesium sulphate 60 mg (2.48 mmol) midazolam 0.015mg/kg 90 seconds before induction dose can reduce the incidence of myoclonus.[12,13,14,15] Nausea and vomiting can be reduced by pre-treatment with anti-emetics. Temporary adrenocortical suppression, as measured by a reduced response to ACTH stimulation, was documented for 6 hours postoperatively and returned to normal by 20 hours.[5]

However the universal lack of demonstrable negative effect from temporary adrenocortical suppression associated with induction doses of etomidate in any study, as well as the finding that mean cortisol levels usually remain in the low normal range after etomidate induction, suggests that the issue of temporary adrenocortical suppression following induction dose may not be clinically significant. Limitation of our study was serum cortisol level could not be estimated.

Conclusion

In conclusion, etomidate is better for its hemodynamic stability over propofol along with less incidence of pain on injection. Only drawback is incidence of myoclonus and post-operative nausea and vomiting which can be prevented by pretreatment with opiods and anti-emetics respectively. We therefore conclude that etomidate is a better option in patients particularly prone to hemodynamic fluctuation at induction like in coronary artery disease, valvular heart disease, hypertensives, patients with shock and critically ill patients.

References

[1] A.K.Bhargava, R.Setlur, and D.Sreevastava, Correlation of Bispectral index and Guedel's

DOI: 10.23958/ijirms/vol02-i11/02

Stages of Ether Anaethesia; Anesth Analg 2004; 98:132-4

[2] Leonara T, Fahy.,Vanmourik, G.A.Utting, J.E. A comparision of the induction characteristics of thiopentone and propofol.Anaethesia, 1985; 40:939-944

[3] Martin, I.G., Edward, C.,Clarie Herrington. A controlled investigation with propofol, thiopentone and methohexitone. Can j Anaesth, 1987; 34(5):478-83

[4] Mc Keating, k,et al. The effects of thiopentone and propofol on upper airway integrity. Anaesthesia, 1998; 43;638-40

[5] Reves, J.G.,Peter, S., Glass, A., David, A : Intravenous anaesthetics: In: Miller's Anaesthesia, seventh edition, Philadelphia: Churchill Livingstone, 2010: p719-758

[6] Stuart.A.Forman. Clinical And Molecular Pharmacolgy Of Etomidate. Anesthesiology. 2011 March; 114(3): 695–707.

[7] Fatma Saricoaglu, Sennur Uzun, Oguzhan Arun, Funda Arun, Ulku Aypar. A clinical comparision of etomidate-lipuro, propofol and admixture at induction. Saudi journal of anaesthesia, 2011; 5:62-65

[8] R.Bloomfield, D.W.Noble.British Journal of Anaesthesia. August 2006.

[9] Prabhat Kumar Sinha, Thomas Koshy. Monitoring Devices for measuring the depth of anaesthesia- an overview .Indian journal of Anaesthesia 2007; 51 (5): 365-381.

[10] V K Grover, Neerja Bharti.V. Measuring depth of anaesthesia-An overview among the currently available montoring systems. The Indian Anaesthetis't Forum; October 2008(1)

[11] Robert K. Stoelting, Simon C.Hiller. Pharmacology and Physiology in Anaesthetic Practice. Non barbiturate intravenous anaesthetic drugs. Fourth edition. p. 155-163.

[12] Paul.F.White, Matthew. R. IV Anaesthetics. Clinical anaesthesia, seventh edition, 2013: p 489-91

[13] H.F. Luan, Z.B. Zhao, J.Y. Feng, J.Z. Cui, X.B. Zhang, P. Zhu and Y.H. Zhang. Prevention of etomidate-inducedmyoclonus during anesthetic induction by pretreatment with dexmedetomidine. Brazilian Journal of Medical and Biological Research (2015) 48(2): 186-190

[14] Aygun Guler, Tulin Satilmis, Seda B. Akinci, Bilge Celebioglu, Meral Kanbak. Magnesium Sulfate Pretreatment Reduces Myoclonus After Etomidate. Anesth Analg 2005; 101:705-9

[15] Lars Huter, Torsten Schreiber, Michael Gugel, Konrad Schwarzkopf. Low-Dose Intravenous Midazolam Reduces Etomidate-Induced Myoclonus: A Prospective, Randomized Study in Patients Undergoing Elective Cardioversion. Anesth Analg 2007; 105:1298 –302.

[16] Moller.A. Petrun, Kamenik..M. Bispectral index-guided induction of general anaesthesia in patients undergoing major abdominal surgery using propofol or etomidate, a double- blind randomized clinical trial, 2012; 1-9.

[17] Anil.K.Pandey, Neeti Makhija, Sandeep Chauhan, Sambhunath Das, Usha Kiran, Akshya Kumar Bisoi et al. The effects of etomidate and propofol induction on hemodynamic and endocrine response in patients undergoing coronary artery bypass graft surgery. World journal of cardiovascular surgery, 2012; 2:48-53.

[18] Nyman.Y, Von.K. Hofsten, Palm.C , Eksberg.S , .Lonnqvist.P.A 7. Etomidate - lipuro is associated with considerably less injection pain in children compared with propofol with added lignocaine. British journal of anaesthesia, 2006; 97:536-39.

[19] Ram Prasad Kaushal, Ajay Vatal, Radhika Pathak. Effect of etomidate and propofol induction on hemodynamic and endocrine response in patients undergoing coronary artery bypass grafting/mitral valve and aortic valve replacement surgery on cardiopulmonary bypass. Annals of Cardiac Anaesthesia; Apr-Jun-2015: Vol 18, Issue 2, 172-78.

[20] M. St Pierre, M. Dunkel, A. Rutherford and W. Hering. Does etomidate increase postoperative nausea? A double-blind controlled comparison of etomidate in lipid emulsion with propofol for balanced anaesthesia. European Journal of Anaesthesiology, Volume 10: October 2000, pg 634-641.

[21] Supriya Aggarwal, Vipin Kumar Goyal, Shashi Kala Chaturvedi,Vijay Mathur, Birbal Baj, Alok Kumar. A comparative study between propofol and etomidatein patients under general anesthesia. Rev Bras Anesthesiology. 2015.

[22] Shagun Bhatia Shah, Itee Chowdhury, Ajay Kumar Bhargava, Bhawnish Sabbharwal. Comparison of hemodynamic effects of intravenous etomidate versus propofol during induction and intubation using entropy guided hypnosis levels. Journal of Anaesthesiology Clinical Pharmacology | April-June 2015 | Vol 31 | Issue 2, pg 180-85.

[23] James R. Miner, Mark Danahy, Abby Moch, BS Michelle Biros. Randomized Clinical Trial of Etomidate Versus Propofol for Procedural Sedation in the Emergency Department. Annals of Emergency Medicine Volume 49, No 1: January2007.

[24] Sowinski P, Symonides M, Jarosz J, Lukaszenska A, Pawlowiscz M, Lessapnoea with etomidate

DOI: 10.23958/ijirms/vol02-i11/02

lipuro than with propofol (with a titrated dose regimen) in outpatient anaesthesia. Eur J Anaesthesiol 2000; 17:14.

[25] Ayuso MA, Luis M, Sala X, Fernandez J, Gomar C. Incidence of pain upon injection of a new formulation of propofol in a fat emulsion of medium and long-chain triglycerides. European journal of anaesthesia 2004; 51:531-6.

[26] Bendel S, Ruokonen E, Polonen P, Uusaro.A. Propofol causes more hypotension than etomidate in patients with severe aortic stenosis: a double-blind, randomized study comparing propofol and etomidate. Anesth Analg.2005; 101(3):622-8.

DOI: 10.23958/ijirms/vol02-i11/02