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A COMPARATIVE STUDY BETWEEN PROPOFOL AND ETOMIDATE WITH RESPECT TO PAIN ON INJECTION AS INDUCING AGENT IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

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Abstract-

Aim and Objective: This study was undertaken in patients undergoing laparoscopic cholecystectomy with aim to compare pain during injection among etomidate and propofol during induction.

Materials and Methods: One hundrade ASA I and II patients of age between 18-60 years scheduled for elective laproscopic cholecystectomy were randomly divided into two equal group(n=50 in each). All the patients were premedicated with inj fentanyl 2 µg /kg, & inj glycopyrrolate 0.2 mg . Group P (n=50) received propofol 2 mg/kg, Group E (n=50) received etomidate 0.3 mg/kg IV as inducing agent. Pain on injection was measured using 4 point graded scales.

Results- Result shows demographic profile and anthropometric profile of both the groups were comparable. Propofol shows Grade-1 pain 20%, Grade-2 pain 10%, Grade-3 pain -4% .That is total 34% pain with propofol where as etomidate shows only 2%.

Conclusion- Injection propofol causes more pain on injection as inducing agent, than injection etomidate in laparoscopic cholecystectomy.

INTRODUCTION- Induction of anaesthesia is crucial part of anaesthesia care. Sudden hypotension, arrhythmia and cardiovascular collapse are dreaded complications following administration ofInducing agent in haemodynamically unstable patients. Therefore it is preferable to use a safe agent with minimal or no adverse effects. Different inducing agents were tried and compared with each other but every agent had their own effect and side effects.

Propofol is a substituted isopropylphenol (2,5-diisopropylphenol) that is administered intravenously as 1% solution in an aqueous solution of 10% soyabean oil,2.25% glycerol, and 1.2% purified egg phosphatide.Administration of propofol,1.5 to 2.5% mg/kg IV as a rapid IV injection(<15sec),produces unconsciousness within about 30 seconds. It is the most popular inducing agent with its favorable characteristics of rapid and smooth induction and recovery, decrease incidence of nausea and vomiting, etc.

Etomidate is a carboxylated imidazole-containing compound that is chemically unrelated to other IV inducing agents. The imidazole nucleus renders etomidate water soluble at an acidic pH and lipid soluble at physiological pH .It provides haemodynamic stability, minimal respiratory depression and cerebral protective .Its lack of effect on sympathetic nervous system, baroreceptor reflex regulatory system and its effect of increased coronary perfusion even on patients with moderate cardiac dysfunction makes it an induction agent of choice in cardiac disease patients.

Present prospective randomized study was designed to compare occurrence of pain on injection of propofol and etomidate in general anesthesia among laproscopic cholecystectomy in a tertiary hospital.

AIMS AND OBJECTIVES- To evaluate pain on injection among propofol and etomidate as inducing agents in laparoscopic cholecystectomy.

MATERIALS AND METHODS- This study is a prospective double blinded randomized trial. This study was conducted at the Department of Anaesthesiology, Nil Ratan Sircar Medical College and Hospital,Kolkata, West Bengal, India.

The study population was formed by adult patients who attended Pre- Anaesthetic Check up(PAC) clinic for surgeries amenable under general anaesthesia at NRSMCH. ASA grade I and II, age 18 to 60 years, both the sex, scheduled for elective laparoscopic cholecystectomy were included in this study. Patient's refusal ,ASA III/IV, pregnant patients, hepatic failure, hepatitis, jaundice, acute cholecystitis, patients with liver, renal and cardiovascular disorders , epilepsy,neurodeficits,COPD,asthma, recent pneumonia or upper respiratory tract infection, patients on antipsy chotics, coagulopathy, history of any drug allergy, anticipated difficult intubation ,hypertension, hypotension, ischemic heart diseases, coronary artery diseases,abnormal echocardiogram,abnormal ECG,presence of primary & secondary steroid deficiency or on

steroid medication were excluded from present study .Written informed consent was obtained from all patients included in the study after proper and thorough explanation of the study procedure and outcome, in their vernacular language.

One hundred sixteen(116) patients were included in this study, among them 6 were excluded due to conversion of laparoscopic procedure to open surgery,3 patients refuse to give consent,5 patients on operation table systolic blood pressure shoot to 140mm of Hg and lastly one patient excluded from my study due to intraoperative gut injury.

One hundred ASA I and II patients of age group 18-60 years scheduled for elective laparoscopic cholecystectomy were randomly divided into 2 equal group, Groups-P(n=50) and Group-E(n=50), in a double blind manner. A detailed history, complete physical examination and routine investigations were done for all patients. On arrival of patient at operation theater, patients were attached with standard anaesthesia monitoring including Electrocardiogram(ECG),Non-invasive blood pressure(NIBP),Pulse-oximeter and baseline vital parameters like heart rate(HR) systolic blood pressure(SBP),diastolic blood pressure(DBP), mean blood pressure(MAP) were recorded. An intravenous linewas (18 G) secured in anti-cubital vein and Ringer's lactate @10ml/kg/hr was started. The patients were pre-oxygenated for 5-7 minutes with 100% oxygen. Then patients were premedicated with inj fentanyl 2microgram/kg IV, and inj glycopyrrolate 0.2mg IV. Group P (n=50) received propofol 2 mg/kg IV as inducing agent. Group E (n=50) received etomidate 0.3 mg/kg IV as inducing agent.

Vital parameters were recorded before induction, at and following induction for comparison, followed by inj vecuronium bromide 0.1mg /kg to provide neuromuscular blockade. After 4 minutes ventilation with 100% 02 laryngoscopy was performed and intubation was done with cuffed endotracheal tube of appropriate size. Anaesthesia was maintained with 33:66 O2 and N2O plus sevoflurane 1%. With intermittent bolus doses of vecuronium 0.02mg/kg as per need with controlled ventilation. EtC02 maintained between 30- 35. Haemodynamic and respiratory parameters were recorded at regular intervals of time 1min,3min,5min,10min following induction,15 min,30 min 45 min,60 min,90 min subsequently and after extubation. At the end of surgical procedure residual neuro muscular blockade was antagonized with Inj neostigmine 0.5mg/kg IV and Inj glycopyrrolate 0.4mg IV ,extubation done when adequate muscle power, regular spontaneous respiration and cough reflex was present. Extubation was carried out as a routine procedure.

Patient was shifted to recovery room (PACU). In PACU side effects were assessed like nausea, vomiting,hypotension,bradycardia,respiratory depression(rate less than 8 per minute),arrhythmias, myoclonus.During induction pain at the site of injection were assessed.Inj ondansetron intravenous given when nausea vomiting occurs. Infusion paracetamol 1gm over 10 min(s) was given 10 min(s) before induction and before taking base line data. During port site closure inj diclofenac sodium 75mg deep intramuscular given in all the patients.

All intubation done by same resident anaesthesiologist.Resident, who administered study drug was also blined.All data were collected in a preprinted computer generated data sheet.

Pain on injection was measured using 4 graded scale; 0 --- no pain, 1 --- verbal complaint of pain, 2 --- withdrawal of arm, 3 ---both verbal complaint and withdrawal of arm.

Statistical Analysis-The results of the present study were recorded and tabulated in Microsoft excel work sheet and then put for statistical analysis using SPSS version 20 IBM for windows. All continuousdata were presented in the tables as mean ± SD. Discrete categorical data were presented as absolute values or relative number of patients, as appropriate. The level of significance set as P< 0.05.The categorical variables were compared using Chi square test and continuous variables using unpaired student's t-test.

Results and analysis -

1. Demographic profile

Parameters	Group P (n=50)	Group E (n=50)	P value
Age (years)	34.47± 6.72	33.90± 6.28	0.178
BMI (kg/m2)	21.99± 1.95	22.77± 2.73	0.704
Gender(M/F)*	24/26	25/25	0.241
Height(feet/inches)	5.41±0.45	5.42±0.38	0.742
ASA(I/II)*	23/27	29/21	0.48

Continuous data is represented as mean ± standard deviation in case of continuous data except those marked with which are categorical data and expressed as number of patients.Continuos data were analysed using Unpaired Student's t-test. Categorical data were analysed using Pearson's Chi-square test. Group P, patients receiving propofol and group E, patients receiving etomidate as inducing agent.

Table shows that the demographic data were comparable between the groups.

2. Duration of surgery

Parameters	Group P (n=50)	Group E (n=50)	P value
Duration of surgery (minutes)	98.71±24.167	102.09 ± 34.515	0.314

Table : Shows that the timing of surgery was comparable between the groups

Table 3:Postoperative complication(side effects)

Parameters	Group-P	Group-E
PONV (No. of Patients)	2 (4%)	9 (18%)
HYPOTENSION	0%	0%
BRADYCARDIA	nil	nil
ARRHYTHMIAS	nil	nil

Table 4: Incidence and grading of pain on injection.

Group	Grade-0	Grade-1	Grade-2	Grade-3
Group-P	33(66%)	10(20%)	5(10%)	2(4%)
Group-E	49(98%)	1(2%)	0	0

Group-P, patients receiving propofol.Group-E, patients receiving etomidate Grade 0- no pain, Grade 1-mild pain, Grade 2-moderate pain, Grade 3-severe pain Table 4- shows higher pain on injection in propofol group.

Figure-1 Severity of pain in two group's

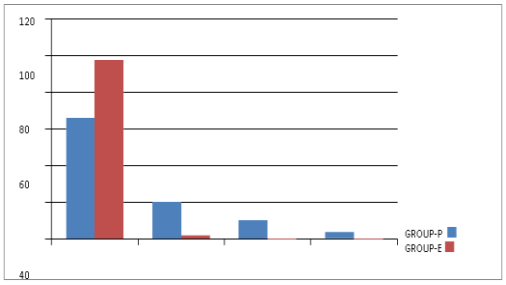

Fig 1: Severity of pain in two group's .X-axis denotes grades of pain.Y-axis denote number of patients.

Figure-2: Comparison of serum cortisol values between baseline and post extubation. Serum cortisol level significantly reduced in etomidate group in post extubation

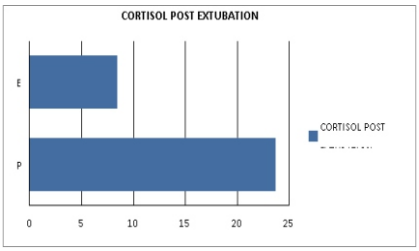

Fig-2: Post-extubation serum cortisol level in both the groups. Group-E shows significantly low value.

DISCUSSION-

Out of 116 patients One hundrade(100) ASA I and II patients of age group 18-60 years scheduled for elective laproscopic cholecystectomy were randomly divided into two equal group, Groups-P(n=50) and Group- E(n=50), in a double blind manner. An IV line was (18 G) secured in anti-cubital vein and Ringer's lactate @10ml/kg/hr was started, multi-para monitor was attached to all the patients and base line SBP,DBP,MAP,HR ,SP02,ECG were recorded. The patients were pre- oxygenated with 100% oxygen. Then patients were premedicated with Inj Fentanyl 2mcg /kg IV, and Inj Glycopyrrolate 0.2 mg IV. Group P(n=50) received Propofol 2 mg/kg IV as inducing agent. Group E(n=50) received Etomidate 0.3 mg/kg IV as inducing agent .Pain on using inducing agent assessed and documented before induction.

Pain on injection was measured using 4 graded scale; 0 --- no pain, 1 - verbal complaint of pain, 2 - withdrawal of arm, 3 - both verbal complaint and withdrawal of arm.

All intubation done by same resident anaesthesiologist.Resident who administered study drug was also blind.Both the study drug were white in colour and we used only tag of paper over syringe.All data were collected in a preprinted computer generated data sheet. Before and after induction period, hemodynamic parameters, hemodynamic response to induction, laryngoscopy, intubation and extubation, necessity of additional anaesthetic agent and possible side effects were also compared among the groups.

Result shows demographic profile and anthropometric profile like age, sex, BMI.height, ASA physical status, height of both the groups were comparable .These prameters appered to be statistically insignificance. Duration of operation was also comparable in both the groups.Duration of surgery in Grp-P 98.71±24.167 min(s) where as in Grp-E it was 102.09±34.515 min(s) .Data were statistically insignificant.

In our study we found Etomidate safer than propofol in respect to pain on injection. Propofol shows Grade-1.pain 20%, Grade-2 pain 10%, Grade-3 pain -4% .That is total 34% pain with propofol where as etomidate shows only 2%. We used lipuro-etomidate that may be the cause lower pain incidence. We administered study drug in anticubital vein.We give both the drug slowly .We used injection fentanyl 2mcg/kg as premedication .All these technique reduces pain of propofol.We used MCT/LCT propofol.

Supriya Aggarwal 2 evaluated 100 ASA I and II patients of age group 18–60 years scheduled for elective surgical procedure under general anaesthesia were randomly divided into two groups of 50 each receiving propofol (2 μ/kg) and etomidate (0.3 mg/kg) as an induction agent.He found 'nopain' with etomidate -96% vs propofol 50%. Propofol group shows Grade-I & Grade –II pain 32% and 18% respectively. Whereas etomidate group shows Grade-I & Grade-II pain only 4% and 0% respectively.We found Grade-I pain-20%, Grade –II pain-10% in propofol group, it was less than the Supriya et al but higher than etomidate group, this is may be due to we use fentanyl 2mcg/kg before induction and we use anti-cubital vein, also we give the drug slowly.All this may be cause of lower pain incidence.

Y. Nyman et al 3 in his study among 110 paediatric patients, aged 2–16 years, scheduled for outpatient surgery. A significantly lower incidence of pain on injection was found in the Etomidate-®Lipuro group as compared with the propofol–lidocaine group (5.0% vs 47.5%, P<0.001). They also used lipiro-etomidate but we did not used lignocaine with propofol. Fatma Saricaoglu et al4 were assigned at random to three groups in which induction was performed with either etomidate- lipuro, propofol or etomidate-lipuro–propofol admixture.

Patients were asked for pain at the injection site and the incidence were (83.8%) in group P and in (63.2%) group E. We also found more injection pain with propofol.

Arvind Khare et al 5 in his study 50 patients of ASA I and II of age group 18-60 years scheduled for elective surgeries under general anaesthesia were randomly assigned in two groups (n=25) receiving etomidate (0.3 mg/kg) in group E and propofol (2.5 mg/kg) in group P as an induction agent. VAS score was recorded for pain on injection. Pain on injection was more in propofol group (P=0.021), While incidence of myoclonus activity was higher in etomidate group (P=0.0027). Though we used different pain assessment scale but result are similar. Pain during injection of anesthetic agent is a bad experience for patient while it is quite embarrassing situation for an anaesthesiologist. Etomidate showed a favorable outcome and it was very well supported by Saricaoglu et al.4 and Wu et al.6SUMMARY- The patients attending PAC clinic at NRSMC&H scheduled to undergo laparoscopic cholecystectomy were assessed for eligibility for this study. After obtaining written informed consent patients were included in the study.

One hundred ASA I and II patients of age group 18-60 years scheduled for elective laparoscopic cholecystectomy were randomly divided into 2 equal group, Groups-P(n=50) and Group-E(n=50), in a double blind manner. An IV line was (18 G) secured in anti-cubital vein and Ringer's lactate @10ml/kg/hr was started, multi-para monitor attached to all the patients and base line SBP,DBP,MAP,HR ,SP02,ECG were recorded. The patients were pre-oxygenated with 100% oxygen. Then patients were premedicated with Inj Fentanyl 2microgram/kg IV, and Inj Glycopyrrolate 0.2mg IV. Group P(n=50) received Propofol 2 mg/kg IV as inducing agent. Group E(n=50) were received Etomidate 0.3 mg/kg IV as inducing agent .Pain on using inducing agent and myoclonus were assessed and documented along with induction. Pain on injection was measured using 4 graded scales.

The results of the present study were decoded and tabulated in Microsoft excel work sheet and then put for statistical analysis using SPSS version 20 IBM for windows. All continuous data were presented in the tables as mean ± SD. The level of significance was set as P< 0.05.

Results showed that the demographic profile and anthropometric profile like age, sex, BMI.height, ASA physical status, height of both the group were comparable.

Duration of operation was also comparable in both the groups.Duration of surgery in Grp- P 98.71±24.167 min(s) where as in Grp-E it was 102.09±34.515 min(s) .Data were statistically insignificant.

In terms of serum cortisol level post-induction we found that in etomidate base line cortisol value

16.72 ± 8.31 mcg/dL and Post-extubation value 8.44 ± 5.00 mcg/dL. In propofol group base line value 13.39 ± 8.39 mcg/dL and post extubation value 23.721± 11.62 mcg/dL.Therefore, etomidateshows significantly reduce cortisol value after single dose injection from base line value .Whereas propofol showed significantly increased cortisol value from base line value.

Regarding pain on injection, we found that etomidate is safer than

propofol. Propofol showed Grade-1.pain 20%, Grade-2 pain 10%, Grade-3 pain -4% .That is total 34% pain with propofol where as etomidate shows only 2%.

CONCLUSION: Injection propofol causes significantly higher incidence of pain on injection as inducing agent, than injection etomidate in laparoscopic cholecystectomy.

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