A COMPARISION OF PROPOFOL INFUSION vs INTERMITTENT BOLUS DOSES OF PROPOFOL IN COLONOSCOPIC PROCEDURES

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1. INTRODUCTION

Gastrointestinal Interventional procedures such as endoscopic retrograde cholangio pancreatography(ERCP) or esophagogastroduodenoscopy (EGD) are complex procedures which make the patient uncomfortable and hence requiring sedation.[1] Performing gastrointestinal (GI) endoscopic procedures under sedation has gained popularity and there have been many efforts to investigate the ideal drug regimen and appropriate depth of sedation for the procedures .[1] Propofol, the most popular agent used for these procedures has a narrow therapeutic window-ranging from mild sedation to deep general anaesthesia rapidly.[2,3]

Propofol administered as a bolus followed by an infusion is the commonest technique. Propofol is an intravenously administered, hypnotic drug initially developed for the induction and maintenance of general anaesthesia. Benefits of propofol sedation involve rapid onset of action, better patient comfort and faster clearance, as well as prompt recovery and discharge. These features of propofol are advantageous for complex gastrointestinal interventional procedures.[4]

Propofol (2,6 di iso propyl phenol) is a short acting intravenous drug. Time for onset of action is 30 – 60 seconds and its duration of action is 4-8 minutes.[4,5] Numerous randomized controlled trials compared propofol with other sedative agents in GI procedures which showed propofol is effective in inducing adequate

sedation with high procedural success rates, rapid recovery and low complications.[6,7,8] A metanalysis showing the comparison of propofol infusion and intermittent bolus doses in procedural sedation showed that continuous infusion group require higher doses than intermittent bolus group and recovery time was same in both groups.[8] There were few studies comparing infusion and intermittent doses of propofol in ERCP and studies show no significant difference between both groups.[9] In our study we wanted to compare propofol infusion vs intermittent doses of propofol in colonoscopy procedure.

Aims and objectives:
To compare propofol infusion and intermittent bolus doses in colonoscopy procedure.
Primary objectives:
1) To compare depth of sedation
2) To compare dosage of propofol required

Secondary objectives:
1) To compare recovery time
2) To compare adverse effects

2. MATERIALS AND METHODS

Study Design: Prospective randomized controlled study
Study Setting: All patients between 18 – 60 years of age undergoing colonoscopy
Sample Size Calculation: a convenience sample of 40 per group was taken.

Inclusion criteria:
- Patients undergoing colonoscopy.
- Adults between 18-60 years of age.
- Patients with ASA grade 1 and 2.
- Patients who are willing to give consent.

Exclusion Criteria:
- Paediatrics and elderly patients.
- Patients with ASA grade 3and 4
- Patients who denied giving consent
- Patients who are allergic to eggs, soyabean oil
- Pregnant and lactating women

3. METHODOLOGY

After obtaining ethical committee clearance and informed consent from all patients, 80 patients of AMERICAN SOCIETY OF ANAESTHESIOLOGISTS [ASA] 1 and 2 physical status were randomly divided into two groups.

GROUP I (n - 40) – received propofol infusion
GROUP B (n - 40) – received intermittent bolus doses of propofol

Minimum monitoring standards including electrocardiography, heart rate, peripheral oxygen saturation, non-invasive blood pressure, temperature monitoring was done for every 5, 10 ,15 ,30 ,45 min and 1 hour. Base line vitals were recorded for all patients before sedation.

For all patients before undergoing the procedure, an intravenous line was secured with continuously running normal saline. All patients received oxygen through nasal prongs throughout the procedure.
The procedure time was defined as first insertion of endoscope until the removal of endoscope. Recovery time was defined as time from endoscope removal to when patient achieved a sedation score of 5 as per OASS score.

Group I: Patients in group A were preoxygenated for 3 minutes. Premedicated with injection GLYCOPYRROLATE 0.01 mg/kg, injection MIDAZOLAM 0.05 mg/kg, injection FENTANYL 1 micro gm /kg. Then received a bolus dose of propofol 0.5 mg/kg followed by propofol infusion at the rate of 3mg/kg/hr.

Group B: Patients in group B were preoxygenated for 3 minutes. Premedicated with injection GLYCOPYRROLATE 0.01 mg/kg, injection MIDAZOLAM 0.05 mg/kg, injection FENTANYL 1 micro gm/kg. Then received a bolus dose of propofol 0.5 mg/kg followed by 20 – 30 mg of propofol bolus intermittently on demand with a gap of 30 seconds in between the doses.

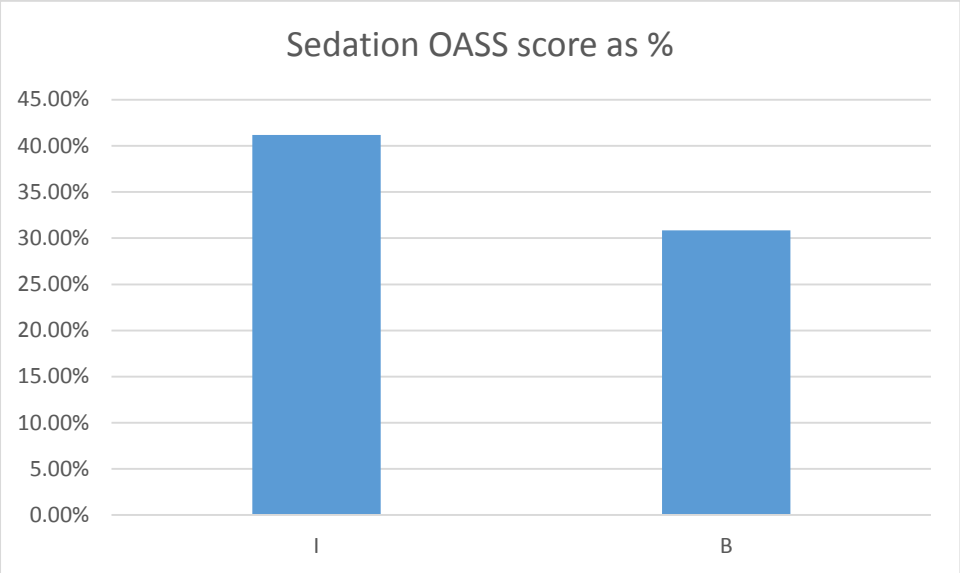
Pulse rate, blood pressure, respiratory rate, oxygen saturation and depth of sedation were continuously monitored and recorded for every 5 , 10 , 15 , 30 , 45 , 60 minutes. Depth of sedation was monitored using OBSERVERS ASSESSMENT OF SEDATION SCORE (OASS SCORE).[14]

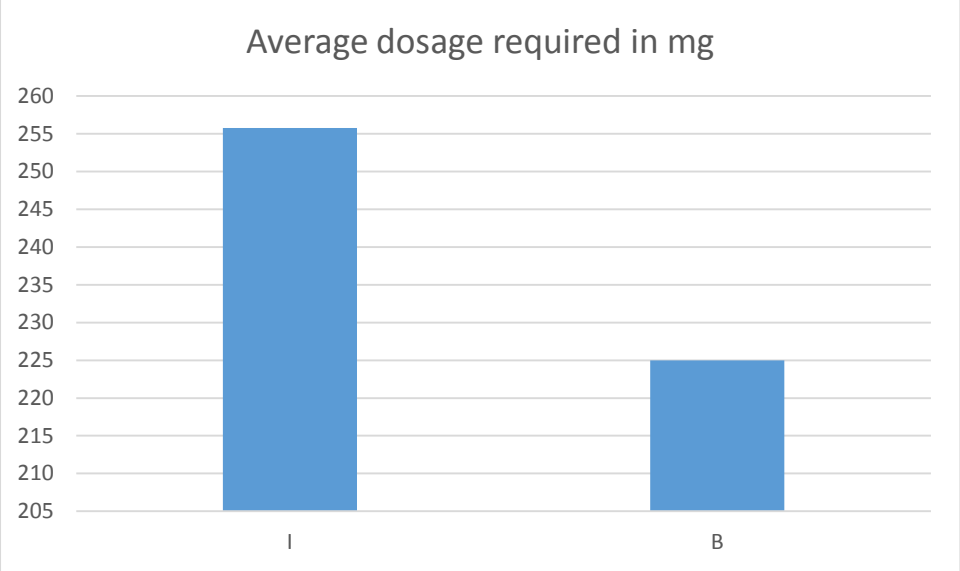
Score 5: Responds readily to name spoken in normal tone
Score 4: lethargic response if name spoken in normal tone
Score 3: Responds when name is called loudly
Score 2: Responds to mild prodding
Score 1: Responds to painful squeeze of trapezius
Score 0: No response to painful squeeze of trapezius

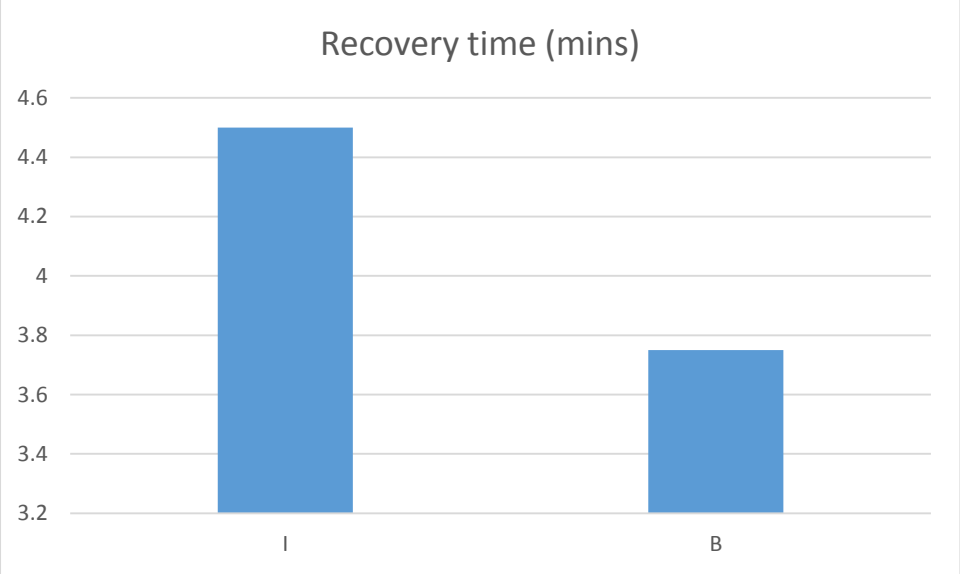
Based on the above scores, depth of sedation was classified as
Deep sedation – OASS score (0-1)
Moderate sedation - OASS score(2-3)
Minimum sedation – OASS score (4)
Following events were considered as complications:
-Decline in oxygen saturation to less than 85% longer than 30seconds.
-Heart rate less than 50 beats per minute
-Blood pressure less than 80/50 mm hg
-Need for mechanical ventilation
Hypoxia was treated with oxygen supplementation, bag and mask ventilation and if required intubation; Bradycardia with ATROPINE and Hypotension treated with crystalloids and if required colloids and vasopressors.

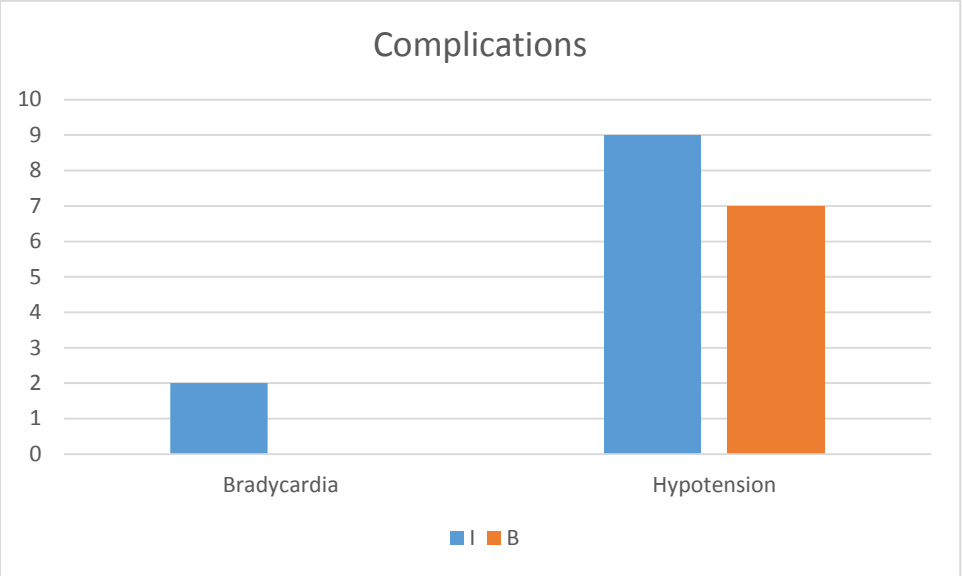
Statistical analysis:
All statistical analyses were performed with MICROSOFT EXCEL, SPSS Statistics version 20.0. A p value of < 0.05 was considered statistically significant.

PARAMETER	GROUP I (Infusion group)	GROUP B (Bolus group)	P VALUE
MALE	62.5%	60%	0.029
FEMALE	37.5%	40%	0.029
WEIGHT (Kg)	60.36	62.45	0656
MEAN AGE (years)	49.08	47.78	1.000
DURATION OF PROCEDURE (mins)	45.24	45.36	0.240
Sedation OASS score	3.53+0.28 (41.17%)	4.15 +0.55 (30.83%)	**<0.0001**
Average dosage required (mg)	255.75+1.5	225+1.3	**<0.0001**
Recovery time (mins)	4.5+0.5	3.75+0.25	**<0.0001**
COMPLICATIONS			
Bradycardia	2	0	0.285
Hypotension	**9**	**7**	


Sedation OASS score as %
45.00%
40.00%
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
I
B


Average dosage required in mg
260
255
250
245
240
235
230
225
220
215
210
205
I
B


Recovery time (mins)
4.6
4.4
4.2
4
3.8
3.6
3.4
3.2
I
B



4. RESULTS

Higher depth of sedation, higher dosage of propofol was required and Recovery time was higher with continuous infusion group than with intermittent group which was statistically significant.

Complications associated with propofol like hypotension, hypoxia and bradycardia shows no statistical significance between both continuous infusion group and intermittent bolus group.

5. DISCUSSION

Gastrointestinal interventional procedures are commonly performed when the patient is under sedation. Some procedures like colonoscopy and esophagogastroduodenoscopy require lighter sedation while some procedures like ERCP which are lengthy and complex procedures require moderate sedation. Conscious sedation is routinely used for gastrointestinal interventional procedures because it provides adequate anxiolysis, acceptance and amnesia for most of the patients.[1]

Many trials were done to investigate the ideal drug regimen for appropriate depth of sedation. Moderate sedation using benzodiazepines and opioids are widely in use for more than three decades and now propofol is gaining importance because of its unique pharmacokinetic properties. Propofol was compared with other traditional sedative agents like benzodiazepines and opioids in many studies.[7]

XIU - LI ZUO ET AL conducted a randomized trial to compare the sedation efficacy of propofol vs midazolam plus fentanyl for upper gastrointestinal endomicroscopy. [8]
This study concluded that propofol is superior to midazolam and fentanyl for conscious sedation. Main limitation in this study was that, although the aim was conscious sedation some patients may have developed deeper sedation during the procedure; but that was not judged during the procedure.

Propofol can be given through intravenous route either by intermittent bolus form or in infusion form which can be through pump controlled or target controlled infusion.Many studies were conducted to show the sedation efficacy between both forms of propofol that is between intermittent bolus form and infusion form.

In our study, Higher depth of sedation was achieved with continuous infusion group I than intermittent bolus group B which is statistically significant. Depth of sedation was more with group I, as a steady state plasma concentration of propofol is maintained, than with group B. This is similar to the study conducted by Gonzalez santiago et al[15] while in the study conducted by Veena kachhwah et al[11] shows no significant difference.
Dosage of propofol required was higher with continuous infusion group I than with

intermittent bolus group B, which is statistically significant. Recovery time was higher with continuous infusion group I than with intermittent bolus group B, making it statistically significant. Recovery time was more with group I as infusion was stopped at the end of procedure, while in group B, last dose was given several minutes before the end of procedure. This is similar to a study conducted by Jaegon lee etal[16] in ERCP procedures while study conducted by Derya seyitoglu et al [12] in ERCP procedures shows no significant difference in dosage of propofol and recovery time. Intermittent bolus form is most cost-effective form as it requires less dose than continuous infusion group.

Complications associated with propofol like hypotension, hypoxia and bradycardia shows no statistical significance between both continuous infusion group I and intermittent bolus group B. This is similar to study conducted by Gonzalez Santiago et al in colonoscopy procedures. ***WEI HUNG CHAN ET AL*** conducted a prospective randomised controlled study for comparison of cardiovascular and respiratory complications between Target controlled infusion of propofol vs intermittent boluses of sedative cocktail regimen which includes a benzodiazepine, an opioid and propofol for GI endoscopy.[13] In their study, Hypotension, hypoxia, and bradycardia were considered as cardiovascular and respiratory complications, while other parameters considered were dosage of propofol required and recovery time in both groups. The conclusion of their study was that Target controlled infusion of propofol was associated with lesser cardiovascular and respiratory complications than intermittent sedative cocktail regimen group in GI endoscopy, with no significant difference between both groups in terms of recovery time during GI endoscopy and showing that continuous infusion group has lesser hospital stay and early discharge.

6. CONCLUSION

This prospective randomised controlled study comparing propofol infusion with intermittent bolus of propofol in 80 patients posted for colonoscopy concludes that the depth of sedation, dose of propofol required and recovery time was higher in continuous infusion group as compared to bolus group. But complications were similar in both and not statistically significant.

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