Original Article

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Anaesthesia Section

Intermittent Manually Controlled versus Continuous Infusion of Propofol for Procedural Sedation during Interventional Endoscopic Procedures: A Single-blinded Randomised Study

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ABSTRACT

Introduction: Sedation with propofol during interventional gastrointestinal endoscopy is usually accomplished with two main modes-intermittent manually controlled using a syringe, and continuous infusion using an infusion device.

Aim: To compare the effect of bolus administration and infusion of propofol on recovery profile during sedation in patients undergoing interventional endoscopy procedures.

Materials and Methods: The present study was a single-blinded randomised study in which 120 patients, belonging to American Society of Anaesthesiologists (ASA) grade I and II, of either gender, and age 18-70 years, were randomly assigned to receive intermittent bolus (Bolus Group, BG) or continuous infusion (Infusion Group, IG) of propofol sedation after induction with 2 mg Midazolam for deep sedation. BG patients received an initial dose of propofol, 1%, according to body weight (<60 kg: 40 mg, >60 kg: 60 mg), followed by boluses of 10-20 mg adjusted to maintain a Modified Observer's Assessment of Alertness/Sedation Scale (MOAA/S) of 0 or 1. In the IG, continuous propofol infusion (4-6 mg/kg/hr) via Graseby 2000 (Smiths Medical) was administered after a bolus of 1 mg/kg of propofol. Vital signs, recovery time, quality of recovery, total dose of propofol, side-effects as well as patient and endoscopist satisfaction score were evaluated. The data was compiled systematically and analysed using unpaired Student's t-test and Chi-square test. The p-value <0.05 was considered significant.

Results: The demographic profile of patients was comparable in both the groups. The recovery time (6.30±2.06 minutes in BG versus 5.71±2.19 minutes in IG) and total propofol dose (327.74±45.52 mg in BG versus 314.46±64.52 mg in IG) were comparable. Similarly, the quality of recovery was identical in both groups. At 10 and 15 minutes after induction, arterial blood pressure was significantly lower in group BG as compared to group IG (114±16.96 in BG versus 120.34±8.78 in IG; p-value=0.031). The endoscopist's satisfaction score was better in IG (p-value=0.001), whereas, the patient satisfaction score was comparable in both the groups (p-value=0.162).

Conclusion: Both regimes allowed good controllability of propofol sedation. However, endoscopist satisfaction score was significantly better and haemodynamic fluctuations were less in infusion group.

Keywords: Bolus vs infusion propofol, Gastrointestinal endoscopy, Out of operating room anaesthesia, Sedation for endoscopy

INTRODUCTION

Sedation, analgesia, or both may be needed for gastrointestinal endoscopic interventional or diagnostic procedures [1]. Propofol is an ideal agent for procedural sedation these days as it possesses many properties like rapid onset of action, short half-life, faster psychomotor recovery and better patient and investigator satisfaction [2]. There are two main modes of propofol administration for sedation-intermittent bolus using a syringe and continuous infusion using an infusion device [3].

The well-known side-effects are hypoxaemia and hypotension, which are related to the total dose as well to the application rate of propofol. Continuous infusion of propofol may be theoretically associated with a less need for user interventions, maintenance of a more consistent level of sedation. Additionally, avoidance of high peak propofol plasma concentration during bolus application may reduce the intensity of hypotensive effects of propofol and a rapid lightening of the sedative effect with subsequent patient movements may be avoided by only minimal fluctuations of the plasma propofol concentration under continuous infusion. Continuous infusion scheme instead of repeated bolus administration can reduce "peaks and valleys" in blood concentration and thereby decrease the total amount of drug given [2]. However, in contrast to these assumptions, some studies, performed outside the field of gastrointestinal endoscopy, showed a significant higher total dose of propofol was required when continuous administration of propofol was compared with the repeated bolus technique [4-6].

The aim of the study was to compare the effect of bolus administration and infusion of propofol on recovery profile during sedation in patients undergoing interventional endoscopy procedures. The primary outcomes measures were recovery time and total dose of propofol required. The secondary outcome measures were adverse events, endoscopist's satisfaction score and patient satisfaction score.

MATERIALS AND METHODS

This single-centered, single-blinded randomised study was conducted from June 2018 to April 2019, at Satguru Partap Singh Hospitals, District Ludhiana, Punjab, India. The approval from Institutional Ethics and Scientific Review Committee was obtained, in the committee meeting dated July 13, 2018. Written informed consent was taken from all patients.

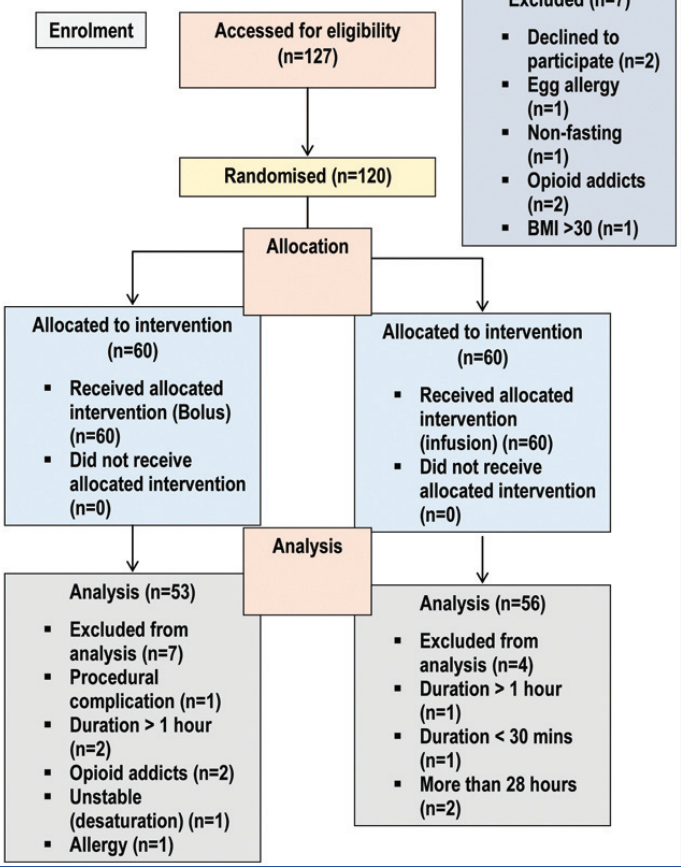
Sample size calculation: Riphaus A et al., studied 100 patients, and observed that the recovery time was 19.0±5.0 minutes in the bolus group and the recovery time was 23.0±6.0 minutes in the perfusion group [2]. Sample size analysis determined that at alpha value of less than 0.05, 60 subjects in each group were required to detect a difference of 3.36 in the recovery time between both the groups to achieve power of 90%. Hence, the sample size of 60 each was considered for each group.

Inclusion criteria: Patients of either gender, aged 18-70 years, belonging to ASA physical status I and II who were planned for interventional endoscopic procedures, were enrolled into the present study.

Exclusion criteria: Obesity (Body Mass Index (BMI) >30 kg/m^2), history of obstructive sleep apnoea, on sedatives, hypnotics or narcotics, anticipated difficult airway, mental illness, hypoxaemia (SpO_2 <90%) on room air, bradycardia (heart rate <50 beats per minutes (bpm)), pregnant and lactating women, and patients allergic to midazolam, eggs, sulphite or soyabean were excluded from the study. The present study was limited to procedures lasting upto 60 minutes.

The patients were divided randomly into two groups using website-based plan generator: Group Bolus (BG) and Group Infusion (IG), comprising of 60 patients each [7].

A total of 127 patients were assessed for eligibility. However, seven patients had to be excluded as they did not meet the eligibility criteria (n=7) or refused to participate (n=2). In total, 120 patients were randomly assigned to receive intermittent propofol bolus application (n=60) or continuous propofol infusion (n=60). During analysis, seven patients from Bolus group and four patients from infusion group were excluded based on exclusion criteria [Table/Fig-1].



[Table/Fig-1]: Participant flow.

Study Procedure

After evaluation of baseline data (age, sex, history, physical examination, airway examination, fasting status), patients were prepared for endoscopy with a temporary intravenous line and standard monitoring (i.e. pulse oximeter, non invasive blood pressure measurement and electrocardiography). All patients also received prophylactic oxygen 2 L/min via nasal prongs throughout the procedure.

All patients received Inj. Midazolam 2 mg bolus and inj Buscopan 20 mg (as per the endoscopist's protocol). The following solutions were randomly administered: inj. propofol, 1%, according to the body weight (bw) (bw <60 kg: 40 mg, bw >60 kg: 60 mg), followed by bolus of 10-20 mg adjusted as needed for the desired level of sedation in bolus group (n=60) and inj. propofol, 1%, at a dosage of 1 mg per kg body weight followed by infusion at a rate of 4-6 mg/kg/hr via Graseby 2000 (Smiths Medical) in infusion group (n=60). Also in group I, bolus of 10-20 mg of propofol adjusted as needed for the desired level of sedation was also given, however patients requiring more than two boluses were excluded from the study. The level of sedation was monitored using clinical criteria, MOAA/S targeted 0 or 1 in both the groups [2]. Vital signs, recovery time, total dose of propofol, side-effects as well as Endoscopist and patient satisfaction scores were observed. In addition, quality of recovery was assessed every 15 minutes till one hour and then every 30 minutes till patient was discharged using Ramsay Sedation score and Post Anaesthesia Recovery Score (PARS) [2].

For PARS, patients were assigned points of 0, 1, 2 for each of the following categories. Complete recovery is indicated by the maximum PARS of 10 points.

i. Activity (inability to move the limbs, ability to move two or four limbs with or without command).
ii. Respiration (evidence of apnoea, laboured breathing or normal breathing pattern).
iii. Circulation (blood pressure compared with baseline prior sedation: ±50% to baseline, ±20±50% to baseline, ±20% to baseline).
iv. Consciousness (hypnotic, arousable or fully awake); and
v. Skin colour (cyanotic, pink or normal).

At the end of procedure, the endoscopist was asked to rate the procedure based on their level of satisfaction from 1=fully satisfied to 5=unsatisfied. Similarly, prior to discharge from recovery room, patients were asked to rate their level of satisfaction from 1=acceptable to 5=unacceptable.

STATISTICAL ANALYSIS

Statistical analysis was done using Statistical Package of Social Science (SPSS) version 21.0. To test the normality Kolmogorov-Smirnov test was applied. Quantitative variables were compared using using unpaired t-test/Mann-Whitney test (when the data sets were not normally distributed). Qualitative variables were correlated using Chi-square test/Fisher's exact test. Categorical variables were presented in the form of numbers and percentages and continuous variables were presented as Mean and Median. The p-value <0.05 was taken as statistically significant.

RESULTS

The demographic and clinical characteristics of study population in both the groups were not statistically significant [Table/Fig-2].

Variables	BG	IG	p-value
Age (years) (M±SD)	46.58±12.76	44.41±12.57	0.537
Gender (Male:Female)	18:35	20:36	0.848
ASA Grade (I:II)	31:22	26:30	0.208
Weight (Kg) (M±SD)	59.32±8.23	58.75±7.94	0.713
Duration of procedure (minutes) (M±SD)	35.75±5.15	35.20±4.32	0.541

[Table/Fig-2]: The demographic profile of the patients.
BG: Bolus group; IG: Infusion group

Primary Outcome

The mean recovery time in BG and IG were comparable (6.30±2.06 min versus 5.71±2.19 min; p-value=0.153) [Table/Fig-3]. Similarly, the quality of recovery (Ramsay sedation score, 5.53±0.87 versus 5.61±0.71) and PARS (6.26±0.49 versus 6.23±0.63) immediately after termination of endoscopic procedure were also comparable.

The total dose of propofol used in BG was 327.75±45.52 mg, while in IG was 314.46±64.52 mg, and the difference in both the groups found to be statistically in significant [Table/Fig-3].

Variables	BG	IG	p-value
Recovery time (minutes) (M±SD)	6.30±2.06	5.71±2.19	0.153
Total dose of propofol (mg) (M±SD)	327.74±45.52	314.46±64.52	0.220

[Table/Fig-3]: Comparison of recovery time and total dose of propofol used in both the groups.
BG: Bolus group; IG: Infusion group

Secondary Outcome

The number of episodes of desaturation (SpO_2 <90%) were comparable in both groups [Table/Fig-4].

However, Endoscopist satisfaction score was significantly better in IG as compared to BG while the patient satisfaction score was comparable between both the groups [Table/Fig-5].

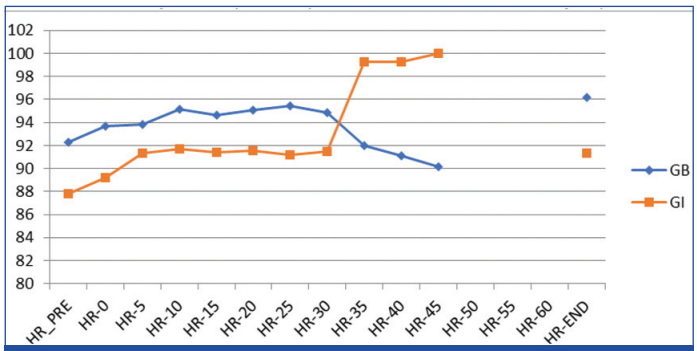
Events	BG (n=53)	IG (n=56)	p-value
Episodes of desaturation (SpO_2 <90%), n	4	2	0.363
Nausea, n	1	0	0.486
Pain on injection, n	5	3	0.481
Muscle movements, n	2	3	0.693

[Table/Fig-4]: Adverse events in both the groups.
BG: Bolus group; IG: Infusion group

Satisfaction score	BG (n=53)	IG (n=56)	p-value
Median endoscopist satisfaction score, mean and range	3 (1-5)	1 (1-5)	0.001*
Median patient satisfaction score, mean and range	2 (1-5)	2 (1-5)	0.162

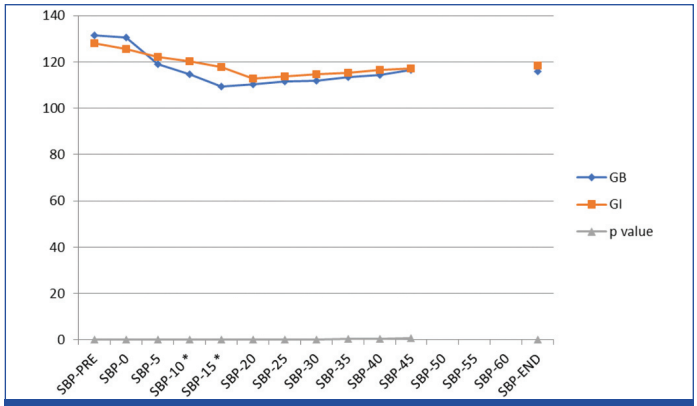
[Table/Fig-5]: Endoscopist satisfaction score and satient satisfaction of both the groups.
BG: Bolus group; IG: Infusion group; *significant p-value

The mean value of heart rate of the two groups was calculated at baseline, after giving the drugs and after five minute intervals. The difference was statistically not significant at all time intervals [Table/Fig-6].



[Table/Fig-6]: Comparison of variation in heart rate in both groups.
HR: Heart rate, GB: Bolus group, GI: Infusion group

Similarly, the mean value of SBP of the two groups was recorded every 5 minutes and was found to be statistically not significant at all time intervals except at 10 minutes and 15 minutes when these were found to be significant [Table/Fig-7].



[Table/Fig-7]: Comparison of variation in systolic blood pressure in both groups.
SBP: Systolic blood pressure; GB: Bolus group; GI: Infusion group; *significant p-value

DISCUSSION

Propofol, a short acting agent is increasingly being used for sedation in interventional endoscopic procedures as it has many properties required for an ideal agent. Besides the traditional intermittent bolus application of propofol, alternative techniques in procedural sedation are Continuous Controlled Infusion (CCI), Target Controlled Infusion (TCI), Patient Controlled Sedation (PCS) and Computer Assisted Personalised Sedation (CAPS). In the present study, bolus administration versus continuous infusion of propofol was compared for sedation for interventional endoscopic procedures. Continuous infusion of propofol showed lesser fluctuations in SBP and more endoscopist's satisfaction when compared to bolus technique. However, the recovery profile and the patient satisfaction were similar in both the groups.

The duration of recovery in the present study was similar in both the groups. The quality of recovery indicated by PARS and RSS were also similar in both the groups. The results regarding duration of recovery were similar to study done by Bennett J et al., [4] and Klein SM et al., [5]. However, Riphaus A et al., [2] showed higher recovery time in infusion group compared to bolus group because unlike in this study, the index study maintained target MOAA/S score of 0 or 1. The quality of recovery indicated by RSS and PARS was similar in two groups of the present study. The mean of PARS in bolus group and infusion group were comparable.The results were similar to the study done by Riphaus A et al., [2], where the quality of recovery as indicated by the PARS was nearly similar in both groups 30 minutes after termination of the endoscopic procedure. However, a prolonged recovery with the use of continuous infusion compared with bolus propofol administration was described in a study by Brownlie GS et al., [6].

The mean total dose of propofol required was similar in both the groups. The results were in concordance with those of Riphaus A et al., [2] and Seyitoglu D et al., [7]. However, studies by Bennett J et al., [4], Klein SM et al., [5] and Brownlie GS et al., [6] contrasted the present study results. The present study results regarding the total dose of propofol might be best explained by the fact that dose required to induce deep sedation might be equal irrespective of technique of propofol administration used. On the other hand, studies that contrasted the results had not provided any convincing evidence of monitoring depth of sedation at target level.

The most striking feature of present study was haemodynamic fluctuations which were more in BG than IG. Although the heart rate fluctuations were minimal in both groups, the perturbations in SBP were more in BG than IG. However, Riphaus A et al., [2] showed that SBP was comparable in both groups, while study done by Klein SM et al., [5] concluded SBP decrease more in continuous infusion group. In present study, more haemodynamic fluctuations were seen in BG which might be due to sudden rise in plasma concentration of propofol during bolus administration leading to significant fall in SBP and heart rate variability.

The rest of haemodynamic parameters such as respiratory rate and oxygen saturation were comparable between both groups. But there were few episodes of desaturation, (four in BG and two in IG) for which chin lift manoeuvre sufficed. The results were consistent with study done by Riphaus A et al., [2] where desaturation was seen in four patients of each group with no need for assisted ventilation.

The side-effect profile of both groups exhibited no significant outcome. Similar results were seen by Riphaus A et al., [2]. Another major significant finding was noted in Endoscopist satisfaction score, where Endoscopist was more satisfied in continuous infusion than bolus group method. These results were consistent with the study done by Bennett J et al., [4]. On the other hand, patient satisfaction score was comparable in between both groups.

Hence, the present study shows more haemodynamic fluctuations in BG and better Endoscopist score in IG. Therefore, infusion technique is proved to be better than intermittent bolus method.

Limitation(s)

Since the present study limited procedures to upto one hour, some dose variability was expected between the two groups for procedures extending beyond an hour. Additionally, the present study used clinical assessment alone as a guide for depth of sedation in titrating propofol dose. EEG guided monitored (BIS Monitor) could have been used.

CONCLUSION(S)

Both the techniques provided good control of sedation for endoscopy and are associated with similar recovery profile and patient safety. However, the haemodynamic stability and Endoscopist satisfaction was more during continuous infusion of propofol than bolus administration. Therefore, continuous administration of propofol should be the standard of care during endoscopic sedation during longer interventional endoscopic procedures.

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