

# Intravenous Sedation Techniques for Gastrointestinal Endoscopy

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## ABSTRACT

Gastrointestinal endoscopic (GIE) procedure has become an essential modality for evaluation and management of gastrointestinal tract abnormalities. The safe sedation of patients for this procedure requires a combination of properly trained physicians and appropriate facilities. Moreover, proper selection and preparation of patients, suitable sedative technique, and application of drugs is essential. Irrespective of regimen used, the safe administration of sedative drugs requires an awareness of the individual needs of the patients. To date, the most commonly used sedation technique for GIE procedure is intravenous technique. The use of short acting drug, adequate dose of sedative agents and sedation endpoint as well as appropriate sedation technique has an important role and also increased the safety. Several intravenous sedation techniques are presently used and evaluated. This article reviews and discusses the current status of the intravenous techniques for sedation in various GIE procedures.

**Key words:** Sedation; Intravenous; Technique; Gastrointestinal endoscopy

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## INTRODUCTION

Recent advances in anesthesia and endoscopic equipment have made gastrointestinal endoscopic (GIE) procedure increasingly popular. Sedation always has been a critical component of performing these procedures. The goal of procedural sedation is the safe and effective control of pain and anxiety as well as to afford an appropriate degree of memory loss or reduced awareness<sup>[1,2]</sup>. To date, sedation practices for GIE procedures vary widely. Intravenous sedation technique is one of the most common anesthetic techniques for GIE procedures. Several intravenous sedation techniques could be performed. GIE sedation requires rapid recovery, decreased duration of care, good quality analgesia, and cost effective techniques. The majority of GIE patients are ambulatory cases. Most of this procedure requires a short time. So, rapid onset, short acting drugs with little adverse effects and improved safety profiles are usually used. Several intravenous drugs may fulfill these criteria and, therefore, GIE sedation could be completed by various intravenous techniques.

Fortunately, extended intravenous sedation techniques are available and their impact on clinical outcomes is demonstrated. Appropriate administration techniques are important to fully benefit from the pharmacological properties of the intravenous drugs. However, their routine use for sedation must be individualized. This article provides an overview of my current knowledge in determining the field of intravenous sedation technique for procedural sedation in GIE procedure. It focuses on commonly used intravenous sedation techniques and also briefly reviews of the literature.

## SINGLE BOLUS ADMINISTRATION

GIE procedure is as an invasive procedure that causes pain or discomfort for the patients. Some endoscopic procedures may be performed without sedation in selected patients. In many countries, GIE sedation is generally provided by physicians to enhance patient tolerance and satisfaction and simplify the procedure. The single bolus administration of sedative drugs is commonly used for short duration and noncomplicated GIE procedures such as esophagogastroduodenoscopy (EGD) and diagnostic colonoscopy. The combination of a benzodiazepine and an opioid has become standard sedative practice

for GIE procedure. Several studies have been confirmed that the addition of a single bolus of meperidine to midazolam improves patient tolerance and decreases pain during endoscopic procedures without significantly increasing the adverse effects or prolonging recovery time<sup>[3]</sup>.

Generally, several practice guidelines recommend physicians for the careful titration of sedative drugs during GIE procedures. However, this titration technique is time-consuming. A previous study compared the safety and efficacy of the titration technique with a single, rapid bolus of sedative drugs before colonoscopy. This study showed the titration required more physician time than the bolus and was related with an increased need for oxygen supplementation. The rapid bolus administration of sedative agents for colonoscopy also provided comparable levels of patient comfort<sup>[4]</sup>.

## INTERMITTENT BOLUS ADMINISTRATION

Conventionally, a single dose of sedative drugs may be inadequate for the long duration of GIE procedures. In addition, the administration of a single full dose of sedative drugs is associated with the risks of cardiorespiratory depression such as hypotension and bradycardia as well as apnea, hypoventilation and upper airway obstruction. For these reasons, an alternative technique is needed to ensure adequate sedation during the procedure. An intermittent bolus administration (split dose) of sedative agents is one of the alternative techniques. It is superior to that of a single dose at the time of removal of the endoscope. However, the boluses frequently create unwanted cardiorespiratory depression and the recovery of the intermittent bolus administration after GIE sedation is delayed.

Lee and Kim evaluated the efficacy and safety of a split dose of midazolam in combination with meperidine for eighty patients underwent outpatient colonoscopic procedures. All patients were randomly assigned into group A (a split dose of midazolam in combination with meperidine) and group B (a single dose of midazolam in combination with meperidine). The results showed that group A had a lower rate of significant hypoxemia and a higher sedation score on removal of the endoscope. The patient controllability, recovery time and pain scores in group B were significantly lower than in group A. The authors concluded that split dose midazolam in combination with meperidine resulted in a safer, more constant sedation status during colonoscopy and a reduction in procedure-related pain and memory<sup>[5]</sup>.

Moreover, a bolus technique could produce higher a sedation level than an intended sedation depth. It is often taken to the level of general anesthesia and is at risk for respiratory depression and hemodynamic instability. The levels of sedation required for patients to comfortably undergo colonoscopy with propofol were assessed<sup>[6]</sup>. The sedation level was monitored with the Patient State Index (PSI), and end-tidal carbon dioxide was monitored via nasal cannula. In one group the PSI value was blinded from the anesthesiologist and in the second group the PSI was visible. Overall 96% of patients achieved levels of deep sedation and 89% accomplished levels of general anesthesia. In addition, the blinded to PSI group was maintained at a deeper sedation level with more respiratory compromise than the unblinded group. This report demonstrated that propofol sedation delivered by a bolus technique was frequently taken to levels of general anesthesia<sup>[6]</sup>.

## TOTAL INTRAVENOUS ANESTHESIA

Total intravenous anesthesia (TIVA) includes induction and maintenance of anesthesia with intravenous drugs alone. To date,

propofol has gained increased acceptance for TIVA because of its excellent pharmacokinetic and pharmacodynamic properties. TIVA might be associated with the administration of nitrous oxide. The objective of TIVA is to maintain a suitable concentration of anesthetic drugs at the site of action in the central nervous system. The continuous infusion of short-acting drugs is the key role of TIVA. This technique could be maintained with a high degree of safety, accuracy and titratability.

Rudner and colleagues compared the combination use of fentanyl, midazolam and propofol to accomplish a state of TIVA with a regimen of remifentanyl infusion and propofol bolus dosing to attain moderate sedation in fifty ASA class I and II patients underwent elective colonoscopic procedures. In the TIVA group, bispectral index monitoring was used to accomplish a stable level of anesthesia and the jaw thrust maneuver was applied to minimize the risk of airway obstruction. The result showed that the recovery time in the remifentanyl infusion and propofol bolus group was significantly shorter than in the TIVA group. The reduction of mean arterial pressure, heart rate, respiratory rate, oxygen saturation and end-expiratory carbon dioxide in the TIVA group was significantly greater than in the remifentanyl infusion and propofol bolus group. Furthermore, no serious adverse events were observed in both groups<sup>[7]</sup>. They also tested the hypothesis that sedation with remifentanyl and propofol might be more effective compared with anesthesia by intravenous administration of midazolam, fentanyl and propofol in colonoscopy. The 100 adult patients received either conscious sedation (sedation group) or total intravenous anesthesia (TIVA group). Sedation was performed by infusion of remifentanyl (0.20-0.25 mcg/kg/min) and propofol in titrated doses. TIVA was carried out by intravenous administration of fentanyl (2 mcg/kg), midazolam (0.05 mg/kg) and propofol in titrated doses. Cardiorespiratory profiles and bispectral index were monitored and recorded. All patients in the TIVA group found the colonoscopy painless. The mean pain score in the sedation group was 0.4. The recovery time in the sedation group was significantly shorter than in the TIVA group. In addition, the alterations of hemodynamic and respiratory parameters in the TIVA group were significantly greater than in the sedation group. This study demonstrated that the combination of remifentanyl and propofol for colonoscopy offered adequate analgesia, acceptable hemodynamic stability, lower respiratory depression and fast recovery<sup>[7]</sup>.

Moreover, our previous study compared and evaluated the success rate of propofol-balanced anesthesia for single balloon enteroscopy between antegrade and retrograde intubation. This study demonstrated that propofol-balanced anesthesia for single balloon enteroscopy procedure in adult patients by experienced anesthesiologist was relative safe and effective. The success rate of the endoscopy did not depend on the route of intubation. Serious adverse events were rare in our population<sup>[8]</sup>.

## MANUALLY CONTROLLED INFUSION

Generally, the continuous infusion technique receives more sedatives than the bolus technique. Several studies have been confirmed that the sedation state in the continuous infusion technique is judged to be better than in the bolus technique. The invasive GIE procedures such as endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS) normally require longer time than the ordinary GIE procedures. Several studies have been evaluated the benefit of intermittent propofol over conventional sedation. A previous study was conducted to compare the continuous infusion

of propofol and conventional sedation in terms of satisfaction, recovery score and the safety parameters for sedation in ERCP procedure<sup>[9]</sup>. One hundred thirty four patients with ASA physical status I-III underwent ERCP were randomly assigned into the two groups. Patients underwent either propofol sedation or meperidine and midazolam sedation. The report showed that time to regain full recovery in the propofol group was significantly shorter than in the conventional group. The rates of oxygen desaturation, bradycardia and hypotension in both groups were low and comparable. As a result, continuous infusion of propofol for ERCP procedure by guidance of gastroenterologist was a safe and effective technique. Consequently, this infusion technique also presented better recovery profiles<sup>[10]</sup>. Our previous study also confirmed that experienced anesthetic nurse and anesthetic trainee administered sedation by using this technique for colonoscopic procedure was safe and effective. The success rate, ease of intubation, patient and endoscopist satisfaction, complications and staff consultation were comparable<sup>[10]</sup>.

To date, nonanesthesiologist-administered propofol sedation (NAPS) is increasingly used for sedation during various GIE procedures. The repeated bolus administration has been recommended for this sedation regimen. A previous abstract also confirmed the safety of NAPS by using an intravenous infusion technique for sedation in ERCP patients<sup>[11]</sup>. Tracheal intubation or death was not observed. Therefore, the NAPS with continuous infusion method for ERCP procedure in the selected patients was safe and effective. In addition, Kulling and colleagues randomized 150 patients to three sedation groups including patient controlled sedation (PCS) with propofol/alfentanil, continuous propofol/alfentanil infusion, and nurse-administered midazolam/meperidine. The authors concluded that PCS with propofol/alfentanil demonstrated a higher degree of patient satisfaction and more of a complete recovery at 45 minutes when compared to conventional sedation and analgesia<sup>[12]</sup>.

Furthermore, the intermittent boluses regimen and pump continuous infusion method for endoscopist-directed propofol administration, targeted to moderate sedation, in colonoscopy was compared by Gonzalez-Santiago and coworkers<sup>[13]</sup>. The 192 consecutive outpatients were randomized to receive the intermittent boluses regimen (20 mg propofol boluses on demand) or pump continuous infusion method (3 mg/kg/h and 20 mg boluses on demand). There were no significant differences in patient, nurse or endoscopist satisfaction and procedural sedation between the two groups. However, propofol doses in the pump continuous infusion group were significantly higher during the induction phase and overall period. The moderate depth of sedation level was about 80% of all assessments. Complications in both groups were minor and comparable. This report confirmed that the intermittent boluses and pump continuous infusion methods for endoscopist-directed propofol administration were safe and effective as well as comparable satisfaction and complication rates. These data also demonstrated that continuous infusion technique resulted in larger propofol delivery compared with intermittent bolus technique. However, the differences in recovery times were not clinically significant<sup>[13]</sup>.

## TARGET-CONTROLLED INFUSION

Target controlled infusion (TCI) is a new techniques of continuous infusions. It uses pharmacokinetic models to predict the patient plasma and effect site concentrations from the infusion design and permits the anesthesiologist to target a selected concentration, the device calculating the appropriate infusion system to achieve this concentration<sup>[14]</sup>. TCI rapidly achieves and maintains a predefined

plasma or effect site concentration of the anesthetic drug. Appropriate target concentrations change with interindividual pharmacodynamic variability and with the nature of the surgery. When an appropriate target concentration for achieving the desired clinical endpoint is chosen, TCI delivery systems perform better than manual systems<sup>[15]</sup>. Currently, TCI devices are approved in many countries, but only for propofol administration.

The TCI has been used for procedural sedation. It provides a safe alternative technique for GIE procedures. The most appropriate drug available for TCI is yet to be established. Several studies confirmed that sedation using TCI for GIE procedures provided effective and safe sedation and was associated with better sedation quality. The depth of sedation appeared to be appropriate and allowed the patients to be easily managed during the procedures<sup>[16]</sup>. A previous trial compared remifentanyl with propofol in the TCI technique for sedating patients during GIE procedures<sup>[17]</sup>. The study demonstrated that propofol in TCI appeared to be an adequate agent for sedation of patients underwent GIE procedures, with fewer adverse effects and higher patient satisfaction. Presumably, the combination of these two drugs might be synergistic. However, the best anesthetic techniques for sedation during GIE procedure are still discussed. The study of Chiang and colleagues compared TCI and manually controlled infusion (MCI) in the same-day EGD followed by colonoscopy in terms of the recovery time, clinical presentations and satisfaction. A total of 220 patients with ASA physical status I or II were enrolled and randomized into the TCI or MCI groups. The recovery time, oxygen desaturation, hypotension and period of bradypnea in the TCI group were significantly lower than in the MCI group. The authors concluded that TCI of propofol combined with alfentanil was correlated with a faster recovery time, and better hemodynamic and respiratory parameters than the manually controlled infusion in same-day bidirectional endoscopy<sup>[18]</sup>.

Moreover, a comparison of the TCI and the PCS of propofol during ERCP procedure was studied. A total of 82 patients underwent elective ERCP were randomized to receive propofol 10 mg/mL using TCI (initial targeted effect-site concentration 2 mcg/mL) or PCS (single bolus 1 mL, lockout time set at zero). Alfentanil was administered if signs of unsatisfactory analgesia happened. The sedation levels and vital signs as well as the consumption of propofol and alfentanil were noted. Additionally, the ease of ERCP performance, speed of recovery, and satisfaction with sedation were assessed. No benefits of TCI over PCS could be demonstrated in this study<sup>[19]</sup>.

Recently, Gotoda and colleagues examined the safety and efficacy of propofol sedation with a TCI pump and Bispectral index monitoring system in 413 elderly patients during gastric endoscopic submucosal dissection. All patients were divided into three groups: group A, age < 70 years; group B, age  $\geq$  70 and < 80 years; and group C, age  $\geq$  80 years. The study demonstrated that elderly patients required lower doses of propofol with this system than younger patients. Hypotension tended to occur in the younger group. However, hypoxemia and abnormal pulmonary function happened at a significantly higher rate in the older groups<sup>[20]</sup>.

## MONITORED ANESTHESIA CARE

Monitored anesthesia care (MAC) refers to a clinical service where in an anesthetic personnel provides analgesia and sedation for a diagnostic or therapeutic procedure. The provider of MAC must be prepared and qualified to convert to general anesthesia when necessary. MAC may include varying levels of sedation,

anxiolysis and analgesia. The American Society of Anesthesiologists recommends that the standards of care be same as for general or regional anesthesia. A wide variety of intravenous drugs have been used during MAC. The use of MAC may be considered medically necessary for GIE procedures in high-risk patients. Benzodiazepines, mainly midazolam, are widely used during MAC because of their properties. In addition, ketamine has been used alone in MAC, but its administration has been related with a high incidence of adverse effects<sup>[21]</sup>. Benzodiazepines have been used in combination with ketamine. Propofol is probably the most appropriate IV agent for MAC. The use of propofol was associated with a more rapid recovery of cognitive functions and less postoperative sedation and confusion. The combination of propofol and small dose ketamine during MAC offers a reduction in the incidence of propofol-induced cardiorespiratory adverse effects<sup>[22]</sup>.

Generally, the general anesthesia with tracheal intubation is utilized for the invasive GIE procedures such as ERCP, EUS and small bowel enteroscopy. However, there is limited data regarding MAC without tracheal intubation for these procedures. One retrospective study was to evaluate the safety and efficacy of MAC sedation during single-balloon enteroscopy procedure and to identify the risk factors for adverse events<sup>[23]</sup>. Of the 178 patients, 166 patients (93%) were performed with MAC and 12 patients (7%) with general tracheal anesthesia. The sedation-related adverse events observed in 17% of patients. The most adverse event was transient hypotension. In the MAC group, the diagnostic yield was 58.4% and the therapeutic yield was 30.1%. The duration of anesthesia was strongly associated with the rate of sedation-related adverse events. This study demonstrated that MAC was a safe and efficacy sedation technique for patients underwent single-balloon enteroscopic procedures. Sedation-related complications were uncommon<sup>[23]</sup>.

## MODERATE (CONSCIOUS) SEDATION

Moderate (conscious) sedation defines as a drug-induced depression of consciousness which patients respond purposefully to verbal commands. Spontaneous ventilation is adequate. Cardiovascular function is usually maintained<sup>[2]</sup>. It ranges from anxiolysis to sleep with preservation of eyelash reflex and purposeful reaction to verbal or mild physical stimulation. Subanesthetic doses of intravenous drugs are often used to provide sedation for GIE procedures. The interest of propofol for conscious sedation was demonstrated at the early stages of clinical use of this drug. Conscious sedation with propofol can be accomplished with intermittent bolus, continuous infusion or TCI. Moderate sedation is generally performed for GIE procedures that require some degrees of patient relaxation and analgesia.

Conscious sedation is typically accepted as an appropriate technique for sedation by non-anesthetic personnel. It could be performed by using benzodiazepines and narcotics. However, propofol might be used for moderate sedation by non-anesthesiologists in some countries. Several studies confirmed that moderate sedation provided a safety margin when compared with deep sedation or general anesthesia. The development of protocols that target sedative agents to moderate sedation will expand the sedative drugs available to non-anesthetic personnel<sup>[24]</sup>.

The detection rate of adenomas is one of the quality indicators in high-quality colonoscopy. The performance of colonoscopy for the detection of polyps in patients sedated with deep and moderate sedation was compared in 520 adult patients. In both deep and moderate groups, sedation was performed by using midazolam and meperidine. There were no significant differences in the overall

detection of polyps and the polyp size as well as the rate of adenoma detection between deep and moderate sedation groups<sup>[25]</sup>.

In patients with obstructive sleep apnea (OSA), sedation is associated with higher risks of cardiorespiratory complications. A study evaluated the safety of conscious sedation during GIE procedure for patients with OSA, and compared this to patients without OSA. All procedures were successfully completed. No complications were noted in the patients without OSA group. In the OSA group, one patient experienced oxygen desaturation during an upper endoscopy and required oxygen supplementation. This study showed that GIE procedure could be safely done in the OSA patients by using conscious sedation<sup>[26]</sup>.

However, the unintended levels of deep sedation can occur when moderate sedation is used during elective GIE procedures. One prospective study evaluated the incidence and risk factors of deep sedation during GIE procedures with meperidine and midazolam intended to maintain a level of moderate sedation. All 80, ASA class I-II, outpatients were enrolled, and intravenous meperidine and midazolam were administered according to a standardized protocol. Hemodynamic parameters and levels of sedation were assessed and recorded by a single observer at 3-min intervals. In this study, deep sedation occurred in 54/80 (68%) patients for a total of 204/785 (26%) of total sedation assessments. Deep sedation occurred at least once in 60% of esophagogastroduodenoscopy, 45% of colonoscopy, 85% of ERCP, and 80% of EUS. Multivariable analysis showed that only ERCP and EUS procedures were independent risk factors of deep sedation. The study confirmed that deep sedation occurred frequently during elective GIE procedures with meperidine and midazolam used with the intent of moderate sedation<sup>[27]</sup>.

## DEEP SEDATION

Deep sedation defines as a drug-induced depression of consciousness which patients cannot be easily aroused but respond purposefully after repeated verbal or painful stimulation. Spontaneous ventilation may be inadequate. However, cardiovascular function is normally maintained<sup>[2]</sup>. Generally, deep sedation should be performed by anesthetic personnel because of its potential in cardiorespiratory depression. The best sedation regimen for deep sedation is still debated. However, many physicians are commonly used propofol with or without other sedative drugs for deep sedation in GIE procedures. Lera dos Santos and coworkers compared deep sedation with propofol and fentanyl with midazolam and fentanyl regimens during upper GIE procedure. The 200 patients were randomized into the two groups. The times to induction of sedation, recovery, and discharge were shorter in the propofol and fentanyl group than the midazolam and fentanyl group. The deep sedation events in the propofol and fentanyl were significantly greater than in the midazolam and fentanyl group. Oxygen supplementation was required in 42% of the propofol and fentanyl group and 26% of the midazolam and fentanyl group. Severe complications were none in both groups. Physician satisfaction was more satisfied with the propofol and fentanyl combination. The authors concluded that deep sedation frequently occurred with the combination of propofol and fentanyl. However, recovery was faster in the propofol-fentanyl group<sup>[28]</sup>.

Most of the ERCP procedures can be performed by using moderate sedation technique. Although, a moderate sedation level for ERCP seems to be sufficient for elderly patients, however, the literature has revealed the superiority of deep sedation in performing ERCP procedure. The anesthesiologist's presence is



mandatory in these cases. Propofol is the sedative agent of choice for sedation in ERCP procedure because of its fast distribution and fast elimination time without a cumulative effect after infusion, resulting in shorter recovery time. Due to its narrow therapeutic spectrum, careful monitoring is much more demanding in order to differentiate between moderate, deep sedation and general anesthesia. In addition, the anesthesiologist's presence is mandatory in these cases. Capnography and Bispectral index or Narcotrend monitoring of the level of sedation might be useful in titrating sedative drugs in ERCP procedure<sup>[29]</sup>. Furthermore, Nayar and colleagues evaluated the sedation-related complications for EUS procedures performed with the use of propofol deep sedation administered by MAC. They also compared these results with moderate sedation provided by the endoscopist. A total of 1,000 patients underwent EUS procedure with propofol deep sedation in two years was assessed. A total of six patients experienced complications. The complication rate in the propofol deep sedation group was 0.60%, compared with 1% in the meperidine and midazolam moderate sedation group. These complication rates were not significantly different between the two groups<sup>[30]</sup>.

In our previous study, we compared and evaluated the clinical efficacy of propofol and pethidine for deep sedation with midazolam and fentanyl for moderate sedation in colonoscopic procedure<sup>[31]</sup>. The study demonstrated that the efficacy of propofol and pethidine for deep sedation showed an advantage over midazolam and fentanyl for moderate sedation used for colonoscopy in term of procedure completion rate, patient's and endoscopist's satisfaction and ease of endoscopy. This might be due to the ease of applying and titrating the combination of propofol and pethidine to the directed target depth likely contributed to better sedation. However, deep sedation created a higher complication rate than moderate sedation<sup>[31]</sup>.

Because of propofol can produce severe cardiorespiratory depression, a combination of propofol and other sedative agents is commonly used. A combination of propofol and ketamine decreases the total dose of the sedative drugs and reduces serious adverse effects<sup>[22]</sup>. In addition, the use of diluted propofol could be utilized in this purpose. Sedation-related hypotension was significantly lower in the diluted propofol group than the undiluted propofol group<sup>[32]</sup>. Our previous study evaluated the efficacy and the rate of completion of colonoscopy in two different combination groups. The use of propofol combined with ketamine and propofol alone for deep sedation in colonoscopic patients was relatively safe and effective. All endoscopies were completely successfully. Sedation-related adverse events in both regimens were mild and transient<sup>[33]</sup>.

## PATIENT-CONTROLLED SEDATION

Patient-controlled sedation (PCS) is a new technique of administration for intravenous sedation. PCS devices deliver a predefined bolus of intravenous drug during a defined time, with or without a lockout interval. GIE procedure requires patient cooperation. The use of PCS for GIE procedure is reported in the literature. A previous study compared anesthesiologist-controlled administration of midazolam and PCS administration of propofol. The results of this randomized study showed that PCS administration of propofol was associated with better cooperation of patients as well as higher endoscopist and patient satisfaction. Time for awakening and discharge in the PCS group was shorter with propofol than with midazolam<sup>[34]</sup>. Patient-controlled TCI may be a further interesting step in the delivery of intravenous sedation.

Gillham and colleagues assessed the safety and efficacy of the

patient-controlled sedation with a TCI of propofol in 20 patients underwent ERCP procedure. An initial propofol target blood concentration (Ct) of 1.0 mcg/mL was supplemented on patient demand with a handset that, when pressed twice within 1 sec, increased the Ct of propofol by 0.2 mcg/mL. The maximum permissible target concentration was set at 3.0 mcg/mL to avoid oversedation. The system failed in one case because of patient confusion. No experiences of hemodynamic instability, airway obstruction, or significant oxygen desaturation were observed. Additionally, endoscopist and patient satisfaction were high. At the end of the procedure, four patients were oversedated, but all were awake within 5 min of arrival in the recovery area. This study demonstrated that patient-controlled sedation with TCI propofol was safe and effective. All patients were well satisfied with this sedation technique<sup>[35]</sup>.

Procedural sedation in the alcoholic patients is challenged. Dexmedetomidine is advocated for procedural sedation and reported effective for alcohol withdrawal. Mazanikov and coworkers evaluated the suitability of the PCS and dexmedetomidine in alcoholic patients during ERCP procedures. Fifty patients with chronic alcoholism scheduled for elective ERCP were randomized into the two groups: dexmedetomidine (loading dose of 1 mcg/kg over 10 min, followed by constant intravenous infusion of 0.7 mcg/kg/h) or normal saline. PCS with propofol-alfentanil was used by patients as a rescue method. Sedation was considered as successful if no intervention of an anesthesiologist was needed. The results demonstrated that dexmedetomidine alone was inadequate in all patients. Sedation was successful in 76% of patients in the dexmedetomidine group and in all patients in the placebo group. The incidence of sedation-related adverse events did not differ between the groups. However, dexmedetomidine was associated with delayed recovery. They concluded that PCS with propofol and alfentanil could be recommended for sedation in the alcoholic patients during ERCP procedure<sup>[36]</sup>.

## COMPUTER-ASSISTED PERSONALIZED SEDATION

Alternative techniques for sedation in GIE procedures have been developed. Improving sedation methods utilizing precise control of preferred target may increase patient satisfaction and practice efficiency. Computer-assisted personalized sedation (CAPS) offers the possibility of safe and effective minimal to moderate propofol sedation by non-anesthesiologists. The SEDASYS is the first CAPS system to receive US FDA approval. It aims to make the delivery of propofol sedation predictable, precise and safe by using computer algorithms to compute and deliver appropriate amounts of propofol, based on physiological parameters. Several studies with the use of SEDASYS system suggest that this system is safe for the use in patients with ASA physical status I and II undergoing routine GIE procedures<sup>[37]</sup>.

The feasibility of CAPS for facilitating the precise administration of propofol by endoscopist/nurse teams, achieving minimal to moderate sedation in patients underwent GIE procedures has been studied by Pambianco and colleagues<sup>[38]</sup>. Twenty-four adults per center in the United States and Belgium were enrolled. This technique demonstrated that patients responded to mild tactile and verbal stimuli in 99% of the time. Mean propofol doses in the United States and Belgium were 65.4 and 72.1 mg, respectively. The mean recovery times were 29 and 10 sec, respectively. Oxygen desaturation

happened in only 6% of patients. No device-related adverse events were noted.

Another study compared the safety and effectiveness of the SEDASYS System to the recent standard of care for sedation during routine GIE procedures. The 1000 adult patients with American Society of Anesthesiologists (ASA) physical status class I to III underwent routine colonoscopy or EGD procedures were randomized to two groups; sedation with the SEDASYS System (group S) and sedation with combination of benzodiazepine and opioid (group C). The oxygen desaturation and recovery time in group S were significantly lower than in group C. The patient and physician satisfaction in group S were significantly greater than in group C. All patients were predominately minimally and moderately sedated in both groups. The incidence of adverse events was 5.8% in the group S and 8.7% in the group C<sup>[39]</sup>.

## ADVANTAGES OF INTRAVENOUS SEDATION TECHNIQUES

The advantages of intravenous sedation in GIE procedures can result from the administrative technique or the pharmacological properties of the intravenous drugs. The therapeutic effect of sedative drug is seen as soon as it is administered to the patient. These effects are dependable and reproducible. Importantly, the entire administered dose reaches the systemic circulation immediately, and the dose can be accurately titrated against its response. In addition, no anesthetic machines or vaporizers are needed when only intravenous drugs are utilized for mild or moderate sedation. This technique could maintain a low level of pollution in the endoscopic theater.

Preventing nausea and vomiting is one priority in ambulatory patients, because post-procedural nausea and vomiting has been recognized as one of the main factors contributing to prolonged stay after ambulatory procedure or unintended return to hospital<sup>[40]</sup>. Several studies have demonstrated the antiemetic effect of propofol when used as an induction bolus or as a maintenance agent for general anesthesia or MAC. To date, propofol is usually used for GIE sedation in ambulatory cases.

Unsurprisingly, sedative drugs are commonly used for GIE sedation because of their anesthetic properties. Our previous study compared the effectiveness of diagnostic EGD with and without intravenous sedation in 170 adult patients. Patients were randomized into two groups: group C (topical pharyngeal anesthesia alone) and group I (intravenous sedation and topical pharyngeal anesthesia). All patients were topicalized with lidocaine viscous and spray. The patients in group I were sedated with midazolam 0.035 mg/kg and maintained with continuous propofol infusion. The result of the study showed that the use of sedation was the major determinant of patient satisfaction, but contributed to an increased recovery room time. Hypertension and tachycardia were the most complications in group C, and hypotension was the most complication in group I. This study confirmed that the efficacy of intravenous sedation technique was significantly greater than the topical anesthetic technique<sup>[41]</sup>.

## LIMITATIONS OF INTRAVENOUS SEDATION TECHNIQUES

Intravenous sedation for GIE procedure is a good strategy to increase efficacy as well as patient and endoscopist satisfaction<sup>[41]</sup>. However, these techniques in GIE procedures have some limitations. The use of specific equipment such as infusion pumps is required to guarantee a proper titration of sedation. These techniques are more expensive

and labor intensive than other techniques. Other limitations are predominantly the result of pharmacokinetic properties of the sedative drugs that direct drug concentration measurements are not available. The associations between infusion rates and acceptable effect-site concentrations are not readily obtainable. The elderly patient is a good example of this issue. Generally, intravenous sedative drugs could produce cardiorespiratory depression. Severe adverse events might be occurred in the patients with cardiorespiratory instability. Appropriate patient selection and adequate patient preparation are needed.

These techniques require a patent intravenous line which must be continued all through the GIE sedation. Venous cannulation is distressing to some patients, especially in children. Intravenous injection of drugs may cause local reactions, pain and technical problems. Consequently, administration and recovery times are required. In ambulatory cases, an escort is also needed. Additionally, costs related to sedation use in GIE procedures have often been considered when compared with topical anesthetic technique. Finally, physicians administered drugs for GIE sedation are required. Although, GIE sedation can be administered by the trained nurse, however, the nurse administering sedation must be skilled to manage the oversedated patients<sup>[42]</sup>. The registered nurse could take the responsibility to monitor the patient during and after GIE sedation. Several guidelines advise that oxygen supplementation should be performed during moderate and deep sedation<sup>[43]</sup>.

## SUMMARY

Sedation for GIE procedure could be effectively and safely accomplished with several intravenous techniques utilizing anesthesiologist or non-anesthetic personnel with appropriate monitoring. The growing importance of sedation for GIE procedures during the past decade has led to the development of efficient sedation techniques in terms of safety and quality of sedation and recovery. In these challenging purposes, intravenous sedation techniques have played an important role, as they provide safe, efficient and cost-effective technique. Significantly, appropriate sedation techniques need to be done. Hence, intravenous techniques used for GIE sedation in this manuscript should be discussed. Most of these techniques are commonly used in recent clinical practice.

## CONFLICT OF INTERESTS

The author declare that has no conflict of interests.

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