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Anesthetic Considerations for Adult Ambulatory Colonoscopy

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ABSTRACT

It is estimated that millions of colonoscopies are performed worldwide and the demand is growing further each year. Despite the introduction of smaller and more flexible endoscopes, colonoscopy is still an invasive procedure, causing physical and emotional discomfort that decrease patient satisfaction leading to unwillingness to participate in colorectal cancer screening with possible negative implications on both diagnosis and treatment. Proper sedation and analgesia, with or without alternative techniques, provide a high level of patient and physician satisfaction with a low risk of adverse events with improved recovery. Sedation providers, anesthesiologist or non-anesthesiologist, should be familiar with the states of sedation and analgesia, pharmacology of sedative and hypnotic drugs as well as cardiorespiratory support when required. Propofol should be administered only by individuals trained in the administration of anesthesia. Any type of sedation or analgesia cannot be considered minor, because it requires training, skill, experience and organization. Therefore, the use of sedation and analgesia should always be evaluated from a safety point of view. Patient preparation, pre-procedural evaluation, sedation and analgesia, recovery care and discharge should be performed according to guidelines.

Keywords: Colonoscopy; Sedation; Analgesia; Drugs; Monitoring; Complications; Recovery; Discharge

INTRODUCTION

Colonoscopy is an invasive procedure, often causing physical and emotional discomfort including pain, embarrassment, anxiety and fear [1]. These concerns may decrease patient satisfaction leading to an unwillingness to participate in colorectal cancer screening affecting negatively both the diagnosis and treatment. [2-5]. If no sedation is offered, the patient and the gastroenterologists should accept a lower chance of completing the procedure. Therefore, sedation and analgesia are commonly provided for the performance of colonoscopy [6,7]. Other non-pharmacologic methods such as music, the use of carbon dioxide instead of air for colon insufflation or warm-water instillation can be used as alternatives to pharmacologic sedation and analgesia [8-12].

This chapter focuses on the efficacy and safety of colonoscopy with or without sedation and analgesia, drug regimens and alternative techniques that may be used.

COLONOSCOPY WITH OR WITHOUT SEDATION AND ANALGESIA

Several earlier studies advocating unsedated colonoscopy reported no differences in terms of examination time, patient or gastroenterologist satisfaction [13-16]. Male gender, higher levels of education, and low anxiety scores were found to be associated with willingness to consider unsedated colonoscopy [17,18]. Although there is debate about whether sedation/analgesia is mandatory for colonoscopy, studies suggest that patients desire sedation [19,20]. Moreover, studies showed that a great amount of such procedures are terminated because of pain [21,22]. There are several factors that may account for pain during colonoscopy including looping of the colonoscope with resultant stretching of the colonic wall and mesentery, distension from air insufflation, force and torque on the insertion of colonoscope, and pain tolerance of the [23]. Therefore, sedation with or without supplemental analgesia is generally necessary for not only patient comfort and safety, but also for successful completion of the procedure [24].

PRACTICE PATTERNS

Sedation practices vary depending on national and cultural differences among countries ranging from no sedation to intentional general anesthesia. Moreover, there is also a wide variation in colonoscopy practice of healthcare facilities, endoscopists, sedation providers and patients among centers in the same country [25]. In United States more than 98% of colonoscopies are performed with sedation [26]. In Canada, more than 90% use sedation during colonoscopy [27]. In Australia, almost all routine colonoscopies are performed with sedation. However, in Europe, Asia and Africa the sedation rates vary among countries [28]. The use of sedation has become a standard practice during colonoscopy in Portugal and Italy [29,30]. Among the members of the Hellenic Society of Gastroenterology 78% use sedation in colonoscopies [31]. In Germany, 87% of

colonoscopies are carried out under sedation [32]. In Spain, 55% of gastroenterology units used sedation is colonoscopies [33].

GOALS OF SEDATION AND ANALGESIA

The main goals of sedation and analgesia during colonoscopy is to relieve anxiety, discomfort and pain, to provide amnesia, to increase patient tolerance for the procedure and to increase satisfaction for both patient and gastroenterologist [34]. On the other hand, sedation may result in catastrophic consequences to the patient including cardiopulmonary events such as hypoxemia, hypoventilation, airway obstruction, apnea, arrhythmias, hypotension, vasovagal episodes and even death [35,36]. Used agent should not suppress spontaneous respiration, cause hemodynamic instability and also should not have any other serious side effects [37]. Additionally, rapid recovery and early discharge is also important [38].

SAFETY OF SEDATION AND ANALGESIA

Besides its beneficial effects, sedation and analgesia may lead to complications including hemodynamic fluctuations, vasovagal response, airway problems and ventilatory impairment [39,40]. Herman et al. [41] reported that 17% of patients experienced a vasovagal episode during colonoscopy. Although many experienced gastroenterologists believe that these transient hemodynamic fluctuations have little clinical significance, Arrowsmith et al. [42] analyzed data from over 21 000 procedures and found that the incidence of serious cardiopulmonary complications and death were 0.5% and 0.03% respectively.

There are important issues in patient safety. These include the definition sedation and its levels, the need for a detailed pre-procedural patient evaluation, the clinical assessment or the use of a specific monitoring for the depth of sedation, the presence of one individual responsible from patient monitoring and trained personnel in anesthetic pharmacology and advanced life support skills [43]. In addition, in patients with significant sedation-related risk factors, or if deep sedation is necessary, it is recommended that an anesthesiologist be consulted [44].

Definition of Sedation and Analgesia

Sedation and analgesia is defined as a continuum of states ranging from minimal sedation through general anesthesia. Patients receiving sedative/analgesic agents may move within one or more of these states during colonoscopy and it is not always possible to achieve the intended state of sedation/analgesia. In these circumstances, inadequate sedation/analgesia may result in patient discomfort, agitation or injury because of lack of cooperation or adverse physiologic or psychological response to stress. Conversely, unintended oversedation may result in cardiac or respiratory depression. Therefore, each individual providing sedation/analgesia should have adequate skills and equipment to successfully rescue patients from deeper levels of sedation and analgesia than intended [44]. Characteristics of minimal, moderate, deep sedation and general anesthesia are given below.

- Minimal Sedation is defined as a drug-induced state during which patients respond normally to verbal commands. Ventilatory and cardiovascular functions are unaffected.
- Moderate Sedation and Analgesia is defined as a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.
- Deep Sedation and Analgesia is defined as a drug-induced depression of consciousness during which patients respond purposefully following repeated or painful stimulation. Ventilatory function of the patient may be impaired requiring assistance in maintaining a patent airway. Cardiovascular function is usually maintained.
- General Anesthesia is defined as a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. Maintenance of ventilatory function is often impaired requiring assistance for a patent airway and positive pressure ventilation for ventilatory depression. Cardiovascular function may also be impaired.

Pre-Procedural Evaluation and Laboratory Tests

A detailed history should include age, pre-existing diseases, previous experience with sedation, analgesia or anesthesia, drug allergies, tobacco, alcohol or substance abuse. Physical examination should include vital signs, auscultation of the heart and lungs, and airway evaluation. Patients may be classified according to a risk stratification. The American Society of Anesthesiology (ASA) scoring system routinely used by the anesthesiologists is helpful in the assessment of patient's physical status. Pre-procedural laboratory testing should be guided by the patient's medical condition [44].

Time and nature of last oral intake should also be questioned. It is recommended that for elective procedures the patient not ingest solid food for 6 h or more prior to the administration of sedation and analgesia, but may have clear liquids up to 2 h before the administration of sedation and analgesia [45]. Fortunately, patients do not eat anything in order to adequate bowel preparation before a colonoscopy. On the other hand, any options for colon preparation [diet and cathartic regimen, gut lavage, and phosphate preparations] may affect electrolyte balance and increase the risk of patients [46].

Monitoring Vital Signs and Depth of Sedation

The literature suggests that monitoring oxygenation and ventilation decreases the likelihood of adverse outcomes in patients receiving sedation and analgesia during colonoscopy. Additionally, monitoring of vital signs including blood pressure and heart rate may reduce the risk of adverse events [44]. The guidelines recommend that pulse oximetry be continually monitored and that vital signs be recorded regularly throughout the procedure. However, because pulse oximetry is a measure of oxygenation not ventilation, patients may have satisfactory oxygenation in the early

course of prolonged apnea, particularly if they are receiving supplemental oxygen. Therefore, guidelines also recommend that ventilation be monitored by clinically [observation, auscultation] or capnography [47]. Especially, if the patient is in a state of deep sedation, an individual whose sole responsibility is patient monitoring should be present. Since, the patient's sedation level may move to another stage during colonoscopy, the literature suggest that the assessment of the state of consciousness periodically from the beginning to the end of the procedure including recovery is beneficial [44]. The most common used scales for depth of sedation are Ramsay Sedation Scale and Observer Assessment of Alertness Score [48,49]. Moreover, Bispectral Index Monitoring can be used during colonoscopy [50].

Trained Personnel

It is also recommended that personnel who administer the sedation and analgesia be trained in the pharmacology of sedative and analgesic medications, as well as their antagonists. These individuals should be trained to recognize the levels and the complications of sedation and analgesia and capable of establishing a patent airway and positive pressure ventilation. An individual or team with advanced cardiac life support should be available [44].

Equipment

The literature and guidelines recommend that a reliable oxygen source, self-inflating resuscitation bag, emergency equipment to establish a patent airway, suction, resuscitation medications, sedative-analgesic drugs, pharmacologic antagonists, monitoring equipment and sufficient space should be present wherever sedation and analgesia are administered [51].

Recovery and Discharge

Each patient should be observed and monitored for sedation level and vital signs until they reach the baseline level of consciousness and are no longer at risk for respiratory depression, because a great amount of adverse events occur in the recovery or postoperative periods [52]. Scoring systems such as Modified Aldrete Scoring System seems to be the most popular tool in the assessment of recovery. During recovery, effects of reversal agents such as flumazenil or naloxone may dissipate while the sedative is still active, leading to re-sedation [53]. Therefore, routine administration of a reversal agent is not suggested [54].

Moreover, each gastroenterology unit should have a policy for discharge criteria [55]. Discharge criteria should be designed to minimize the risk of unexpected readmission as well as morbidity following discharge.

COMPLICATIONS RELATED TO SEDATION AND ANALGESIA

Sedation and analgesia may lead to adverse events depending on a number of factors, including the type, dose and mode of administration of sedative drugs, as well as the patient's age and physical status. Hypotension, hypertension, desaturation, bradycardia, arrhythmia, respiratory

depression, vomiting, cardiac arrest, angina, hypoglycemia, and/or allergic reactions have been reported [44]. It has been suggested that a greater level of sedation has the potential to result cardiorespiratory complications and an increased risk of colon perforation because patients are not able to report pain, an important warning signal of impending perforation although there is no strict evidence to support this claim [56,57]. O'Connor et al, [58] reported that 54% of patients receiving diazepam or midazolam plus meperidine had an oxygen saturation [SaO_2] of less than 90% . The administration of propofol as a sedative agent resulted in a severe hypotension and desaturation in 0.5% and 2.4% of patients respectively [59]. Patients who are ASA physical status III and IV are found to be at greater risk for oxygen desaturation than ASA physical status I and II patients [60].

Type of Sedation

Minimal and deep sedation have advantages and disadvantages. Several studies showed that minimal sedation is associated with more intraoperative agitation and recall rates, but resulted in less cardiorespiratory complications and faster recovery than deep sedation [61,62]. Patient movement during colonoscopy may affect the procedure negatively leading to inadvertent perforation of the colon [63]. However, there are safety concerns with deep sedation. In patients receiving deep sedation, there was a lower rate of procedural recall and fewer episodes of patient movements during the procedure. On the other hand, more than 20% of patients required basic airway maneuvers [38].

Medication for Sedation and Analgesia

Traditionally, colonoscopy procedures have been performed with conscious sedation, which involves the administration of a benzodiazepine and an opioid [64]. The benzodiazepine is utilized to decrease anxiety and provide amnesia while the opioid is used for pain relief. However, the use of propofol with a shorter recovery time in colonoscopy practice is significantly increased [65].

Benzodiazepines

Midazolam: A large number of clinical trials showed that midazolam is the most likely used drug for amnesia and sedation in colonoscopy [66]. It has been used alone or in combination with a variety of other drugs including meperidine, opioids, ketamine and propofol [67,68].

Remimazolam: Remimazolam, a short-acting benzodiazepine with organ-independent metabolism with rapid onset, appears to have potential advantages over other currently available benzodiazepines. However, its respiratory depressant effect has been reported in numerous studies [69].

Hypnotics

Propofol: The use of propofol for sedation during endoscopic procedures has increased in recent years mainly because of its favorable pharmacokinetic profile compared with traditional sedative

drugs such as benzodiazepines and opioids [26]. Clinical trials and meta-analyses reported that propofol is frequently used during colonoscopy, alone or in combination with opioids, benzodiazepines or other sedative agents [70]. Its sedative, hypnotic, antiemetic and amnesic properties has advantages of rapid onset of action and short recovery profile with high patient satisfaction for outpatient colonoscopy [71,72]. The disadvantages are its narrow therapeutic range, pain on injection and potential to cause respiratory and cardiopulmonary depression [73]. Even low-dose propofol used for minimal-to-moderate sedation may impair ventilation [74]. Moreover, in contrast to benzodiazepines and opioids, no reversal agent is available.

Fospropofol: Fospropofol is a water-soluble prodrug of propofol, with pharmacokinetic and pharmacodynamic properties differ from propofol emulsion [75]. After intravenous injection, propofol is released from fospropofol by tissue alkaline phosphatases, resulting in lower peak concentrations and a more gradual decline in drug concentrations compared with standard propofol administration. Adverse events such as paresthesia and pruritus are mostly transient and self-limiting [76].

Etomidate: In two randomized double-blind trial, etomidate in combination with fentanyl and remifentanil has been compared with propofol. Toklu et al. [77] reported that etomidate-remifentanil administration results in more stable hemodynamic responses and shorter recovery and discharge times than propofol-remifentanil administration during colonoscopy. In a similar study, Banihashem et al. [78] found that the combination of etomidate-fentanyl provided faster recovery time with comparable hemodynamic stability than the combination of propofol-fentanyl in adult patients undergoing colonoscopy.

Ketamine: Ketamine, has been safely used to complement sedation for colonoscopy [79]. Khajavi et al. [80] found that ketamine-propofol combination resulted higher patient satisfaction than ketamine-fentanyl combination. Türk et al. [81] reported that ketamine-propofol combination provided better hemodynamic stability and quality of sedation compared with alfentanyl-propofol combination in elective colonoscopy with a prolonged discharge time. In a randomized double blind prospective trial, addition of low-dose ketamine to midazolam-fentanyl-propofol-based sedation for outpatient colonoscopy resulted in more rapid and better quality of sedation, less propofol consumption, more stable hemodynamic status, and less adverse effects with similar recovery times [82].

Dexmedetomidine: Dexmedetomidine is a selective α [2]-adrenergic receptor agonist used for the sedation of mechanically ventilated adult patients in an intensive care setting and in non-intubated adult patients prior to and/or during surgical and other procedures [83]. Dexmedetomidine has been shown to be safely used as a sedoanalgesic agent in colonoscopies [84]. However, Jalowiecki et al. [85] concluded that sole use of dexmedetomidine to provide analgesia/sedation for colonoscopy may lead to pronounced hemodynamic instability and prolonged recovery.

Nitrous oxide: Nitrous oxide [N_2O] and Oxygen [$O_{2]}$ mixture has been shown as an alternative to intravenous analgesia in patients undergoing colonoscopy [86]. Systematic reviews and randomized clinical trials reported that N_2O provides more rapid recovery and discharge with comparable analgesia to intravenous sedation [87,88].

Opioids

Fentanyl: Fentanyl, a μ-opioid receptor agonist, is characterized by a rapid onset and short duration of action. The action of the drug is related to its agonism of the opioid receptors. Its 100 μg is equivalent to 75 mg of meperidine in terms of analgesic activity. It has been used in combination with midazolam, mainly in patients undergoing lower GI endoscopy [52,56,68,78,80,82,86].

Alfentanyl: Alfentanyl is an opioid analgesic with a rapid onset and short duration of action. Recently, it was shown that patient-controlled analgesia pumps and sedation with alfentanyl and fentanyl for colonoscopy are safe, feasible, and acceptable to most patients, although a shorter sedation time makes alfentanyl more attractive, as it reduces the recovery time [81,89].

Remifentanil: Remifentanil, alone or in combination with propofol has been used in several clinical trials in patients undergoing gastrointestinal endoscopic procedures. Manolaraki et al. [90] reported that remifentanil during colonoscopy provides sufficient pain relief with better hemodynamic stability, less respiratory depression, and significantly faster recovery and hospital discharge than moderate sedation with midazolam and pethidine. Moerman et al. [91] showed that remifentanil is superior in terms of pain relief, recovery profile and hemodynamic profile with higher patient satisfaction than propofol during colonoscopy. It seems that remifentanil patient-controlled analgesia is safe and effective for inducing sedoanalgesia during colonoscopy [92]. Similarly, Mandel et al. [93] showed that patient-controlled sedation with propofol/remifentanil provided more rapid recovery than midazolam/fentanyl group. Akcaboy et al. [94] concluded that low-dose remifentanil infusion with intermittent bolus injections can provide adequate sedation, amnesia and better analgesia than propofol infusion, but nausea and vomiting may be a problem during the recovery phase of sedation and analgesia.

Mode of Administration

Sedation and analgesia can be administered by an anesthesiologist or non-anesthesiologist as intermittent boluses or continuous infusion throughout the procedure. Moreover, patient controlled sedation and target controlled infusion are alternative modes of drug delivery.

Anesthesiologist versus non-anesthesiologist debate

Debate exists on whether the staff administering sedation should be an anesthesiologist, a gastroenterologist or a non-anesthesiologist. Although, reports suggesting the safety of sedation administered by non-anesthesiologists exist in the literature, incidence of adverse hemodynamic and airway events were reported as 1.44% and 0.74% respectively [95-100]. The reasons behind nurse rather than physician organizations seems to be likely economic [101-102].

Anesthesiologist administered sedation leads to a substantial increase in healthcare costs, which is challenged by healthcare insurance companies in some countries [20]. Another advantage is the autonomy of not having to wait for anesthesiologist. In some countries, nurses are trained to administer sedation, others have used computer feedback systems to provide sedation during colonoscopy [103]. In United States, anesthesiologists and certified registered nurse anesthetists are involved when propofol is used in approximately 70% and 18% of endoscopies, respectively [26]. American gastroenterology associations agree that routine anesthesiologist assistance with endoscopy is not warranted for average-risk patients except high risk patients [20]. On the other hand, improper use of sedation agents by unqualified persons may result complications. Anesthesiologists involved in the care of many patients undergoing colonoscopy with their specific expertise in the pharmacology, physiology and clinical management of patients receiving sedation and analgesia [44]. Therefore, although the debate seems to be continued for a long time, anesthesia provider participation rates for colonoscopies are increasing [66,102]. The role of the anesthesiologists in the field of colonoscopy is important not only for participating in the care of high risk patients, but also contributing in the improvement of sedation guidelines for both anesthetic and non-anesthetic personnel for safety and quality of care [44,104].

There is also controversy regarding the safety of propofol when administered by non-anesthesiologists. Most authors recommend that sedation with propofol should be performed by a registered nurse only in low risk patients [105]. ASA and the American Association of Nurse Anesthetists issued a joint statement in 2004 that, propofol for sedation/analgesia should be administered only by persons trained in the administration of general anesthesia. This restriction is concordant with specific language in the propofol package insert [106]. In 2010 members of the European Society of Gastrointestinal Endoscopy (ESGE), the European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) and the European Society of Anaesthesiology (ESA) published a guideline on non-anesthesiologist administration of propofol for gastrointestinal endoscopy [107]. However, at the ESA General Assembly held in Amsterdam on 15 June 2011, the majority of the active members approved the motion to retract the endorsement, because a majority of the national societies of the ESA felt unable to support this guideline following publication [108]. Consequently, the ESA retracted its endorsement of this guideline [109].

Patient-controlled sedation (PCS)

Patient-controlled sedation (PCS) has been evaluated and found to be safe and effective method in colonoscopy [110]. In PCS, the medication is self-administered by the patient in response to pain or discomfort. Specialized pumps with a lockout time are used that deliver a preset dose of medication in response to a patient pressing a handheld button. However, because the patient press the button after the feeling of pain the desired sedation effect may delay resulting in inadequate sedation and analgesia [111].

Target-controlled infusion (TCI)

Target-controlled infusion (TCI) is a computer-controlled infusion system designed to deliver intravenous drugs according to the drug's pharmacokinetics, using an infusion pump controlled by a computer. These systems use complex mathematical models to compute the drug dosage and they may account for various patient characteristics that alter drug disposition [112]. Propofol is the most frequently infused drug via TCI [113]. However, most of these techniques are limited to provide minimal sedation to minimize hemodynamic changes and allow faster recovery [114].

Patient's Physical Status

The incidence of morbidity and mortality increases in ASA III or higher patients compared with ASA I-II patients [44,97]. Additionally, male sex, increased body mass index and high level of sedation are found as independent predictors of sedation-related adverse events [115].

NON-PHARMACOLOGİCAL METHODS

Traditionally, air insufflation was used to advance the colonoscope through the colon. However, many studies and meta-analyses showed that carbon dioxide insufflation is safe in patients without severe pulmonary disease, and is associated with decreased bowel distension and post-procedural pain [116]. Several studies investigated the effect of instillation of warm water [hydro-colonoscopy] instead of air and found less pain, reducing the need for sedation/analgesia, and improving patient acceptance for colonoscopy [117]. Listening relaxing music has been shown to decrease anxiety levels and discomfort during colonoscopy [10,118].

CONCLUSION

Although more than fifty years past since the introduction of flexible colonoscope in clinical practice, psychological and religious barriers, fear of the procedure related to pain or possible unfavorable diagnosis, are still making colonoscopy difficult. Pharmacological sedation and analgesia as well as non-pharmacological methods have beneficial effects, in terms of willingness to participate colonoscopy, control of pain and discomfort, ease of cecum intubation leading to high patient and gastroenterologist satisfaction. However, the controversy regarding the administration of sedation by an endoscopist or an anesthesiologist continues. It is essential for sedation providers to be familiar with the states of sedation and analgesia, use of sedative and hypnotic drugs as well as cardiorespiratory support. Another controversy on whether or not a non-anesthesiologist can administer propofol for colonoscopy seems to be continued, despite the recommendations of Anesthesiology Societies regarding propofol should be administered only by persons trained in the administration of general anesthesia. Any type of sedation, analgesia or anesthesia performed outside the operating room cannot be considered minor, because it requires training, skill, experience and organization. Needs for sedation and analgesia should be evaluated from a safety point of view. Patient preparation, pre-procedural evaluation, sedation and analgesia should be performed utilizing the same standards as used in the operating room.

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