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Sedation-Related Adverse Events in Gastrointestinal Endoscopy

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Review

Gastrointestinal endoscopy is a means to improve the accuracy of clinical diagnosis and effectiveness of treatment of gastrointestinal diseases and is widely used in the treatment of gastrointestinal diseases. Most gastrointestinal endoscopy examinations are performed under anesthesia under non-tracheal intubation conditions, lacking airway protection. In addition to operation-related complications such as bleeding, perforation, local infection, and gas-related complications, the occurrence of sedation-related adverse events also raises concerns.

1.Respiratory system

1.1 Hypoxemia

The current anesthetic protocol for Gastrointestinal endoscopic (GIE) procedures is mainly based on propofol sedation, supplemented by opioid analgesics. hypoxemia is one of the most common sedation-related adverse events, often occurring due to respiratory depression, airway obstruction, and ventilation difficulties, with an incidence of 7% - 31% **[1,2]**. Episodes of hypoxemia are usually mild and improved by jaw support, placement of oropharyngeal or nasopharyngeal ventilation tubes, etc. But severe or prolonged hypoxemia requiring intermittent mask ventilation or tracheal intubation. Prolonged hypoxemia can further lead to serious complications, including myocardial ischemia, cardiac arrhythmias, or permanent neurological damage. However, even transient hypoxemia reduced to 90% is associated with prolonged hospitalization, postoperative admission to the ICU, high costs, and increased chances of readmission after discharge **[3]**. Previous studies have shown that elderly (>65 years) and obese patients (BMI >28 kg/m2) are prone to angry tract obstruction; patients with combined chronic obstructive pulmonary disease and severe reflux esophagitis are more likely to have choking cough. In addition to the above factors, risk factors for hypoxemia include hypertension, diabetes mellitus, heart disease, high ASA classification, and concurrent gastroscopy and colonoscopy **[4,5]**. Several methods have been reported to reduce the incidence of hypoxemia, with continuous low dose propofol administration6 and reduced drug push rate, as well as to reduce other adverse effects and improve comfort **[6]**. High-flow nasal oxygenation (HFNO)5, using high-flow constant-concentration warmed and humidified oxygen, provides continuous positive airway pressure (8 cmH2O), reducing the risk of hypoxemia and the need for airway interventions, while improving patient comfort. However, it may lead to gastric insufflation and increase the risk of regurgitant aspiration due to its maintenance of high positive air pressure **[7]**.

1.2 Pulmonary aspiration

Because the protective reflexes of patients disappear under anesthesia, once the gastric contents reflux, it is easy to enter

the respiratory tract causing reflux misaspiration. Despite the routine abstinence from drinking and eating before painless endoscopy, the risk of aspiration pneumonia during painless gastroscopy is significantly increased, the risk of aspiration pneumonia was significantly increased when gastroenteroscopy was performed under sedation **[8]**.

The increased risk of reflux aspiration is associated with gastroesophageal reflux, esophageal stricture, and impaired gastric emptying, for which guidelines recommend appropriate prolonged fasting and placement of gastrointestinal decompression if necessary **[9]**. However, studies have shown that routine fasting does not achieve complete gastric emptying and differences in gastric acid pH, and gastric ultrasound in patients undergoing elective surgery without risk factors for delayed gastric emptying It was found that after fasting, there was still a large amount of gastric fluid in about 6% of patients and solid contents in 1.7% of patients **[10]**. Even in the absence of relevant high-risk factors, unanticipated gastric retention can occur during endoscopy, and such patients may have undiagnosed diabetes mellitus, gastrointestinal tumors, etc. Gastric ultrasound can provide a visual basis for judgment, and before induction of anesthesia, gastric ultrasound is more effective than simple fasting instructions It is more likely to ensure gastric emptying, and if solid gastric contents are found, anesthesia should be delayed or appropriate precautions should be taken to prevent inadvertent aspiration. However, for such patients, the ASA classification may not suggest the presence of relevant high-risk factors, so is there a better evaluation index for the risk of reflux aspiration in such patients who are not extubated.

In patients clearly at high risk for regurgitant malaspiration, the choice of conscious analgesia allows both the preservation of protective reflexes and the ability to reduce examination discomfort. In patients with unanticipated gastric retention under sedation, choosing a head-high position to avoid retraction of the scope and timely arousal may be beneficial in reducing the incidence of reflux. During the examination, if reflux occurs, the oropharynx should be immediately suctioned; the patient should be placed in a head-down position and changed to a right-sided position **[9]**.

2.Cardiovascular system

Endoscopic operation itself on the stimulation of the vegetative nerves, sedation and the role of anesthetic drugs may cause arrhythmia, sinus bradycardia or tachycardia to suspend the operation, timely symptomatic treatment can be improved. Hypotension is defined as systolic blood pressure below 90 mmHg or 20% below the basal value, loss of body fluids due to fasting and bowel washes, myocardial depression and vasodilation of anesthetic drugs may cause hypotension **[11]**. Patients with reduced cardiovascular function are more susceptible to cardiovascular system events, including intraoperative hypotension, malignant arrhythmias, myocardial ischemia, and myocardial infarction. Optimizing preoperative preparation is particularly important, and it was found that preoperative ultrasound measurement of IVCD, when IVCDmax <1.25, was more likely to result in hypotension during anesthesia **[12]**. Both oral multivitamin carbohydrate or intravenous infusion before surgery were beneficial in maintaining circulatory stability and did not significantly reduce the occurrence of intraoperative hypotension, which may also be due to a relatively small sample size **[13]**. While different intraoperative drug regimens, propofol combined with diazoxide did not differ from sufentanil and fentanyl on intraoperative circulatory effects, but the diazoxide group reduced respiratory risk, which could reduce propofol dosage and shorten the time to awakening **[14]**.

With or without sedation, increased myocardial oxygen demand and decreased myocardial perfusion during endoscopy, hypertension and tachycardia are associated with increased oxygen consumption, whereas hypotension and bradycardia are capable of causing inadequate coronary blood supply, and angina pectoris or myocardial infarction may occur. Preoperative identification of high-risk patients, detailed information on current antihypertensive medications, anti-anginal and anti-arrhythmic therapy, continuation of relevant medications before the examination, and intraoperative preoxygenation and continuous oxygen for high-risk patients are all beneficial in reducing circulatory complications **[11]**. In addition, the relevant departments should be consulted before the examination to assess and improve the current comorbid

conditions, inform patients of the relevant risks before the examination, and use relevant at the same time, the dose of anesthetic drugs should be reduced to shorten the examination or operation time, and for very high-risk patients, gastroscopy can be performed in the operating room. For patients with angina pectoris during endoscopy, sublingual nitroglycerin and oxygen inhalation should be given and the examination should be stopped, and electrocardiogram and other tests should be performed in time to detect myocardial infarction.

3.Internal environment

Electrolyte disturbance and dehydration are relatively common problems in gastrointestinal endoscopy, and intravenous rehydration is not routinely performed after the administration of bowel preparation fluid to patients who undergo bowel preparation, which can cause electrolyte disturbance in addition to water loss. 23.6% of patients developed hypokalemia after bowel prep **[15]**. And, depending on the degree of hypokalemia, oral or intravenous potassium supplementation was chosen preoperatively, with no serious adverse events related to hypokalemia, but recovery from anesthesia was not studied. In one meta-analysis, hypokalemia was found to occur in 17.2% of patients in the general population after bowel preparation with sodium phosphate preparations, compared with 4.8% of patients after PEG bowel preparation, and the current clinical use of small volume preparations such as SPMC and PEG-asc is more frequent, but no large sample studies are available **[16]**. Hypokalemia may cause muscle weakness, constipation and nausea and vomiting and other symptoms, but may also cause severe symptoms such as paralysis, convulsions, arrhythmias, coma and death. Fasting with solids for at least 8 hours and liquids for at least 2 hours is routine before painless endoscopy; in practice, patients may be fasted for longer due to the uncertainty of the examination time, and dehydration may cause adverse effects such as thirst, anxiety, hypoglycemia, irritability, postoperative nausea and vomiting, as well as being associated with increased postoperative delirium, which affects the patient's rapid postoperative recovery **[17]**. European guidelines for bowel preparation for colonoscopy recommend using high or low volume PEG-based, SPMC and PEG-asc bowel preparation regimens without routine use of NaP, especially in patients with renal insufficiency or high-risk factors. The combination of drugs is not recommended for constipated patients **[18]**. In contrast, in our gastrointestinal endoscopic bowel preparation, pre-administration of laxatives or gastrointestinal stimulants is recommended for constipated patients, and there are no reports on the effects of this drug regimen on the body's electrolytes **[19]**.

Even if only an examination is performed, preanesthetic intravenous fluids not only replenish blood volume, maintain water and electrolyte balance, improve patient comfort, and shorten the time to complete recovery from anesthesia.12 In addition, a shorter fasting period not only maintains preoperative glucose, insulin, potassium, and sodium levels at higher levels, but also reduces the incidence of postoperative nausea and vomiting **[20]**.‘In a study related to thyroidectomy thyroidectomy-related study’ **[21]** oral low-concentration carbohydrate 2 hours before surgery relieved patients' discomfort such as hunger, thirst, and anxiety, increased patient comfort, and also reduced the incidence of postoperative nausea and vomiting, but whether there was any effect on electrolytes was not compared, and whether there was an increased risk of reflux aspiration for gastrointestinal endoscopy performed in an unintubated general anesthetic fashion without gastric emptying checks. Although the guidelines recommend prolonging the duration of abstinence from alcohol and food for patients with combined gastroesophageal reflux, gastrointestinal obstruction, and impaired gastric emptying, for most outpatients, the use of oral carbohydrates 2 hours before surgery, along with the assessment and correction of patients' preoperative electrolyte disturbances, may also reduce the incidence of related adverse effects.

4.Nausea and vomiting

PONV refers to nausea and vomiting within 24 h after surgery, one of the most common adverse reactions to anesthesia, with an incidence of up to 30% and up to 70% in high-risk patients, and is influenced by individual patient quality, anesthetic medication, type of surgery and operating time and other factors. Previous studies have shown that

young women are the main independent and strongest risk factors for PONV, non-smoking, history of PONV and motion sickness, opioid use will increase the occurrence of nausea and vomiting. General anesthesia, inhalation anesthetics, and length of anesthesia can have an effect on nausea and vomiting. In addition, patients undergoing painless gastrointestinal endoscopy, the mechanical irritation of the endoscope to the mucosa of the gastrointestinal tract, inadequate suction after insufflation, and irritation of the throat are related to the guidelines recommend prophylaxis for patients with moderate and high risk of PONV, butylphenols, corticosteroids, anticholinergics, 5-HT3 receptor antagonists, neuro kinin (NK)-1 antagonists and other drugs have some intervention effect on nausea and vomiting **[22,23]**.

As mentioned previously, electrolyte disturbance, dehydration, and prolonged fasting may be associated with postoperative nausea and vomiting. In addition to routine application of antiemetic medications for prevention in high-risk patients, whether preoperative volume assessment, electrolyte examination to assess the internal environment and correct hypovolemia, hypoglycemia, and electrolyte disturbance may also reduce the occurrence of postoperative nausea and vomiting. Different anesthetic regimens also have an impact on complications, and the incidence of hypotension, arrhythmias, oxygen saturation below 85%, respiratory depression, and regurgitant aspiration is significantly higher in painless gastrointestinal endoscopy performed under general anesthesia compared with conscious sedation **[24]**. For patients with risk factors, conscious sedation may be more beneficial for rapid postoperative recovery.

Although painless gastrointestinal endoscopy has been widely used, complications related to intraoperative and postoperative sedation still occur. The type, dose, and mode of intraoperative anesthetic drugs, as well as the patient's age and underlying disease, are among the risk factors for related complications. Although most of these adverse reactions are mild and can improve rapidly with symptomatic treatment, more serious complications can occur. Therefore, preoperative assessment of anesthesia risks and taking appropriate preventive measures are currently important aspects that can improve patient prognosis and enhance comfort.

At present, there is no uniform standard for preoperative assessment of painless endoscopy, including painless gastroscopy, painless colonoscopy and painless fibrinoscopy, and the American Society of Anesthesiologists (ASA) classification and grading of patients' physical condition is the most widely used index among the tools for assessing painless endoscopy. The ASA score is the most widely used tool for assessing painless endoscopy, and many hospitals in China also use the ASA score as the main assessment basis, but its scope is broad. Previous studies have identified a risk screening index system for painless gastroscopy through expert consultation and interviews, and subsequently included patients 844 for risk index screening, and finally further tested the efficacy of the risk model and proposed a model for predicting adverse events in painless gastroscopy **[25]**, but it has not been further practiced. In painless endoscopy, it is important to establish a better and more applicable preoperative assessment program for endoscopy, screen high-risk patients, and develop standard preventive measures to reduce complications and improve patient comfort, as to how to perform rapid and accurate preanesthesia assessment.

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