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Review Article

Anesthetic premedication: New horizons of an old practice

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ABSTRACT

The practice of anesthetic premedication embarked upon soon after ether and chloroform were introduced as general anesthetics in the middle of the 19th century. By applying opioids and anticholinergics before surgery, the surgical patients could achieve a less anxious state, and more importantly, they would acquire a smoother course during the tedious and dangerous induction stage. Premedication with opioids and anticholinergics was not a routine practice in the 20th century when intravenous anesthetics were primarily used as induction agents that significantly shorten the induction time. The current practice of anesthetic premedication has evolved into a generalized scheme that incorporates several aspects of patient care: decreasing preoperative anxiety, dampening intraoperative noxious stimulus and its associated neuroendocrinological changes, and minimizing postoperative adverse effects of anesthesia and surgery. Rational use of premedication in modern anesthesia practice should be justified by individual needs, the types of surgery, and the anesthetic agents and techniques used. In this article, we will provide our readers with updated information about premedication of surgical patients with a focus on the recent application of second generation serotonin type 3 antagonist, antidepressants, and anticonvulsants.

1. Introduction

Modern anesthesia thrived in the middle of the 1840s when the Scottish obstetrician Simpson discovered the anesthetic qualities of chloroform and applied it to his patients during childbirth, and the American dentist Morton first publicly demonstrated diethyl ether as an inhaled anesthetic at the Ether Dome of Massachusetts General Hospital in Boston, USA. Compared with the halogenated inhalational anesthetics we use today, diethyl ether is notorious for its long duration of induction time. Patients often suffered a long period of involuntary movement, anxious feeling, and excessive salivation before they could finally be put to sleep. Such behaviors can be attributed mainly to the high blood solubility of diethyl ether. The partition coefficient of diethyl ether is 12, compared with that of 1.4, 0.65, and 0.45 of other ether derivatives of isoflurane, sevoflurane, and desflurane, respectively. Guedel's signs were used to describe the long induction time of ether anesthesia, which included four stages (analgesia stage, excitement stage, surgical anesthesia stage, and respiratory paralysis stage); Stage 3, i.e., surgical anesthesia can be divided into four planes, according to the patterns of muscle tone, breathing, and eye movement.[1] The Guedel's signs are scarcely used today during induction with either an intravenous anesthetic or an inhalational anesthetic that has a lower blood solubility.

2. Past, present, and future of premedication

2.1. History of premedication

The concept of anesthetic premedication was initially developed to counteract the side effects of general anesthesia when ether and chloroform were widely used as inhalational anesthetics in the 1850s.[2] Two physicians, Nussbaum in Germany and Bernard in France, in 1864 simultaneously found that subcutaneous morphine can relax patients and intensify chloroform anesthesia. At the same time, another French scientist Dastre found that atropine can decrease salivation and antagonize the effects of respiratory

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depression and vomiting associated with morphine. As a result, morphine and atropine became popular as anesthetic premedication in the late 19th century.[3] It was not until 1911 when Dudley Buxton published the first paper regarding the use of morphine, atropine, scopolamine, and other similar agents prior to inhalation anesthesia that anesthetic premedication became a debated issue and drew more attention of anesthesiologists.[4]

2.2. Current practice of premedication

The practice of anesthetic premedication in surgical patient is no longer a routine procedure today. There are several reasons to explain why we do not give medication to every patient before sending them to the operating theater. The main reason is that the induction time of general anesthesia in current practice is much shorter than that of ether anesthesia. We now routinely use intravenous anesthetics as induction agents; for most intravenous agents, onset of action occurs within 60 seconds. Patients who do not have venous access, such as children undergoing an operation in an outpatient setting, can be given sevoflurane as an induction agent via a face mask. Despite having some involuntary movements (excitement stage of Guedel's sign), these children can easily be made sleep in 1 minute due to the low blood solubility of sevoflurane.

The issue of patient safety is another concern of anesthetic premedication. When patients are premedicated, they must be put into surveillance to monitor the vital signs and the potential side effects of medication when they are in the ward, during transport to operating theater, or when they are in the waiting area of the operating theater. We usually do not monitor vital signs of patients while they are still in the waiting lounge. If premedication becomes a routine practice in a hospital, more manpower is needed to take care of these patients, leading to an increase in costs; for this reason most of the hospitals do not perform this at present. From the viewpoint of efficacy of medication, patients will not obtain the beneficial effects of premedication if they receive their medication too early or too late prior to operation. In a busy operating theater of a medical center where a lot of patients are ready to undergo surgery, the operation is often delayed or conducted earlier, making the efficacy of premedication unpredictable.

We should also take “street readiness” of patients into account. At present, more operations are performed on an outpatient service basis in medical centers. After surgery, patients need to resume their normal daily activity as soon as possible. If the side effects of a premedication affect the functional recovery following an outpatient operation, most patients will not be willing to accept the medication.

2.3. Future direction of premedication

Although premedication was initially developed to fight back the adverse effects of anesthesia, we now emphasize more about the efficacy of premedication in improving the general well-being of patients and patient satisfaction after their surgery. There are still many people in whom the quality of recovery from anesthesia is not good, and many of them have not been treated adequately. Although we already have guidelines for some preventive measures, for instance, to manage postoperative nausea and vomiting (PONV) or to deal with a difficult airway, we have yet to develop a complete list of statements or guidelines on premedication to manage all possible anesthesia-related side effects. It is clear that new consensus guidelines need to be established, and more clinical trials on anesthesia premedication need to be conducted.

3. Purposes of premedication

The two general purposes of premedication proposed by Beecher[5] in 1955 are as follows: (1) to present a tranquil and well-rested patient to the surgeon and (2) to decrease the hazards incurred by anesthesia and surgery. Atropine was once used before anesthesia to prevent “vagal inhibition” and to decrease secretion induced by chloroform or ether. Morphine had also been used to reduce reflex irritability of patients and decrease the amount of ether requirement.[6] As the new halogenated inhalational anesthetics and intravenous anesthetics have dramatically shortened the induction time of anesthesia, the main purpose of premedication today is no longer to prevent radical movement or reduce secretion of patients, but to allay patient fears and lessen patient anxiety.

Other purposes of anesthetic premedication, as found in the literatures, are to: (1) prevent postoperative pain, (2) provide effective prophylaxis against PONV, (3) decrease perioperative shivering, (4) decrease postoperative pruritus, (5) decrease gastric secretions, (6) prevent allergic reactions, (7) suppress reflex responses to surgical stimuli, and (8) decrease anesthetic requirement for the surgical procedure.[7]

3.1. To decrease anxiety

Preoperative anxiety can occur in as high as 80% of surgical patients. Two vulnerable groups of patients are females and children. While most female adults are usually concerned about the uncertainty of their future, their family, the success of the operation, and the safety of anesthesia, the children, by contrast, will experience varying degrees of separation anxiety before an operation. Both psychological and pharmacological approaches are effective in decreasing preoperative anxiety. A study conducted as early as 1963 showed that patients visited by an anesthesiologist before surgery are more likely to remain calm in the operating theater than those who did not receive reassurance.[8] Another study found that the brochure educating patients about the effects of anesthesia is less effective in reducing anxiety than a personal interview.[9] Midazolam has been proved to be effective in reducing the preoperative anxiety level in many studies. It will not delay discharge from the recovery room in outpatient surgery. Except for midazolam, α2-agonists, antidepressants, and anticonvulsants are all effective in reducing the preoperative anxiety level (see below).

3.2. To reduce postoperative pain

Preemptive analgesia, a concept of delivering an analgesic regimen prior to the surgical stimulus to reduce the severity and duration of postoperative pain, originated from the experimental findings of Woolf and Chong[10] in 1983 that the central nervous system will be hypersensitized after peripheral tissue injury. The goals of preemptive analgesia would therefore be as follows: (1) to decrease acute postoperative pain after peripheral nerve damage and tissue injury; (2) to prevent central neuron sensitization; and (3) to inhibit the development of chronic postsurgical pain (CPSP). During the past 3 decades, there have been many clinical applications of different analgesic interventions to try to achieve these goals. Many papers had reviewed and analyzed the numerous results of such efforts, but with a controversial and debating conclusion.

An extensive review published by Moiniche et al[11] in 2002 analyzed more than 3700 patients from 80 randomized controlled trials between 1983 and 2000 to study the effects of preemptive analgesia with different techniques: 20 trials on nonsteroidal anti-inflammatory drugs (NSAIDs), eight trials on NMDA receptor