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REVIEW

Intravenous anesthetics most commonly used in pediatrics

Anestésicos endovenosos más utilizados en pediatría

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ABSTRACT

Introduction: anesthesia is described as the provision of medication to induce amnesia, analgesia, and muscle relaxation, allowing surgical intervention in a patient.
Objective: to describe the most commonly used intravenous anesthetics in pediatric patients.
Development: the best type of anesthesia to be used is evaluated depending on the type of surgical intervention the child will undergo. For surgical procedures that require total numbness, general anesthesia is the most common, however, it is one of the types of anesthesia that presents the greatest risks after the postoperative period, so constant monitoring by the anesthesiologist is important. Intravenous anesthetics such as propofol, remifentanil, fentanyl, and ketamine are widely used intravenously, so it is always necessary to act with great caution, never with overconfidence, and be prepared for any eventuality.
Conclusions: the type of anesthesia used will depend on the type of surgery. Regardless of the type of anesthesia to be administered, the anesthesiologist must be highly trained and perform preoperative tests, especially in cases of general anesthesia where the child's weight and the dose to be administered are key factors.

Keywords: Anesthesia; Intravenous; Pediatric Patients.

RESUMEN

Introducción: la anestesia la describe como la provisión medicamentosa de amnesia, analgesia y relajación muscular que permiten la intervención quirúrgica en un paciente.
Objetivo: describir los anestésicos endovenosos más utilizados en pacientes pediátricos.
Desarrollo: dependiendo del tipo de intervención quirúrgica a la que vaya ser sometido el niño es que se evalúa cual es la mejor anestesia a aplicar. Para las intervenciones quirúrgicas que requieren adormecimiento total la más común es la anestesia general, sin embargo, es una de la anestesia que mayores riesgos presenta después del post operatorio, para ello es importante el monitoreo constante del anestesiólogo. Los anestésicos endovenosos: propofol, remifentanil, fentanyl y ketamina son muy utilizados por via endovenosa por lo que siempre se debe actuar con mucha cautela, nunca con exceso de confianza, y hay que estar preparado para cualquier eventualidad.
Conclusiones: la anestesia a utilizar va a depender del tipo de intervención quirúrgica. Independientemente del tipo de anestesia que se vaya a suministrar, el anestesiólogo debe tener una excelente preparación y realizar las pruebas pre operatorias, en los casos de anestesias generales donde el peso del niño y la dosis a administrar es clave.

Palabras clave: Anestesia; Endovenosa; Pacientes Pediátricos.

INTRODUCTION

The most practical definition of anesthesia describes it as the provision of medication to induce amnesia, analgesia, and muscle relaxation, allowing surgical intervention in a patient.[1]

During a patient's state of anesthesia, the anesthesiologist is responsible for maintaining the homeostasis of vital processes and providing a safe and comfortable perioperative experience. All surgical or interventional procedures, regardless of the medical specialty, require the support of anesthesia, which in turn must be tailored to the patient's baseline characteristics (age, sex, comorbidities) and the type of procedure to be performed.[2]

Historically, pediatric anesthesia has been primarily inhalation-based. With the advent of intravenous anesthetics, their effects require greater attention due to the complexity of their pharmacokinetic interactions, which can interfere with hemodynamics, making it more or less predictable, depending on the characteristics of the age group.[3]

The anesthetic procedure involves the administration of drugs with specific pharmacological actions, aimed at controlling a systemic response to various noxious stimuli.[4]

Various drugs and anesthetic techniques have been studied to determine the modulation of this response, as well as to evaluate the release of catecholamines in response to the stimuli above.[1]

Opioid drugs are highly effective in preventing such responses and are used in balanced anesthesia as well as in intravenous general anesthesia. The primary mechanism by which analgesia is achieved through opioid drugs is the activation of N-methyl-D-aspartate receptors.[5]

Induction in pediatric anesthesia has been the subject of constant controversy regarding the nature and type of drugs, the use of muscle relaxant premedication, and collaboration with the anesthesiologist.[6]

A recent controversy has been the type of induction. The stepwise induction technique has been proposed as superior to the standard rapid induction technique because it is expected to improve the child's surgical experience.[6]

Over the years, the advancement and use of the aforementioned types of anesthesia have contributed significantly to the successful performance of surgical procedures. However, the state of anesthesia alone has been considered an intrinsic risk. During anesthesia, the patient is subject to the injection/inhalation of drugs with potential adverse effects, primarily cardio-respiratory and allergic. The induced state of unconsciousness carries with it the risk of airway obstruction, pulmonary contamination, and the inability to detect peripheral injuries.[7]

Finally, neuromuscular blockade and loss of self-control of autonomic responses make the patient dependent on mechanical ventilation and the anesthesiologist and their team.[1]

The objective is to describe the most commonly used intravenous anesthetics in pediatric patients.

DEVELOPMENT

Various general principles have been proposed for treating pain in children, and it is worth noting that the preventive aspect of pain management is paramount. It is not difficult to foresee that a child will suffer pain, for example, as a result of surgery, painful examinations, and in some pathological circumstances. Therefore, prophylactic treatment is required.[8]

It is unacceptable, both from a human and pharmacological point of view, to expect a person to suffer to treat them if the pain can be prevented. Lower analgesic doses are required to avoid pain than to treat it. Thus, in the course of a surgical procedure in which pain is known to occur, it is necessary to administer analgesics preventively without waiting for the pain to appear to relieve it. This principle has become the cornerstone of pain management.[8]

Currently, most published reviews emphasize this point. Other essential elements in managing pain in children are the simultaneous use of pharmacological and non-pharmacological procedures. Distraction, percutaneous electrical nerve stimulation, hypnosis, and other non-drug methods have an effect that enhances the action of analgesics. This highlights the fact that comprehensive pain management encompasses several key facets.[8]

Pain management should not cause suffering in itself, especially when it comes to administering analgesics. Intramuscular, rectal, or intranasal routes of administration should only be used when no other options are available, as there is a risk that the child will silence their pain for fear of parenteral drug administration.[8]

Parents should be involved as much as possible in decisions about their child's treatment and pain management, as they are more accustomed than anyone else to recognizing their child's reactions to pain. Taking their opinion into account should be part of the treatment plan. It is also advisable to ensure that parents are present, if possible, during the practice of techniques that may cause the child pain, involving them to provide reassurance in difficult moments, which are always a source of anxiety.[8]

Pain management techniques encompass both non-pharmacological and pharmacological approaches. Non-pharmacological techniques include physical and psychological methods, such as applying local cold, using

vigorous vibration at the site of pain, and employing distraction techniques, as well as hypnosis. Pharmacological techniques, on the other hand, may involve the use of analgesics, sedatives, or anesthetics. Analgesics can be non-steroidal (NSAIDs) or opiates, and the routes of administration are very diverse.[8]

In high-demand emergency services with limited infrastructure, physicians, as the cornerstone of patient management, must master a series of techniques and procedures that enable them to control pain and treat certain acute conditions, thereby allowing children to be returned to their families more quickly. Thus, for example, the reduction of certain types of fractures, dislocations, and listhesis in traumatic pathologies, as well as the repair of wounds or lacerations, the reduction of inguinal hernias, or the removal of foreign bodies (coins) in the upper third of the esophagus, can be performed in the Pediatric Emergency Department with a well-directed sedation and analgesia technique.[8]

This procedure is also helpful for diagnostic procedures, such as topographic or sonographic studies in challenging patients, taking into account the appropriate medication according to the underlying pathology.[8]

To apply a sedation and analgesia protocol in pediatrics in the Emergency Department, three factors must be taken into account:[9]

1- Patient's pathology and health conditions: The patient should be classified to assess their risk according to the American Society of Anesthesiologists, and preferably choose those who are previously healthy or have mild systemic pathology.

2- Resources available in the emergency department: This includes monitoring equipment, cardiopulmonary resuscitation equipment, sedation, or anesthesia.

3- The capacity of the pediatric emergency department: This factor refers to the training of emergency personnel to work as a team in performing a procedure under sedation or anesthesia.

For the procedure to be successful, sedation should ideally be harmless, the ideal candidate should be selected, the best technique should be used, the characteristics of the drugs to be used should be known, and the team should be adequately trained.[10]

Physicians generally have no difficulty in administering certain analgesics or sedatives. Still, when it comes to inducing conscious or unconscious sedation to perform a procedure, the number of those who do so is reduced. For this reason, guidelines for managing sedoanalgesia in pediatric emergencies are provided.[10]

It is essential to consider the specific circumstances of certain medications before using them, as they can exacerbate a patient's condition if not selected appropriately. Always act with great caution, never with overconfidence, and be prepared for any eventuality.[10]

Some of the most commonly used intravenous anesthetic drugs in pediatric practice are:[10]

Propofol

Propofol is a short-acting intravenous anesthetic commonly used for induction and maintenance of anesthesia in pediatrics. It is a hypnotic agent that acts on GABAergic receptors in the brain, having a rapid onset of action and a short duration. Propofol is rapidly metabolized in the liver and eliminated mainly by the kidneys.

Clinical use

- Induction of general anesthesia in children from 1 month of age.
- Maintenance of general anesthesia: in children aged 1 month and older.
- Sedation for surgical procedures and diagnostic techniques: in children over 1 month of age.
- Sedation in intensive care units: in adolescents aged 16 years and older.
- It can also be used as an antiemetic at very low doses.

Dosage and administration guidelines

- Induction of general anesthesia: administered slowly until clinical signs of anesthesia appear. The dose should be adjusted according to age or body weight. Most patients over 8 years of age require approximately 2,5mg/kg body weight of propofol 10mg/ml for the induction of anesthesia. Younger children, especially those between 1 month and 3 years of age, may require higher doses of 2,5-4mg/kg body weight.
- Maintenance of anesthesia: Propofol administration can be maintained by infusion or repeated bolus injections. The required rate varies between patients, but rates of 9 to 15 mg/kg/h usually achieve satisfactory anesthesia.
- Sedation in intensive care: despite its contraindication in patients under 16 years of age, doses of 1-4 mg/kg/h have been used with a recommended duration not exceeding 24 hours.
- Superficial sedation for surgical procedures and diagnostic techniques: most pediatric patients require 1-2 mg/kg body weight of propofol 10 mg/ml for the onset of sedation.

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Remifentanil

The pharmacokinetics of remifentanil are unique. It is characterized by its rapid onset of action, reaching plasma levels quickly with onset of action at 1,6 minutes, and its action ends just as quickly, 3 to 10 minutes after the infusion is stopped. It is metabolized directly by nonspecific plasma esterases, and its elimination is not affected by liver or kidney disease. There are no significant changes in the elimination of the drug in different pediatric age groups. An important disadvantage is that, upon completion of its action, there is no analgesic effect; therefore, it is necessary to administer analgesics promptly during painful procedures to mitigate pain. Similar to other opioids, remifentanil causes dose-dependent bradycardia, hypotension, respiratory depression, nausea, and muscle rigidity. This drug can be used with excellent results in painful procedures that require maintaining spontaneous ventilation and analgesia, such as bronchoscopies or nasolaryngoscopies, whether diagnostic or therapeutic, for example, in cases of foreign bodies in the airway, which can be achieved with an intravenous infusion of 0,08 to 0,1 g/kg/min.

Fentanyl

This is a commonly used, highly lipophilic drug that crosses the blood-brain barrier rapidly, accumulates in fatty tissue, and causes less histamine release compared to morphine. For this type of procedure during deep sedation, 2 to 3 g/kg can be used in combination with a hypnotic such as midazolam or propofol, as well as with inhaled anesthetic agents. We must consider that its hepatic metabolism produces active metabolites, which are then excreted biliary. Additionally, in full-term and premature newborns, hepatic and renal function is immature, which can prolong the elimination half-life.

Ketamine

Ketamine is a drug that binds to NMDA receptors and sigma opioid receptors, producing analgesia and a state of dissociative anesthesia; patients do not respond to nociceptive stimuli but can maintain airway reflexes and cardiovascular stability. Ketamine rapidly crosses the blood-brain barrier, reaching its peak effect in 1 minute. The duration of a single dose is 10 to 15 minutes. It should be noted that it causes excessive salivation and may increase the risk of airway obstruction. The intravenous dose is 1-2 mg/kg.

Inhalation Anesthetics[11,12]

Inhalation anesthetics such as sevoflurane, isoflurane, and desflurane have the advantage of a rapid onset of action, as well as termination, providing the patient with unconsciousness, immobility, and amnesia, but not analgesia. They are associated with several hemodynamic variations, although hemodynamic stability is dose-dependent and can lead to vasodilation, myocardial depression, and arrhythmias. They are also bronchodilators and can be used in patients with bronchospasm or asthma. Sedation is achieved through the lungs as the primary route of access and elimination; however, depending on the metabolism and elimination of each agent, care must be taken with patients who have liver or kidney failure. The onset of adverse effects can be reversed immediately by decreasing the concentration of the agent in the inspired air. Deep sedation can be achieved with a MAC of 0,5, adjusted to the patient's age.

Benzodiazepines

Midazolam is the most commonly prescribed drug and can be administered orally, intranasally, intramuscularly, intrarectally, or intravenously. It is a potent amnesic and anxiolytic and provides short-acting sedation. It has no analgesic properties and needs to be combined with a drug that gives analgesia, such as local anesthetics or opioids. The combination of fentanyl and midazolam is very effective, with a rapid onset of action in sedation and analgesia. However, respiratory depression with the combination of midazolam and opioids is dose-dependent.

The metabolism of benzodiazepines (glucuronidation) utilizes the same metabolic pathway as bilirubin, with a decrease in the metabolism of the latter. This situation must be taken into account in newborn patients, especially premature infants. The administration of benzodiazepines is used for the premedication of pediatric patients before the IV administration of moderate sedation or anesthesia. Peak serum concentrations and effects on the central nervous system of midazolam are reached 10 minutes after intranasal administration and approximately 20 to 30 minutes after oral ingestion.

Clonidine

the most common adjuvant drug for single-dose caudal blocks. Several mechanisms have been proposed to explain its effect, the most likely being that it binds to alpha-2 receptors in the dorsal horn of the spinal cord. A dose of 1-2 µg/kg is recommended for prolonging the analgesic effect. The use of clonidine in premature infants and infants under 3 months of age is being debated due to a hypothetical risk of apnea in this group of children.

Dexmedetomidine

Has a shorter half-life than clonidine. European guidelines do not specify specific doses, but several authors have suggested 1-2 µg/kg as an effective dose. Caudal anesthesia will last longer with dexmedetomidine than with morphine as an adjuvant, while remaining on par with clonidine in quality. Hemodynamic effects, particularly bradycardia, are rare and are primarily associated with the higher dose concentration (2 µg/kg).

Opioids

These have a long tradition as adjuvant drugs in caudal anesthesia. Current guidelines recommend 10-30 µg/kg for morphine. Side effects of epidural caudal morphine include reduced intestinal motility and postoperative nausea/vomiting. Pruritus is another well-known and common problem, but the real risk is respiratory depression, sometimes with a delayed onset. Thus, the use of morphine should be limited to strictly selected patients.

Ketamine

Binds to opioid and N-methyl-D-aspartate receptors and has no respiratory side effects. In preservative-free form, both racemic ketamine and esketamine can be safely administered at 0,5-1 mg/kg in the epidural space. However, as animal models have revealed neuronal apoptosis following intrathecal application, current European guidelines recommend conservative dose concentrations of 0,5 mg/kg to minimize side effects.

Mepivacaine

- Use in subcutaneous infiltration and neuraxial blocks. Medium potency.
- Recommended concentration in pediatrics: 1-2 %. Dose up to 6 mg/kg.
- Onset of action: 5 min. Duration of effect: 1-3 hours. When combined with adrenaline, the duration of its effect increases to 2-6 hours (do not use in distal parts).

Bupivacaine

- Use in subcutaneous infiltration and neuraxial blocks. High potency.
- Recommended concentration in pediatrics: 0,25 %. Dose up to 2,5 mg/kg.
- Intermediate onset of action: 5-10 min. Duration of effect: 4-6 hours.

Ropivacaine

- Used in epidural blocks. Medium potency.
- Recommended concentration in pediatrics: 0,2-1 %. Dose 1,7-2 mg/kg.
- Intermediate onset of action: 5-10 min. Duration of effect: 4-6 hours. Less toxic, but also less potent than bupivacaine. With its own vasoconstrictor effect.

Levobupivacaine

- Isomer of bupivacaine, with similar potency and pharmacokinetics and lower toxicity. For this reason, it is currently replacing bupivacaine.
- Recommended concentration in pediatrics: 0,2-0,5 %. Dose up to 2,5 mg/kg.

The safety of successful anesthetic management depends on knowing the physiological, anatomical, and pharmacological characteristics of each group. In fact, infants have a higher risk of anesthetic morbidity and mortality than older children; in general, this risk is inversely proportional to age, with newborns are at greater risk.[13]

Among the most commonly reported incidents when using intravenous general anesthesia, according to different bibliographies, the following complications may occur: bradycardia, laryngeal spasm, apnea, vomiting, bronchoaspiration, the patient waking up during the procedure, hypoglycemia, and agitation.[13]

Clinical outcomes in pediatric anesthesia have improved significantly over the last 20-30 years, but unexpected laryngospasm that is difficult to treat can still lead to patient morbidity, increased postoperative medical management, and unnecessary hospitalization. The incidence of laryngospasm in pediatric anesthesia, it is difficult to determine, with incidences ranging from 0,9 % to a maximum of 14 %.[14]

Multiple studies have analyzed related to adverse events in children requiring gastrointestinal endoscopic procedures in settings where deep sedation is the preferred anesthetic technique during anesthesia general anesthesia, but not for the opposite case.[15]

Another factor to consider is that childhood obesity is associated with numerous respiratory disorders, which can worsen when general anesthesia.[15]

Spinal anesthesia (SA) is one of the most commonly used types of anesthesia in operating rooms due to its effectiveness and safety. However, it is not without complications such as hematomas, tears in neighboring structures, and infection at the puncture site. Other less common but more serious complications include

nerve damage due to anesthesia toxicity and hypotension/bradycardia leading to arrhythmias and excitation or depression of the central nervous system.[16]

General anesthesia has optimized drugs and techniques for use in major surgery, but post-surgical complications such as the following may occur: shock, hemorrhage, wound infection, pulmonary disorders (panting, chest pain, fever, cough), urinary retention, and reaction to anesthesia (dizziness, wheezing, rash, low blood pressure, high fever, liver disorders, agitation, and confusion).[17]

Local anesthetics, on the other hand, easily cross the blood-brain barrier and can alter brain function. When their concentrations rise to very high levels, they inhibit excitatory and inhibitory pathways, causing CNS depression, loss of consciousness, and ultimately coma. Today, it is known that life-threatening allergic responses related to the use of amide-type local anesthetics are extremely rare. Their clinical presentation can trigger skin symptoms such as dermatitis, respiratory system involvement with h, bronchospasm, and respiratory distress, and even fatal systemic anaphylaxis. At higher concentrations, a direct myocardial depressant effect occurs, manifested by ventricular arrhythmias, delayed myocardial conduction, and profound contractile dysfunction, ultimately leading to cardiovascular collapse.[18]

CONCLUSIONS

In general terms, determining the type of anesthesia to be used in children undergoing surgery will depend on the type of surgical procedure the child is undergoing. In most cases, for high-risk surgeries or procedures performed due to a diagnosis that may put the child's life at risk, general anesthesia is commonly used. Logically, this carries risks that may arise when the effects of the anesthesia wear off and the patient begins to wake up, such as edema, respiratory problems, and bronchospasms, among others. If the surgery does not require total anesthesia, depending on the type of procedure, regional or local anesthesia may be administered.

Regardless of the type of anesthesia to be administered, the anesthesiologist must be highly trained and perform preoperative tests, especially in cases of general anesthesia, where the child's weight and the dose to be administered are key factors.

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CONFLICT OF INTEREST

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