

Propofol as Inducing Agent of Elective Cesarean

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Abstract

Propofol as an inducing agent in selective caesarean section is considered one of the most effective methods to carry out the surgical procedure without any type of complication, however, studies have shown that anesthetics such as Thiopental produce similar effects, therefore A bibliographic review and a brief comparison with this drug are carried out in order to determine the effectiveness and efficacy of both, and their effects on the mother and the newborn.

Keywords: Propofol, elective caesarean section, caesarean section operation, general anesthesia.

Introduction

Like most anesthetics, Propofol is a γ -aminobutyric acid (GABA) receptor agonist. It has a favorable pharmacokinetic (PK) and pharmacodynamic (PD) profile, which has made it the most widely used intravenous anesthetic for the past three decades. The rapid and gentle induction with almost no arousal phenomenon, a relatively short context-sensitive time, a fast terminal half-life, and a low incidence of postoperative nausea and vomiting (PONV) make it a highly versatile hypnotic drug. It is used for sedation and anesthesia in almost all types of surgery, but it is especially suitable for anesthesia in patients undergoing ambulatory and neurosurgery where rapid psychomotor recovery is of the utmost importance. It has also been shown to be effective and useful for the sedation of patients in the intensive care unit (ICU) and the conscious sedation of patients undergoing diagnostic or invasive procedures [1].

Propofol exerts its hypnotic actions by activating the central inhibitory neurotransmitter, gamma-aminobutyric acid (GABA). GABA receptors are ion channels activated by ligands composed of several subunits (α 1-6, β 1-4, γ 1-3, δ , ϵ and ρ 1-3) that form a pentameric structure containing a central chloride channel (Figure 1). Binding of the Propofol molecule to the receptor leads to an increased influx of chloride ions and hyperpolarization of the neuron, leading to a lack of response to external stimuli. Propofol also influences the presynaptic mechanisms of GABAergic transmission, such as uptake and release of GABA. Not only does Propofol facilitate GABAergic transmission by presynaptic and postsynaptic mechanisms, but it has also been shown to selectively block the release of acetylcholine in the basocortical and hippocampal septum pathways that are under tonic innervation by GABAergic

impulses [2].

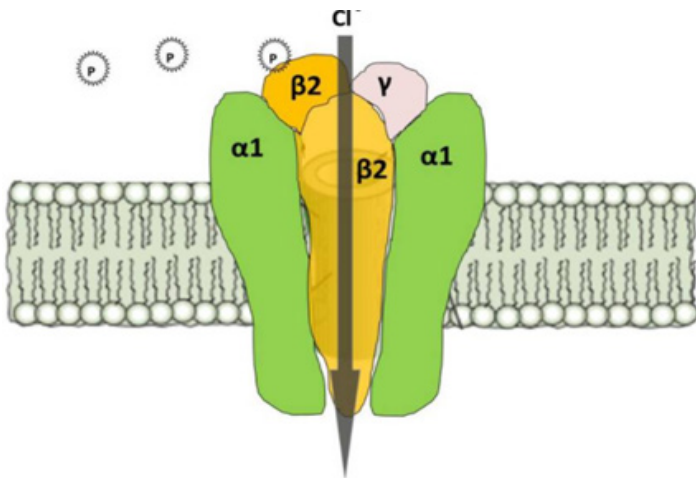


Figure 1: Schematic representation of the gamma-aminobutyric acid (GABA) A receptor in the cell membrane with its α , β and γ subunits where Propofol interacts mainly to cause its anesthetic effect in the central nervous system. The star “P” structures represent Propofol drug molecules. By interacting with the GABA A receptor, entry of chloride ions occurs through the central chloride channel.

From an obstetric point of view, regional anesthesia is preferred during cesarean section, but general anesthesia may be the only option in certain circumstances, such as patient preference, back deformities not amenable to spinal anesthesia, failed spinal anesthesia, hypertension intracranial, maternal coagulopathy and certain neurological diseases. A safe induction agent for obstetrics should, among other things, provide gentle and rapid induction, maintain maternal hemodynamic function, and exert little or no effect on the Apgar score, therefore it is important to know the effects of Propofol. In relation to neonatal Apgar score and maternal recovery time after cesarean section since Propofol is widely used for induction and maintenance of anesthesia in other surgeries, but not in obstetric procedures. It has a short induction time and blunts the airway reflexes during laryngoscopy; Compared to thiopental, patients emerge more quickly from Propofol anesthesia, which can depress the fetal central nervous system, resulting in a low Apgar score at birth [3].

Methods

A bibliographic search of information published since 2015 was carried out in the databases of Scielo, PubMed, Academic Google, Elsevier, Medline. The search was carried out with articles in Spanish and English and the use of keywords such as: Propofol, elective cesarean section, cesarean section operation, general anesthesia.

Results

Cesarean delivery is defined as the delivery of a fetus, alive or dead, through an incision in the abdominal and uterine wall. Removal of the fetus from the abdominal cavity is excluded as in the case of ruptured uterus or abdominal ectopic pregnancy. Cesarean delivery was classified as elective if the decision to perform the

operation was made before the start of labor and after preoperative preparation at a pre-established time during office hours to ensure the best quality of obstetric and anesthetic services., neonatal and nursing, including during labor [4]. Around the world, an increase in cesarean section rates has been observed in developed and emerging countries. In sub-Saharan regions, the cesarean section rate is only 3%; in Central America it is 31% and in North America it is 24%. The rate in Europe is around 25% of all deliveries, while in the US the rate is estimated at 32.2%. In 2000, in the European Union, 221 cesarean sections were performed for every 1000 live births; by 2011, the number had risen to 268 per 1,000 live births. In Europe, cesarean section births increased from 172.49 per 1,000 live births in 1997 to 253.23 per 1,000 live births in 2010 [5]. In relation to the incidence of cesarean sections in the study carried out by Soukayna et al., It was reported that in the Souissi maternity hospital the incidence was 17.83% and the Overall cesarean delivery rate was 24.15% for elective cesarean sections and 75.85% for emergency cesarean sections, giving an approximate 4: 1 ratio for emergency cesarean versus elective cesarean [4].

Therefore, failed tracheal intubation and the risk of aspiration and the resulting aspiration pneumonitis have historically been the most feared complications of general anesthesia in relation to elective cesarean section. Propofol, despite being the most used intravenous anesthetic in the last 30 years, is considered the most used in the induction phase while volatile anesthetics are responsible for the maintenance phase. However, in recent years and through multiple descriptive studies, the implementation of this drug in both phases has been proposed, which is called total intravenous anesthesia (TIVA) based mainly on the combination of this drug and an opioid. through which the multiple benefits conferred by the use of Propofol as an anesthetic during the intervention performed are evidenced, among which are less invasive long-term effects, fewer harmful cognitive effects, potential for improvement, among others, which makes Further study is needed on its implementation and the effects it has on the induction of elective cesarean section [6].

Gutiérrez et al. Describe in their descriptive and prospective study the effects of Propofol in pregnant women and neonates when used as an inducer in general anesthesia for elective cesarean sections, evaluating the period of induction to the birth of the neonate by means of doses consisting of 2.5 mg / kg, with oxygen and 50% nitrous oxide. And as for the results, the anesthetic plane reached was adequate, there was no incidence of consciousness during the induction-birth interval. There were no anesthetic complications and 70% of the cases had no adverse reactions. The induction-birth times on average were 7 + -2.8 minutes and the uterine incision-birth time of 69.7 + -60 seconds. Only two neonates had low Apgars at the first minute and in all the Apgars was high at 5 and 20 minutes. The technique was generally well accepted by women [7].

Claude et al. Carried out an exhaustive bibliographic review of approximately 20 articles, between 1989 and 2016, where after an analysis of methodological studies and case reports it is concluded that Propofol was an alternative induction agent for general anesthesia in cesarean section and it has few disadvantages in the

newborn's Apgar score at 1 minute, which lays the foundation for it to be a definitive agent today [8].

Munender and others in their comparative study with 103 patients conducted a detailed study on the use of Propofol as a suitable alternative to thiopental as an induction agent in obstetric anesthesia, in which their results showed that Propofol proved to be an agent of action. rapid, without consequence at the level of significant cardiovascular depression in obstetric patients with a result that is comparable to the use of thiopental, as well as minimal side effects, pain being the main effect, therefore these desirable properties of the drug offer an advantage in obstetric patients considering different aspects compared to this procedure, therefore its use in obstetric anesthesia seems to be adequate [9]. The study was carried out with a group of 103 female patients with 36 weeks of gestation, with immediate delivery by elective cesarean section, of this group 51 patients were administered Thiopental 5 mg / kg, while the remaining 52 were administered Propofol 2.5 mg / kg, both with satisfactory results in terms of the period from administration to unconsciousness, however, the differences obtained lie in the type of induction and pain as an adverse effect.

Of the 52 patients who were administered Propofol, 80.8% (42) had a mild induction and 19.2% (10) had an altered induction. On the other hand, of the 51 patients who were administered Thiopental, 71.6% (37) presented a mild induction and 28.4% (14) presented altered induction (Figure 2).

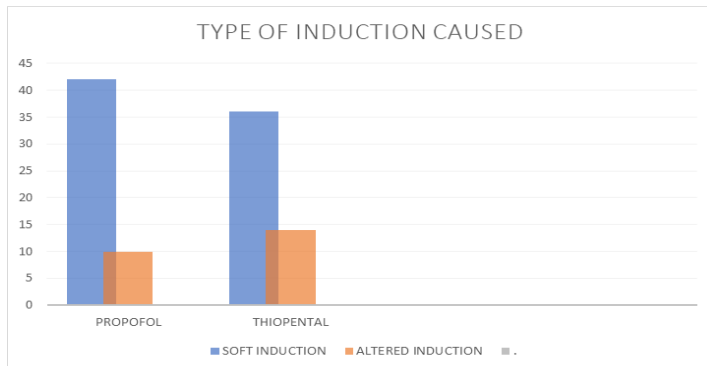
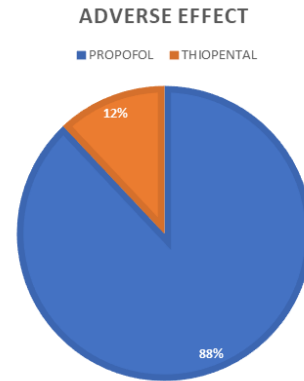


Figure 2: Number of patients who presented mild and altered induction, depending on the type of drug administered.

Regarding adverse effects, of the 52 patients who were administered Propofol, 15 reported pain at the moment of feeling the injection, while of the 51 patients who were administered Thiopental only 2 reported pain (Figure 3). In this vein, taking into account the statistics, Propofol provides greater effectiveness at the time of cesarean section induction, since the rates are higher in terms of mild induction, however, Thiopental is a good alternative for use for induction.



A safe induction agent for obstetrics should have minimal or preferably no effect on the Apgar score in the newborn, therefore Tumukunde and others in their simple randomized clinical trial from 2015 showed the primary results of the scores of Apgar up to 10 minutes postpartum compared to Propofol and thiopental, the participation of 74 neonates with an Apgar <7, discriminating 43 in the Propofol administration group and 31 in the thiopental group. At 0 min, 43 infants in the Propofol group had an Apgar score <7, compared with 31 infants in the thiopental group. At one minute, in the Propofol group 35 had an Apgar score <7 and 24 in the thiopental group. At the 5-minute progress, 13 and 8 infants had an Apgar score <7 in the propofol and thiopental group, respectively. And finally, after 10 minutes, 3 neonates in the Propofol group and 2 neonates in the thiopental group, which shows that the proportion of Apgar scores <7 decreased significantly (Table 1) [3].

Table 1: Number of newborns with Apgar score <7 after cesarean section

Apgar score in relation to time	Propofol Group	Thiopental group
Minute 0	43	31
Minute 1	35	24
Minute 5	13	8
Minute 10	3	2

Discussion

The administered concentrations of propofol for the induction of unconsciousness are strongly rooted in the pharmacokinetic models that use this drug. Coetzee et al. Describe the classic recirculatory model in which, first, the drug mixes in the venous flow before entering the pulmonary circulation, through which it must pass through a first pass before entering the circulation. systemic. The lungs delay the passage of drugs and may even eliminate

some. The systemic circulation then distributes the drug to various organs (including the target organ) through which it also undergoes a first-pass process. Subsequently, a part is returned to the venous flow and recirculated, which is directly related to the cardiac output since as the cardiac output increases, the maximum arterial concentrations decrease in response to a bolus dose and the area under the arterial concentration-time curve decreases, which leads to a decrease in the effects on the target organ [10].

During the surgical procedure, it is necessary to administer an effective anesthetic drug that maintains minor adverse effects, mainly in hemodynamic stability, since alterations in both heart rate and blood pressure cause the development of bleeding during the procedure, which constitutes a cause of death. Previously, the drug most used for this purpose was Thiopental, however, it has been necessary to compare this anesthetic with Propofol, in order to know the influence of both on the hemodynamic stability of the patient and determine which is the most suitable. Thus, Kushwaha et al. In their comparative study conducted a study carried out at the southern Rajasthan tertiary care university hospital for a year, in which patients aged 18 to 60 underwent surgical procedures, divided in group P and T where group P received propofol 2.2 mg / kg and group T received thiopental 5 mg / kg intravenously for the induction of anesthesia. All patients had a pulse oximeter, ECG, and continuous blood pressure monitoring. Hemodynamic parameters such as pulse rate, systolic and diastolic blood pressure were recorded during induction and at 1-minute, 2-minute, 3-minute, and 4-minute intervals after intubation [11].

According to what was observed, in both groups there was a drop in systolic blood pressure, which subsequently increased and, for its part, diastolic pressure also decreased in both groups, with a subsequent increase in it. Although both had variations in the hemodynamic parameters, the group administered with Thiopental registered a significantly greater increase in blood pressure, for which it was concluded that propofol presented less risky alterations.

In obstetrics, previously the most widely used anesthesia was epidural, however, the use of Propofol as an anesthetic has positioned itself as the most useful technique for the induction of cesarean section, being predominantly implemented in hypovolemic patients. On the other hand, it has been shown that, due to its mechanism of action, it requires a considerable interval to achieve the desired effect, which in turn means that the time necessary to achieve hypnosis is prolonged, which increases the chances that the patient wakes up during the surgical procedure, which makes it the object of study and analysis.

The state of unconsciousness during cesarean section and the degree of it are the most important factor in determining the appropriate drug to be administered and in countries such as England, Thiopental was the drug par excellence used in this type of procedure together a Opioids such as fentanyl, alfentanil and remifentanyl for induction associated with a reduced risk of SAGA and better neonatal outcomes, compared to other agents, however, an increase in the use of Propofol and rocuronium has been observed. Due to this, encephalogram studies have been carried out in order

to compare the degree of consciousness induced with the administration of both Thiopental and Propofol, where the behavior of the delta and beta waves under the effects of both anesthetics is studied [12].

Hee Sun and others, in their comparative encephalogram study, between September 2017 and May 2019 with pregnant women with elective caesarean section, between 20 and 44 years of age. All parturients received at least 3 min of pre-oxygenation with 100% oxygen, followed by RSI with cricoid pressure. Thiopental 5 mg / kg or propofol 2 mg / kg was administered, followed by succinylcholine 1.5 mg / kg to facilitate intubation. After the fasciculation and electromyography (EMG) activity bar disappeared on the BIS monitor, all patients were intubated with a 6.5 cuff tracheal tube using a video endoscope. After confirming successful intubation, 0.5 mg / kg rocuronium was administered immediately to achieve further muscle relaxation. Anesthesia was maintained with 50% nitrous oxide (N₂O) in oxygen (6 L / min) and sevoflurane. And in terms of results, the thiopental group experienced a more significant decrease in slow delta wave activity and an increase in beta activity after intubation before neonatal delivery compared to the propofol group, however, in the encephalogram BIS (Bispectral Index), spectral entropy and RPE (Renyi Permutation Entropy) have the same tendency in stages I, II and III, which clearly indicates that general anesthesia induced by thiopental has an increased risk of consciousness in comparison with propofol-induced anesthesia [13].

Aspects such as hemodynamic response to intubation, depth of anesthesia, and postoperative recovery are favorable characteristics that were demonstrated in the use of propofol for induction of anesthesia, as well as a lower increase in blood pressure during laryngoscopy and intubation. providing better hemodynamics during the intervention [14]. In addition, Capote et al., In their retrospective study evaluating the rates of failed or difficult intubation in a group of 895 women, concluded that the use of propofol is associated with a lower risk of difficult or failed intubation, and may protect against intubation. appearance of difficult intubation which is important for the surgical procedure, as confirmed by Sie and others in their comparative study between Thiopental and Propofol where they reported that the risk of consciousness increases if the intubation presents alterations [15, 16].

Regarding the postoperative period, it is important to maintain neonatal stability, without apparent depression and uterine atony, for which the incidence and severity of the aforementioned problems can be reduced using appropriate agents such as remifentanyl and mainly propofol, which have a profile Favorable pharmacodynamic and pharmacokinetic characterized by rapid onset and compensation of obstetric anesthesia [17].

On the other hand, the few adverse reactions that it presents, demonstrate and classify this anesthetic as the most effective in analgesia in patients with selective caesarean section, since its effects both at the maternal and fetal level consist in the maintenance of hemodynamics, reducing any risk of bleeding, increasing neuronal tolerance to hypoxia, improving the quality of brain recovery and in general preserving the well-being of both, as well as fewer side

effects during the postoperative period [18].

In their comparative study, Montandrou et al., Compared the Apgar score in newborns by caesarean section with Thiopental and Propofol, two periods were compared, depending on the hypnotic drug used: thiopental before May 2011 and propofol afterwards. The primary outcome was to compare the proportion of newborns with an Apgar score at 5 minutes <7 between both groups and which resulted in that the proportion of newborns with an Apgar score at less than 7 was significantly higher in the group. propofol group [19].

Regarding the respiratory conditions of patients requiring mechanical ventilation, Lopez et al., In their observational study where propofol-remifentanyl and midazolam-fentanyl were administered, conclude that both the combination of propofol-remifentanyl and midazolam-fentanyl appear to be effective as Sedo-analgesic regimen of patients treated by mechanical ventilation after surgery, which is still the object of study [20].

Conclusion

Propofol, administered intravenously for induction in selective caesarean section, is an alternative that has become the most widely used in recent years, due to its multiple and varied benefits, regarding both maternal and neonatal health, where it remains hemodynamics, without complications during the intervention and with satisfactory evolution during the postoperative period, in addition to a good response of the newborn to the Apgar test, so that, compared to other anesthetics such as Thiopental, it is considered the most suitable and least invasive method for the induction of unconsciousness and the correct surgical procedure.

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