

Propofol Versus Barbiturates as an Inducing Agent in Elective Cesarean Section: Systematic Review and Meta-Analysis

Marcelino Sánchez Tamayo^{1*} | Miguel Liván Sánchez Martín² | Eivet García Real² | Dianamary Brito Herrera¹ | Lisbet Díaz Fonseca¹ | Cirilo Piedra Torres¹

*Correspondence: Marcelino Sánchez Tamayo

Address: ¹Anesthesiology and resuscitation service. Comandante Pinares General Teaching Hospital, Cuba; ²Anesthesiology and resuscitation service. Abel Santamaria General Teaching Hospital, Cuba

e-mail ✉: marcelino881230@gmail.com

Received: 26 February 2021; Accepted: 01 April 2021

Copyright: © 2021 Sánchez Tamayo M. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided that the original work is properly cited.

ABSTRACT

Introduction: The choice of the anesthetic agent when it is necessary to provide general anesthesia to the obstetric patient to perform the cesarean section is a controversial issue, especially because the short and long-term effects that it could develop in the newborn are not fully known.

Objective: To evaluate the neonatal results of the use of Propofol versus Barbiturates as an inducing agent for anesthesia for elective cesarean section.

Methods: A systematic review was carried out with meta-analysis of clinical trials and randomized comparative studies showing neonatal outcomes taking into account the pharmacological comparison according to the neonatal physical state, the adaptive and neurological capacity, the presence of hypoxia and acidosis, as well as the need admission to the intensive care unit. The review was performed in the Cochran library, MEDLINE, EMBASE, Cochran Central Register of Controlled Trial (CENTRAL), PubMed, SCISEARCH, Clinical Trial Registries, EBSCO, LILACS, Sciencedirect, Hinari databases in Spanish and English during the last 35 years, selecting articles from pregnant patients, with single fetuses, without maternal or fetal complications, who are scheduled for elective surgery. Data selection and analysis was carried out by two independent reviewers.

Results: 17 studies with 1898 patients were included, 15 compared Propofol vs Thiopental, one study compared Propofol vs Methohexital, one investigation compared Propofol vs Tiamilal. Physical state at one minute of life favored the control group (RR: 1.26; 95% CI: 1.07 and 1.48). There was no relationship between the groups for the rest of the outcomes. Heterogeneity was low in the primary outcome.

Conclusions: There was not enough scientific evidence to indicate the superiority of one drug over the other, so both could be good options for elective induction of caesarean section.

Keywords: Neonatal Outcomes, Propofol, Barbiturates, Neonatal Depression, Neonatal Hypoxia

Background

The ideal anesthetic method for caesarean section does not exist. There are, general and regional procedures, each with indications and contraindications. The choice of those methods is based in the physiological change pregnancy, surgery indication, maternal and fetal status, and the experience and skills presented by anesthesiologists and surgeons (Delgado *et al.*, 2020).

Although the complications related with the general anesthesia, there are many clinical situations where this technique is necessary and summarizes the contraindications of the regional procedures. Those are: patient refusal of regional anesthesia, unbalance coagulopathy, anticoagulant and antiplatelet medications, moderate or severe mitral valvular disease, uncontrolled hemorrhage, infectious lesions at the puncture site, occupying lesions of the intracranial space, uncontrolled epilepsy (Mekonen *et al.*, 2020; Afolabi and Lesi, 2012; Madkour *et al.*, 2019).

When it is necessary to provide general anesthesia, there is uncertainty about which anesthetic agent should be used for induction of anesthesia. The fundamental concern consist in the impact that the drug may have on the fetus due to the placental transfer or drugs and the maternal hemodynamic level.

Therefore, it is valid to ask yourself: what is the effect of the use of propofol as an inducing anesthetic agent compared to barbiturate drugs in pregnant patients who undergo elective cesarean section in terms of neonatal outcomes?

Description of the Condition

Cesarean section is a procedure that allows the fetus to be removed through the abdomen through an incision in the uterus (Sarduy Nápoles *et al.*, 2018). The introduction of the cesarean section in the clinic, made possible a marked reduction in maternal and fetal mortality, and is considered as one of the greatest contributions in contemporary perinatal medicine. However, it is a procedure that is not without risks and surgical and anesthetic complications, and that are exacerbated when the indication is not adequate (Siles Levy, 2018).

It is one of the most frequent major abdominal surgeries in secondary and tertiary health centers. The Latin American Center for Perinatological Care showed that there was an excess of 650,000 caesarean sections, with an equivalent cost of 400,000,000 dollars, which transforms its beneficial effect into a health problem (Salud Perinatal, 1989; FLASOG, 2015). The World Health Organization also stated that when the cesarean section rate is greater than 10%, it is not associated with a decrease in maternal

and perinatal mortality rates [3].

In 2018 there was an overall cesarean section rate of 77.4%. In the same way, in 2019, a rate for Europe, Africa, Asia and the Americas of 76.5%, 55.8%, 75.1% and 82.7% was published. In Cuba from 1970 to 2011, the incidence of the operation increased from 3.7 to 30.4%, and until 2016, the figure ranged from 30.5%, showing an increase of 10 times the figure initial (Nápoles Méndez and Couto Núñez, 2017; [1]).

Cesarean section is a procedure that is used when vaginal delivery is risky for the mother and / or the fetus or it is not possible to perform it. It presents short- and long-term complications, with possible chronic repercussions on the well-being of the woman, the newborn and future pregnancies (Fonseca Pérez, 2017; Chen *et al.*, 2018).

Description of the Intervention

To meet the objectives of general anesthesia in any surgical intervention including caesarean section, there is a fairly wide arsenal of inducing drugs, from which they act on inhibitory neurotransmitters such as gamma aminobutyric acid A, such as Thiopental, Propofol, Midazolam; on excitatory neurotransmitters (glutamate, aspartate) such as Ketamine; and etomidate. The prototype drug for this process is Thiopental, but since Propofol was introduced in the clinic in 1977, it has aroused great interest, although the results have not been conclusive (Baker and Naguib, 2005).

It was first used by Kay and Rolly, as a water-insoluble drug in the form of a lipid emulsion. It is an alkyphenol, with a rapid onset of action and completion of its effect and few adverse effects. It is metabolized in the liver by glucuroconjugation and sulfate without metabolites with pharmacological action, and presents extrahepatic metabolism (renal and intestinal) and is excreted by the kidney and other organs such as the lungs. It follows a two-compartment distribution model and as a three-compartment model. Its pharmacokinetics are very sensitive. It is used for sedation, amnesia, hypnosis, anticonvulsant (controversial effect), antiemetic, antipruritic, and antinociceptive. With doses of 1 to 1.5 mg / kg, loss of consciousness is obtained, but the duration of the hypnotic effect is greater, 10 to 15 minutes, if doses between 2 to 2.5 mg / kg are administered. The initial distribution half-life is 2 to 8 minutes, with an elimination half-life between 4-23.5 hours. It has a volume of distribution in the central compartment of 20 to 40 liters. Maintains a high clearance under normal conditions, between 1.5 and 2.2 liters / minute (Vanegas Saavedra, 2014; Vuyk *et al.*, 2020).

In Cuba, the Center for State Control of Medicines, Equipment and Medical Devices, published that the safety of the use of Propofol was not proven during pregnancy and lactation, so it is not

recommended as an inducer or at high doses, more than 2.5 mg / kg in induction, nor more than 6 mg / kg / h for maintenance. This publication refers to the absence of sufficient scientific evidence to affirm the safety of the drug in obstetric patients [3].

How the Intervention Might Work

The placenta is considered an exchange membrane, of solute, proteins, nutrients, oxygen, carbon dioxide, among others, but also as a pathway for drugs that may or may not affect the fetus (Martínez Segura, 2014; Gin *et al.*, 1990). Some of the factors on which the placental transfer of drugs depends are: maternal (maternal pH, lipid solubility and degree of ionization of drugs, physicochemical characteristics, cardiac output, exposure time), placental (membrane thickness, size of the exchange surface, the presence of placental alterations), and fetal (fetal cardiac output, drug protein binding, fetal metabolism) (Vuyk *et al.*, 2020).

It is part of the maternal central compartment for the distribution of any drug and is related to the rapid distribution half-life after intravenous bolus, where each drug follows a pharmacokinetic profile, which determines the drug concentration in plasma and at the effect site (brain), which results in an adequate anesthetic state (Soens and Tsen, 2020). It is recognized as a critical period for anesthesiologists, neonatologists and obstetricians, the time that elapses between anesthetic induction and extraction of the product, which in skilled hands ranges between 3 and 5 minutes. During this time, the maternal concentrations of the drug gradually, to establish a state of pseudo-equilibrium between the plasma and the effect site, and then undergo a decay by distribution and elimination of the drug (Delgado *et al.*, 2020).

For its part, the fetus constitutes a pharmacokinetic model that is somewhat independent from that of the mother, where low concentrations of anesthetics are found after bolus, which depends on maternal cardiac output, uteroplacental blood flow, fetal metabolism, protein binding, volume of fetal distribution with greater amount of water, maternal-fetal pH gradient, dose and exposure time (Martínez Segura, 2014).

After birth, most newborns have few residual anesthetic effects, since only a small part reaches the fetal brain (Santos *et al.*, 2015).

Why This Review is Important

No systematic review was found that had been carried out previously in the country. In addition, there are controversies regarding the safety of propofol as an inducing anesthetic agent for caesarean

section based on neonatal outcomes. In particular, the purpose of this drug is to examine the physical state of the newborn as well as the adaptive and neurological capacity, the acid-base state, the risk of hypoxia and the incidence of admission to the neonatal intensive care unit. The evidence suggests that Propofol is a good therapeutic option to provide general anesthesia in this situation, surpassing Barbiturates and other agents depending on the quality of maternal recovery, the lower incidence of adverse effects and intraoperative awakening.

Objective

To evaluate the neonatal results of the use of Propofol versus Barbiturates as an inducing agent for anesthesia for elective cesarean section.

Methods

For the preparation of the systematic review and meta-analysis, the Cochrane collaboration guidelines established in the Cochrane manual of systematic reviews of interventions version 5.1.0 will be followed (Centro Cochrane Iberoamericano, 2011).

The PRISMA guidelines for this purpose will be followed during the review (Fleming PS *et al.*, 2013).

Type of Studies: randomized controlled clinical trials, comparative studies.

Type of Participants: pregnant patients, with a single fetus, without maternal or fetal complications, who arrive for elective surgery for cesarean section.

Types of Interventions: general orotracheal anesthesia, where Propofol is compared against Thiopental or other barbiturate drugs.

Types of Outcome Measures

Primary Outcome

Neonatal depression at one minute and at five minutes of life according to the significant Apgar score when it was <7 points.

Secondary Outcomes

Low adaptive and neurological capacity according to the score of the adaptive and neurological capacity scale at 15-30 minutes, 2 hours and 24 hours of life, significant when it was <35 points.

Neonatal acidosis (respiratory or metabolic) defined by alterations in the acid base status according to pH, BE (mmol / l), HCO₃ (mmol / l), pCO₂ (mmHg).

Neonatal hypoxia defined by pO₂ figures.

Need for admission to the neonatal intensive care unit.

Exclusion Criteria

Retrospective research, systematic reviews, non-systematic reviews, case presentation and case series, letters to the editor, review articles, studies that were conducted outside the time range in which the review was conducted, randomized and controlled clinical trials were excluded for emergency cesarean section, pregnancies with multiple fetuses, comparison of general and regional anesthetic techniques, where various drugs were administered for anesthetic induction, pregnant women with maternal or fetal complications.

Search Methods for The Identification of Studies

Electronic Search

A systematic review will be carried out of the works published in the databases of the Cochran library, MEDLINE, EMBASE, Cochran Central Register of controlled trials (CENTRAL), PubMed, SCISEARCH, Registries of clinical trials, EBSCO, LILACS, Sciencedirect, Hinari, in Spanish and English for the last 35 years, using keywords such as: (anesthetic induction OR general anesthesia OR) AND (propofol OR Thiopental OR) AND (cesarean section OR cesarean section OR).

Looking for other sources In addition, the search for "pearls" will be implemented in the bibliographic references of the most relevant investigations, with the purpose of increasing the number of articles in the review. On the other hand, we will try to establish contact with the authors of the works with incomplete data publication, publication of the abstract, or that the necessary information will be represented in the form of a graph. Data extraction and analysis Two review authors: Dr. Marcelino Sánchez Tamayo and Dr. Miguel Liván Sánchez Martín, individually completed the data collection and evaluation before comparing the results and reaching a consensus. In the event of discrepancies, a third reviewer, Dr. Eivet García Real, will be consulted to resolve the disagreement.

Selection of studies The Zotero version 5.0.89 bibliographic reference manager was used to store the search results and eliminate duplicate documents. All titles and abstracts will be evaluated by two reviewers individually, according to provenance and authorship, deciding if the work was included,

excluded or not clear. In the event of any discrepancy between these, the criteria of a third evaluator will be requested. For the titles that with the potential to be included in the review, the full text was obtained, in order to assess the agreement with the inclusion and exclusion criteria, and if they provide sufficient information to be chosen. The number of items chosen at each stage will be recorded, which will be reported on a PRISMA flow chart.

Data Extraction and Management

The data of the studies that were included and that were extracted in a data collection sheet were: author, year of publication, study groups, participants, measurement scales and the fundamental results. Each result will be extracted independently by an author, and if there are discrepancies between them, the opinion of a third evaluator will be requested.

Assessment of Risk of Bias in Included Studies

The Cochrane collaboration tool, Review Manager version 5.1 (RevMan) was used to determine the level of bias and the quality of the papers that were included. Two investigators carried out the process of completing the items that evaluated the bias independently, requesting a third criterion if there was any discrepancy.

The following aspects will be evaluated:

- Random sequence generation (selection bias).
- Allocation concealment (selection bias).
- Blinding of participants and staff (performance bias).
- Blinding of outcome assessment (detection bias).
- Incomplete outcome data (attrition bias).
- Selective reporting (reporting bias).

Other Biases

The evaluation of each aspect will be carried out in low risk, high risk or unclear level of risk. This information will be recorded and displayed in a chart of risk of bias on included research and another for stratifying the quality of included research.

Measures of Treatment Effect

Dichotomous data (number of patients) will be collected for neonatal depression outcomes at 1 minute and 5 minutes; low adaptive and neurological capacity at 15-30 minutes, at 2 hours and at 24 hours; and the need for admission to the neonatal intensive care unit.

Continuous data (mean value and standard deviation) will be collected for the variables values of excess base, pH, arterial pressure of carbon dioxide, arterial pressure of oxygen and quantification of bicarbonate.

The relative risk will be determined for dichotomous data and the standardized mean difference for continuous values. The overall effect will be measured by the value of "Z".

Handling of Unavailable Data

Information from the primary investigation will be compared with the protocol when possible, in order to know if all measured outcomes were reported. It will be verified whether all the patients who were included at random were included in the research results. This element will be considered within the guidelines that evaluate the bias of the studies.

Assessment of Heterogeneity

It will be evaluated by observing the overlap of the confidence intervals, where the coincidence of these denotes greater consistency between the investigations. The I² statistical test will also be determined (indicates which proportion of the variance is due to the difference in the effect and not secondary to sampling errors), with the value of Tau (indicates the variance of the true effects) and with the value of the chi². In the case of I², a value of 0% was categorized as homogeneous studies, up to 25%: low heterogeneity, up to 50%: moderate heterogeneity, up to 75% high heterogeneity, and up to 100%, it was classified as considerable heterogeneity. On the other hand, a result of $p < 0.05$ in the chi² test indicated a result of moderate to considerable heterogeneity (Borenstein *et al.*, 2011; Garcia Alamino and Lopez Cano, 2020).

Assessment of Reporting Bias

The research protocols that were included will be sought, with the aim of establishing a comparison between them and evaluating their differences. To show the publication bias, a funnel plot (Funnel Plott) will be used, when the number of investigations included for a given variable is eight or more (Sterne *et al.*, 2011).

Data Synthesis

The meta-analysis will be carried out in those variables where there is more than one investigation. The results will be presented depending on the outcomes to be studied. The RevMan version 5.1.0 calculator will be used to determine the relative risk using the Mantel-Haenszel model. The

random effects model will also be used if there is variation between the research groups. A 95% confidence interval will be set, with a p value = 0.05 or less to establish statistical significance. The statistical analysis of the works and the preparation of the forest graphs (Forrest Plott) will be obtained with the collaboration of RevMan version 5.1.0.

Summary of Findings Table

The GRADE system was used to evaluate the degrees of scientific evidence, which were related to the following outcomes:

- Neonatal depression at the minute of life.
- Neonatal depression at five minutes of life.
- Adaptive and neurological capacity at 24 hours of life.
- Neonatal hypoxia.
- Neonatal acidosis.

The GRADE approach assesses the certainty of a body of evidence based on the extent to which one can be sure that an estimate of effect or association reflects the item being assessed. The assessment of the certainty of a body of evidence considers the risk of bias within the study, openness of the evidence, heterogeneity of the data, precision of the effect estimates, and risk of publication bias. A four 'Summary of findings' tables were constructed using the GRADEpro GDT software to create 'Summary of findings' tables for the following comparison in the review:

Propofol vs Barbiturates

The composition of the table was carried out by two authors in the review.

Results

Description of The Studies

The general characteristics of the patients in the studies in terms of maternal age, gestational age, height, weight, parity, history, and anesthetic protocol, were similar between the comparison groups and between the investigations.

Search Results

4420 studies were found plus 61 works through other sources (pearl search) in the initial search; where 394 records that were duplicated in the different electronic databases were eliminated and 1015 full-text papers were approved for review, of which 984 articles were excluded, being included in the

qualitative analysis of the review 21 investigations and in the meta-analysis 17 of them that included 1898 patients (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Celleno *et al.*, 1989; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Mamidi *et al.*, 2011; Miranda *et al.*, 1992; Montandrau *et al.*, 2019; Moore *et al.*, 1989; Saharei *et al.*, 2014; Tolyat *et al.*, 2016; Tumukunde *et al.*, 2015; Valtonen *et al.*, 1989; Yau *et al.*, 1991; Cakrtekin *et al.*, 2015) (Fig. 1).

Included Studies

Outcomes

Seventeen investigations (Table 1) were included in the systematic review that establish a comparison of neonatal outcomes between the use of Propofol and Barbiturate drugs.

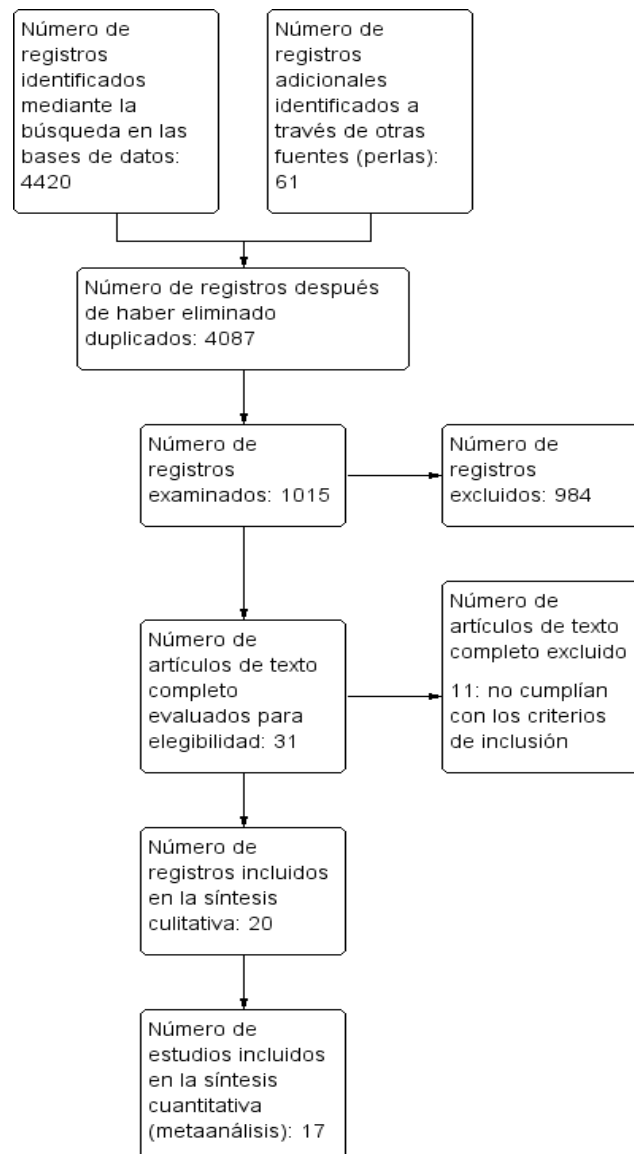


Figure 1: Research selection process within the review

Table 1: General characteristics of the studies that were included

| Author and year | Desing | Intervention (total participants) | Measurement of variables | Outcomes | Results |
|-----------------|---|---|--|--|--|
| Abboud, 1995 | Clinical trial | Experimental group (Propofol): 37 patients Control group (Tiamilal): 37 patients | Physical state 1 and 5 minutes (Apgar scale) acid base state adaptive and neurological capacity 2 hours and 24 hours (Neurological and Adaptive capacity score NACS) | Apgar <7 Alterations in the acid-base state NACS <35 | Neonatal status (Apgar scale), acid-base status, and adaptive and neurological capacity were good in both research groups. |
| Capogna, 1991 | Randomized double-blind clinical trial | Experimental group (Propofol): 28 patients Control group (Thiopental): 28 patients | Physical state 1 and 5 minutes (Apgar scale) acid base state adaptive and neurological capacity at 15 minutes, 2 hours, 24 hours (Neurological and Adaptive capacity score NACS) | Apgar <7 Alterations in the acid-base state NACS <35 | Neonates in the Propofol group obtained a low Apgar score at one minute of life, but there were no differences between the groups at five minutes of life. |
| Celleno, 1989 | Randomized comparative clinical study | Experimental group (Propofol): 20 patients Control group (Thiopental): 20 patients | Physical state 1 and 5 minutes (Apgar scale) adaptive and neurological capacity at 24 hours (Neurological and Adaptive capacity score NACS) | Apgar <7 ENNS <35 | Infants in the Propofol group were lowest at 1 and 5 minutes, with 25% muscle hypotonia at 5 minutes. Hypotonia was not found with the early neuroadaptation |
| Celleno, 1993 | Randomized comparative clinical study | Experimental group (Propofol): 30 patients Control group (Thiopental): 30 patients | Physical state 1 and 5 minutes (Apgar scale) adaptive and neurological capacity at 15 minutes, 2 hours, 24 hours (Neurological and Adaptive capacity score NACS) | Apgar < 7 NACS < 35 | The Apgar score was lower in the Propofol group than in the Thiopental group. There was no difference between the groups and the acid base state. |
| Dailland, 1989 | Randomized comparative clinical study | Phase I group: propofol for bolus induction iv. Phase II group: propofol for induction and maintenance. | Physical state 1 and 5 minutes (Apgar scale) acid base state adaptive and neurological capacity 2 hours and 24 hours (Neurological and Adaptive capacity score NACS) adaptive and neurological capacity at 15 minutes, 2 hours, 24 hours (Neurological and Adaptive capacity score NACS) | Apgar <7 Alterations in the acid-base state NACS <35 | Minimal deleterious effects on the health of newborns were observed in the Propofol group |
| Gin, 1993 | Randomized comparative clinical study | Experimental group (Propofol): 30 patients Control group (Thiopental): 32 patients | Physical state 1 and 5 minutes (Apgar scale) acid base state adaptive and neurological capacity at 15 minutes, 2 hours, 24 hours (Neurological and Adaptive capacity score NACS) Admission to Neonatal Intensive Unit Care | Apgar <7 Alterations in the acid-base state NACS <35 Need for income | Neonatal Apgar scale, neuroadaptation scale, umbilical cord catecholamines, blood gases, oxygen content were similar in both groups |
| Gregory, 1990 | Randomized comparative clinical study | Experimental group (Propofol): 10 patients Control group (Thiopental): 10 patients | Physical state 1 and 5 minutes (Apgar scale) adaptive and neurological capacity at 15 minutes, 2 hours, 24 hours (Neurological and Adaptive capacity score NACS) | Apgar <7 NACS <35 Alterations in the acid-base state | The Apgar scale and blood gas analysis were similar in both groups |
| Mamidi, 2011 | Randomized double-blind controlled clinical trial | Experimental group (Propofol): 115 patients Control group (Thiopental): 115 patients | Physical state 1 and 5 minutes (Apgar scale) | Apgar < 7 | The Apgar scale at 1 and 5 minutes of life were higher in the Propofol group than in the Thiopental group |
| Miranda, 1992 | Randomized comparative clinical study | Experimental group (Propofol): 30 patients Control group (methohexytone): 30 patients | Physical state 1 and 5 minutes (Apgar scale) | Apgar < 7 | There were no differences between the groups in the Apgar score and blood gas analysis. |

| | | | | | |
|------------------|---|---|--|---|---|
| Montandrau, 2019 | Randomized comparative clinical study | Experimental group (Propofol): 189 patients Control group (Thiopental): 178 patients | Physical state 1 and 5 minutes (Apgar scale) acid base state Neonatal intensive care admission | Apgar <7 Alterations in the acid-base state NACS <35 Need for income | The use of Propofol was a risk to obtain low Apgar at one minute of life. Blood gas analysis and admission to therapy were similar in both groups |
| Moore, 1989 | Randomized clinical trial | Experimental group (Propofol): 21 patients Control group (Thiopentone): 21 patients | Physical state 1 and 5 minutes (Apgar scale) acid base state Neonatal intensive care admission | Apgar <7 Alterations in the acid-base state NACS <35 Necesidad de ingreso | Fetal evaluation was slightly better in the Thiopental group than in the Propofol group. |
| Sahraei, 2014 | Double-blind randomized controlled clinical trial | Experimental group (Propofol): 54 patients Control group (Thiopental): 54 patients | Physical state 1 and 5 minutes (Apgar scale) | Apgar < 7 | There were no statistically significant differences in neonatal vitality between the groups. |
| Tolyat, 2016 | Double-blind controlled clinical trial | Experimental group (Propofol): 28 patients. Control group (Thiopental): 28 patients. Experimental group (Propofol + Thiopental): 28 patients. | physical state 1 and 5 minutes (Apgar scale) | Apgar < 7 | There were differences between the groups and Propofol is proposed as the most appropriate agent for anesthetic induction. |
| Tumukunde, 2015 | Randomized controlled clinical trial | Experimental group (Propofol): 75 patients Control group (Thiopental): 75 patients | Physical state 1 and 5 minutes (Apgar scale) Neonatal intensive care admission | Apgar <7 Need for income | There were no differences between the two study groups. |
| Valtonen, 1989 | open clinical trial | Experimental group (Propofol): 16 patients Control group (Thiopentone): 16 patients | Physical state 1 and 5 minutes (Apgar scale) acid base state | Apgar <7 Alterations in the acid-base state | There were no differences between the two study groups in terms of the Apgar scale and blood gas analysis. |
| Yau, 1991 | Randomized comparative clinical study | Experimental group (Propofol): 20 patients Control group (Thiopentone): 20 patients | Physical state 1 and 5 minutes (Apgar scale) acid base state adaptive and neurological capacity at 15 minutes, 2 hours, 24 hours (Neurological and Adaptive capacity score NACS) | Apgar <7 Alterations in the acid-base state NACS <35 | The Apgar scale and the neurological adaptation scale were similar in the two groups |
| Çakırtekin, 2015 | Randomized comparative clinical study | Experimental group (Propofol): 35 patients Control group (Thiopentone): 35 patients | Physical state 1 and 5 minutes (Apgar scale) acid base state | Apgar <7 Alterations in the acid-base state | The Apgar score at 1 and 5 minutes of life, blood gas analysis was similar in both groups |

Seventeen studies report the physical state of the newborn in the first minute (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Celleno *et al.*, 1989; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Mamidi *et al.*, 2011; Miranda *et al.*, 1992; Montandrau *et al.*, 2019; Moore *et al.*, 1989; Saharei *et al.*, 2014; Tolyat *et al.*, 2016; Tumukunde *et al.*, 2015; Valtonen *et al.*, 1989, Yau *et al.*, 1991; Cakrtekin *et al.*, 2015); seventeen investigations report data on the physical state of the newborn at five minutes (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Celleno *et al.*, 1989; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Mamidi *et al.*, 2011; Miranda *et al.*, 1992; Montandrau *et al.*, 2019; Moore *et al.*, 1989; Saharei *et al.*, 2014; Tolyat *et al.*, 2016; Tumukunde *et al.*,

2015; Valtonen *et al.*, 1989, Yau *et al.*, 1991; Cakrtekin *et al.*, 2015); six studies evaluate adaptive and neurological capacity between 15 and 30 minutes of life (Capogna *et al.*, 1991; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Yau *et al.*, 1991); seven studies acquire data on adaptive and neurological capacity at two hours (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Yau *et al.*, 1991); seven studies confirmed adaptive and neurological capacity at 24 hours of life (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Yau *et al.*, 1991); nine investigations report the newborn's pH values (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Dailland *et al.*, 1989; Gin *et al.*, 1993; Montandrau *et al.*, 2019; Moore *et al.*, 1989; Valtonen *et al.*, 1989; Yau *et al.*, 1991; Cakrtekin *et al.*, 2015); seven studies show the BE values of the newborn (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Dailland *et al.*, 1989; Gin *et al.*, 1993; Valtonen *et al.*, 1989; Yau *et al.*, 1991; Cakrtekin *et al.*, 2015); Nine studies report newborn pCO₂ values (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Dailland *et al.*, 1989; Gin *et al.*, 1993; Montandrau *et al.*, 2019; Moore *et al.*, 1989; Valtonen *et al.*, 1989; Yau *et al.*, 1991; Cakrtekin *et al.*, 2015); nine studies show the pO₂ values of the newborn (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Dailland *et al.*, 1989; Gin *et al.*, 1993; Montandrau *et al.*, 2019; Moore *et al.*, 1989; Valtonen *et al.*, 1989; Yau *et al.*, 1991; Cakrtekin *et al.*, 2015); four investigations on HCO₃ values (Capogna *et al.*, 1991; Gin *et al.*, 1993; Valtonen *et al.*, 1989; Cakrtekin *et al.*, 2015); and four studies stated the need for intensive care (Gin *et al.*, 1993; Montandrau *et al.*, 2019; Moore *et al.*, 1989; Tumukunde *et al.*, 2015) as key outcomes.

Intervention and Comparison

Propofol vs Tiamilal

One study compared Propofol and Thiamilal as inducing anesthetic agents in caesarean section (Abboud *et al.*, 1989).

Propofol vs Methohexitone

One work carried out the comparison between Propofol and Methohexitone as inducing anesthetic agents in caesarean section (Miranda *et al.*, 1992).

Propofol vs Thiopental / Thiopentone

Fifteen investigations developed the comparison of Propofol versus Thiopental as anesthetic inducing agents in cesarean section (Capogna *et al.*, 1991; Celleno *et al.*, 1989; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Mamidi *et al.*, 2011; Montandrau *et al.*, 2019;

Moore *et al.*, 1989; Saharei *et al.*, 2014; Tolyat *et al.*, 2016; Tumukunde *et al.*, 2015; Valtonen *et al.*, 1989, Yau *et al.*, 1991; Cakrtekin *et al.*, 2015)

Country of Origin

The studies were carried out in one of the following countries: USA (Abboud *et al.*, 1995); Italy (Capogna *et al.*, 1991; Celleno *et al.*, 1989; Celleno *et al.*, 1993); Iran (Mamidi *et al.*, 2011; Saharei *et al.*, 2014; Tolyat *et al.*, 2016); France (Dailland *et al.*, 1989; Montandrau *et al.*, 2019); China (Gin *et al.*, 1993; Gregory *et al.*, 1990; Yau *et al.*, 1991); Malaysia (Miranda *et al.*, 1992); England (Moore *et al.*, 1991); Uganda (Tumukunde *et al.*, 2015); Finland (Valtonen *et al.*, 1989); Turkey (Cakrtekin *et al.*, 2015).

Excluded Studies

Some studies, despite meeting the inclusion criteria, are not part of the review as the full work could not be obtained or the full text was in other languages despite the title and abstract being published in the selected languages of the review.

Risk of Bias of Included Studies

Figure 2 shows the risk of bias according to the Cochrane methodological bases. Regarding random sequence generation, allocation concealment, blinding of participants and staff, blinding of outcome assessment, selective reporting, and other risks, an unclear risk was mostly detected due to the absence or exposure of incomplete data in the publication work; The incomplete results data exposure parameter had a low risk of bias, since all the data that were operationalized were exposed as results. High risk of bias was only detected in the randomization of the groups, in which it was done by the number of medical records (Montandrau *et al.*, 2019) and the presentation of incomplete data in the study results (Gregory *et al.*, 1990). (Fig. 2).

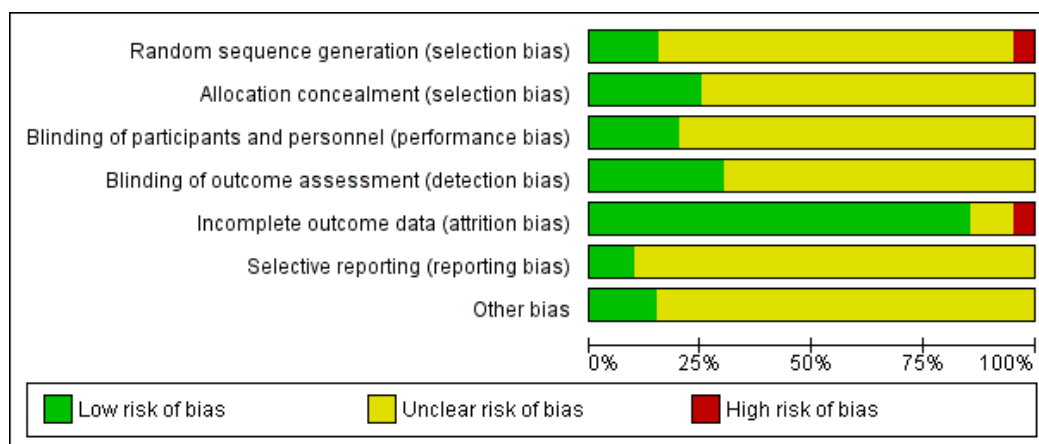


Figure 2: Assessment of risk of bias

The independent quality assessment of each investigation is shown in the figure (Fig. 3).

| | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|-------------------|---|---|---|---|--|--------------------------------------|------------|
| Abboud 1995 | ? | ? | ? | ? | + | ? | ? |
| Çakırtekin 2015 | ? | ? | ? | ? | + | + | ? |
| Capogna 1991 | ? | + | ? | ? | + | ? | ? |
| Celleno 1989 | ? | ? | ? | ? | + | ? | ? |
| Celleno 1993 | + | + | + | + | + | ? | + |
| Dailland 1989 | ? | ? | ? | + | + | ? | ? |
| GIN 1993 | ? | ? | ? | + | + | ? | ? |
| Gregory 1990 | ? | ? | ? | ? | - | ? | ? |
| Mamidi 2011 | ? | ? | ? | ? | + | ? | ? |
| Mamidi 2016 | ? | ? | ? | ? | + | ? | ? |
| Mehdi 2012 | ? | + | + | + | + | ? | ? |
| Miranda 1992 | ? | ? | ? | ? | + | ? | ? |
| Montandrou 2019 | - | ? | ? | ? | + | ? | ? |
| MOORE 1989 | ? | ? | ? | ? | + | ? | ? |
| Sahraei 2014 | ? | ? | ? | ? | ? | ? | ? |
| Tolyat 2016 | + | + | + | + | + | ? | + |
| Tumukunde 2015 | + | + | + | + | + | + | + |
| VALTONEN 1989 | ? | ? | ? | ? | ? | ? | ? |
| Venkatareddy 2018 | ? | ? | ? | ? | + | ? | ? |
| Yau 1991 | ? | ? | ? | ? | + | ? | ? |

Figure 3: Independent research quality assessment

The analysis of publication bias was carried out using the funnel plot for the variables: neonatal Apgar result 1 minute (Fig. 4), neonatal Apgar result 5 minutes (Fig. 5), neonatal result pH values (Figure 6), result neonatal pCO₂ values (Fig. 7), neonatal pO₂ values (Fig. 8).

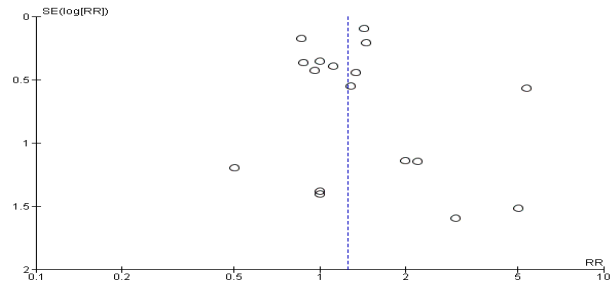


Figure 4: Analysis of publication for the analysis of the Apgar neonatal 1 minute of life

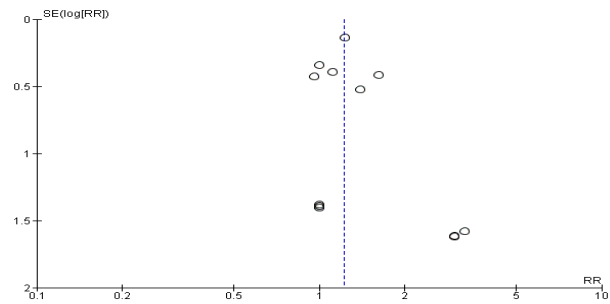


Figure 5: Analysis of publication for the analysis of the Apgar neonatal 5 minute of life

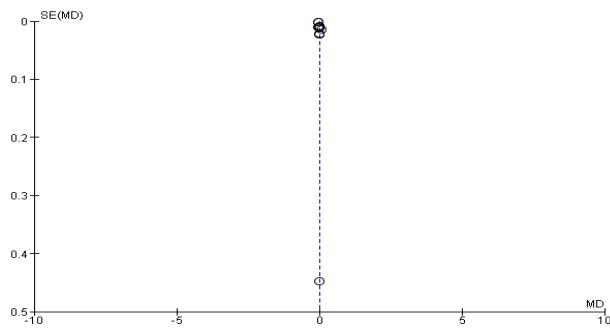


Figure 6: Analysis of publication bias for the neonatal pH analysis

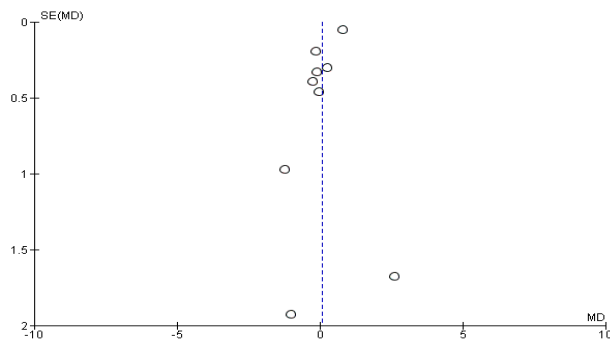


Figure 7: Analysis of publication bias for the neonatal pCO₂ analysis

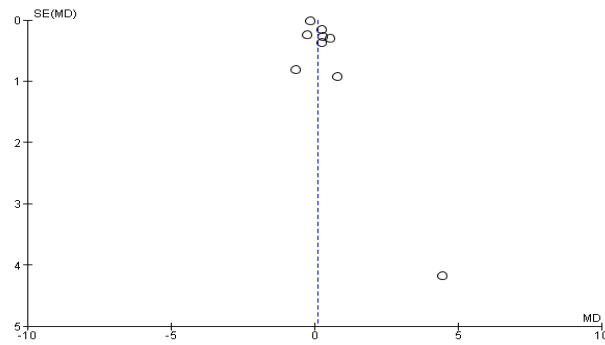


Figure 8: Analysis of publication bias for the neonatal pO₂ analysis

Analysis of The Results

Neonatal Depression in The First Minute of Life

Seventeen studies reported data on neonatal depression within the first minute of life (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Celleno *et al.*, 1989; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Mamidi *et al.*, 2011; Miranda *et al.*, 1992; Montandrou *et al.*, 2019; Moore *et al.*, 1989; Sahraei *et al.*, 2014; Tolyat *et al.*, 2016; Tumukunde *et al.*, 2015; Valtonen *et al.*, 1989, Yau *et al.*, 1991; Cakrtekin *et al.*, 2015)

The physical state of the newborns according to the Apgar scale at the first minute (Figure 9) showed a positive association between the study groups, with which it could be said that patients whose mothers were administered Propofol have a higher risk of present neonatal depression. (RR: 1.26; 95% CI: 1.07 and 1.48; patients 1898). The analysis of heterogeneity included chi2 values of 17.05 with df = 16 and the I2 value was 6% (low heterogeneity).

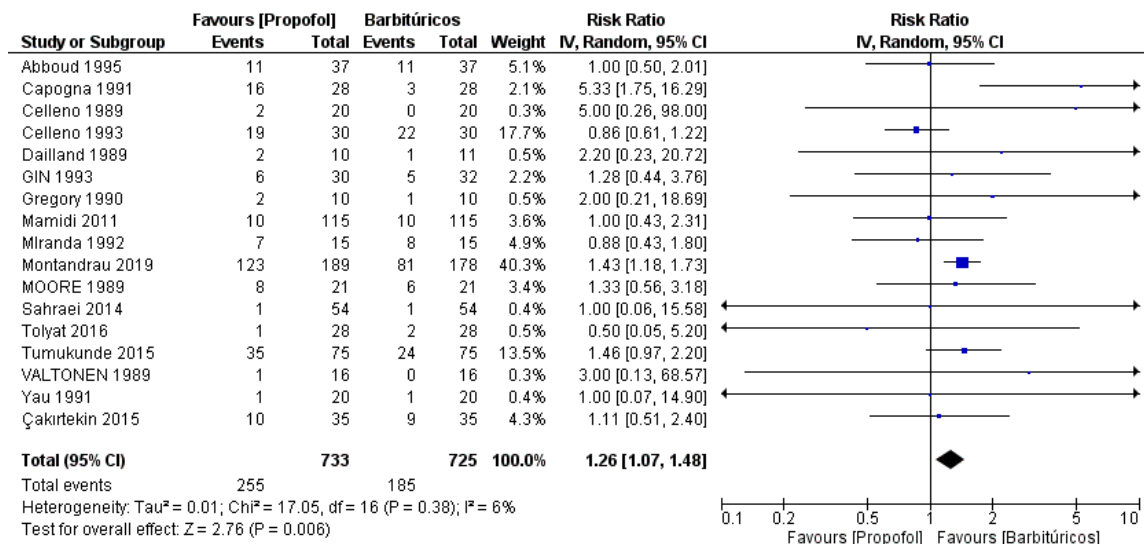


Figure 9: Forest graph for the analysis of neonatal Apgar at 1 minute of life

The GRADE approach was used to determine the level of evidence. In this case, a moderate level of evidence was obtained, especially due to the number of elements that assess the research risk that were classified as unclear risk (Table 2).

| Certainty assessment | | | | | | | Nº de pacientes | | Efecto | | Certainty | Importance |
|---|------------------|--------------|-------------------|-------------------|-------------------|-----------------------|-----------------|-----------------|------------------------|---|---------------|------------|
| Number of studies | Study desing | Risk of bias | Inconsistency | Indirect evidence | Vageness | Others considerations | Propofol | Barbiturates | Relative (95% CI) | Absolute (95% CI) | | |
| Neonatal depression at the first minute of life | | | | | | | | | | | | |
| 17 | Randomized trial | Serious | It is not serious | It is not serious | It is not serious | none | 255/733 (34.8%) | 185/725 (25.5%) | RR 1.26 (1.07 to 1.48) | 66 more per 1000 (from 18 more to 122 more) | ⊕⊕⊕○ Moderate | |
| Neonatal depression at the five minutes of life | | | | | | | | | | | | |
| 17 | Randomized trial | Serious | It is not serious | It is not serious | It is not serious | none | 130/733 (17.7%) | 101/725 (13.9%) | RR 1.22 (0.99 TO 1.51) | 31 More per 1000 (from 1 less to 71 more) | ⊕⊕⊕○ Moderate | |
| Low adaptative and neurological capacity at 24 hours of life | | | | | | | | | | | | |
| 7 | Randomized trial | Serious | It is not serious | It is not serious | It is not serious | none | 5/129 (3.9%) | 5/130 (3.8%) | RR 0.96 (0.32 to 2.83) | 2 less per 1000 (from 26 less to 70 more) | | |
| Neonatal acidosis | | | | | | | | | | | | |
| 9 | Randomized trial | Serious | It is not serious | It is not serious | It is not serious | none | 381 | 372 | - | 0 (0 to 0) | ⊕⊕⊕○ Moderate | |
| Neonatal hypoxia | | | | | | | | | | | | |
| 9 | Randomized trial | Serious | It is not serious | It is not serious | It is not serious | none | 206 | 204 | - | 0 (0 to 0) | ⊕⊕⊕○ Moderate | |
| Need for admission to the Neonatal Intensive Care Unit | | | | | | | | | | | | |
| 4 | Randomized trial | Serious | It is not serious | It is not serious | It is not serious | none | 91/314 (29.0%) | 90/300 (30.0%) | RR 1.11 (0.49 to 2.54) | 33 more per 1000 (dfrom 153 less to 462 more) | - | |

Neonatal Depression at Five Minutes of Life

Seventeen studies reported data on neonatal depression at five minutes of life (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Celleno *et al.*, 1989; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Mamidi *et al.*, 2011; Miranda *et al.*, 1992; Montandrou *et al.*, 2019; Moore *et al.*, 1989; Saharei *et al.*, 2014; Tolyat *et al.*, 2016; Tumukunde *et al.*, 2015; Valtonen *et al.*, 1989 ; Yau *et al.*, 1991; Cakrtekin *et al.*, 2015)

The physical state of the newborns according to the Apgar scale at five minutes of life (Fig. 10) showed that there were no significant differences between the experimental and the control group (RR: 1.22; 95% CI: 0.98 and 1.51; p = 0.07; participants: 1898 patients). The analysis of heterogeneity included chi2 values of 2.36 with df = 11 and the I2 value was 0% (homogeneous studies).

The GRADE approach was used to determine the level of evidence. In this case, a moderate level of evidence was obtained, especially due to the number of elements that assess the research risk that were classified as unclear risk. (Table 2)

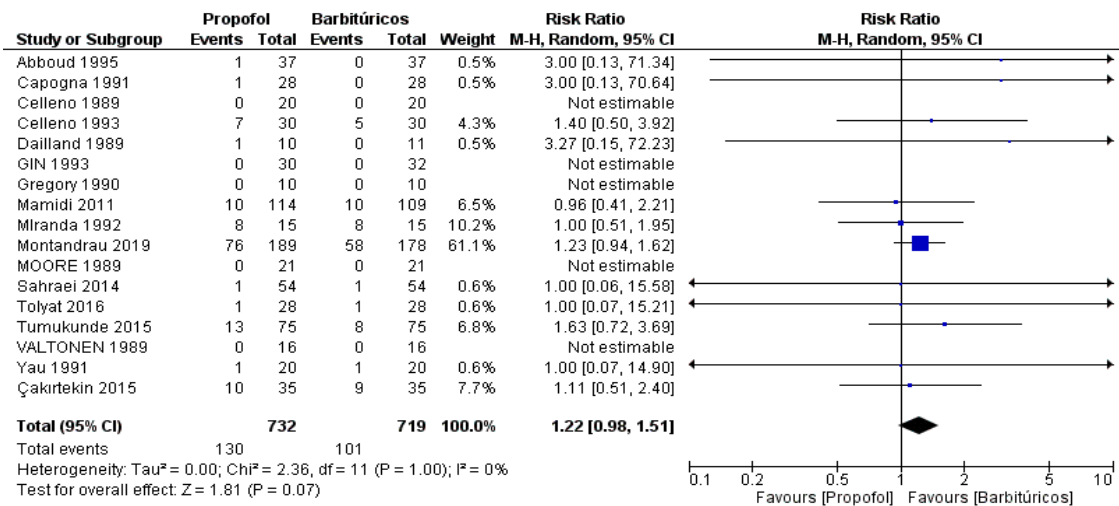


Figure 10: Forest graph for the analysis of neonatal Apgar at 5 minute of life

Adaptive and Neurological Capacity

Seven studies assess adaptive and neurological capacity between the first 15 and 30 minutes, 2 hours and 24 hours of life (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Celleno *et al.*, 1993; Dailland *et al.*, 1989; Gin *et al.*, 1993; Gregory *et al.*, 1990; Yau *et al.*, 1991).

The adaptive and neurological capacity of newborns between 15 and 30 minutes, at 2 and 24 hours of life, shown in Figures 11-13, did not show significant differences between Propofol and Barbiturates (RR: 1.14; 0.88 and 0.96 respectively; 95% CI: 0.61 and 2.12; 0.42 and 1.84; 0.32 and 2.83 correspondingly; p = 0.68, 0.73 and 0, 94; participants: 281). Despite not finding a significant result, at 2 and 24 hours of life there was a lesser tendency to low adaptive and neurological capacity in the group whose mothers were administered Propofol. The analysis of heterogeneity included chi2 values of 3.90; 3.73 and 1.76, with df of 5; 5 and 4 respectively and the I2 values were 0% in the three results. (Homogeneous studies).

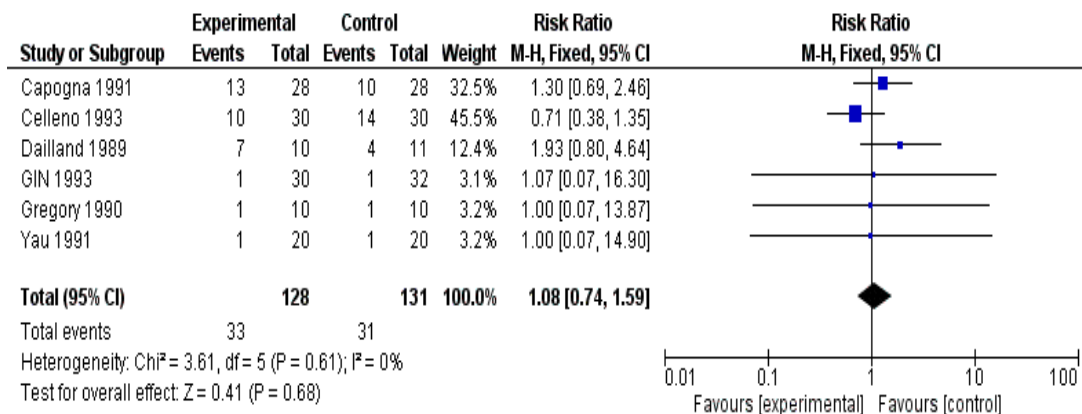


Figure 11: Forest graph for the analysis of neonatal adaptive and neurological capacity at 15 minutes of life

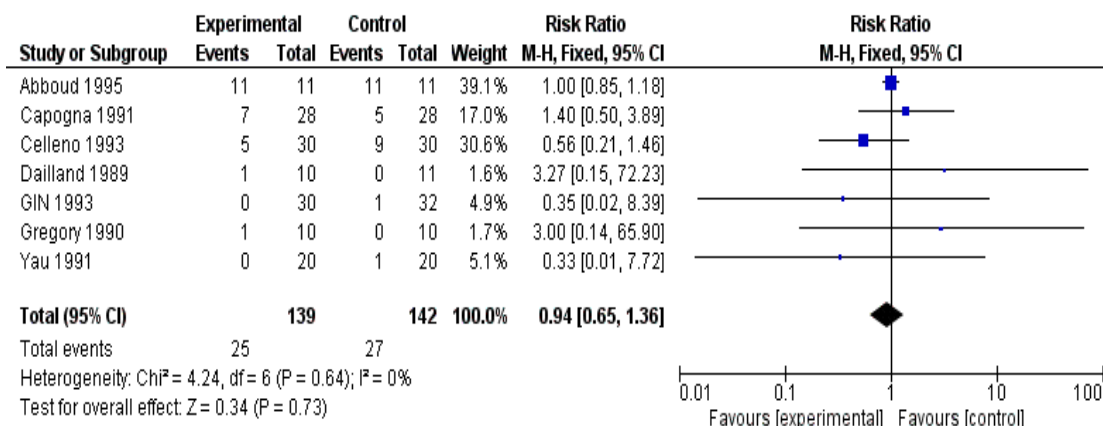


Figure 12: Forest graph for the analysis of neonatal adaptive and neurological capacity at 2 hours of life

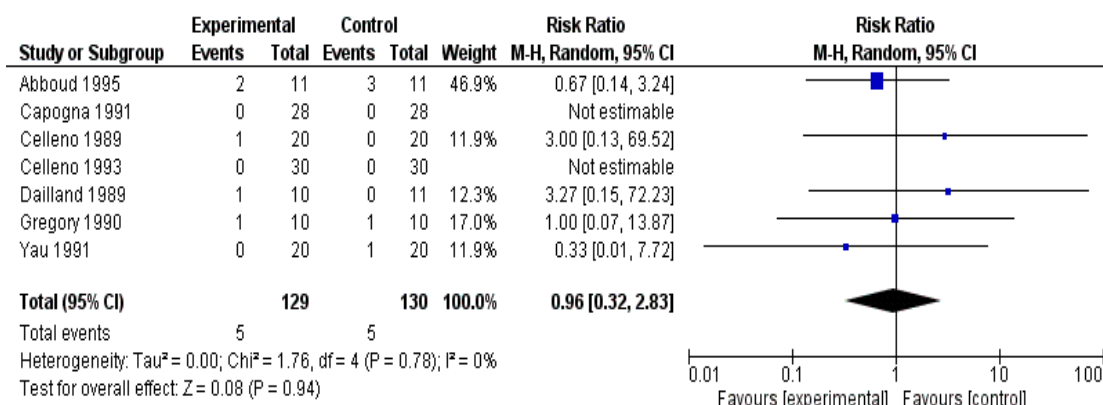


Figure 13: Forest graph for the analysis of neonatal adaptive and neurological capacity at 24 hours of life

Neonatal Acidosis

Between seven and nine investigations report data on neonatal acidosis status (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Dailland *et al.*, 1989; Gin *et al.*, 1993; Montandrou *et al.*, 2019; Moore *et al.*, 1989; Valtonen *et al.*, 1989; Yau *et al.*, 1991; Cakrtekin *et al.*, 2015).

In the evaluation of the acid-base status of the newborns for pH, pCO₂, and HCO₃ values at birth (Fig. 14-16), no statistical difference was observed between the treated and control groups. (SMD: 0.34, 0.96, 1.24, and -0.17 respectively; 95% CI: 0.98 and 0.31, 0.26 and 1.66, -0.06 and 2.53; and -0.97 and 0.62 correspondingly; p = 0.31, 0.06 and 0.66; participants: 753 patients).

Regarding the BE value (Fig. 17), if it was statistically significant (SMD: 0.96; 95% CI: 0.26-1.66; p = 0.007; participants: 344 patients), thus expressing a positive association between the comparison groups, and therefore, the infants in the experimental group have a higher risk of negative BE than the control group.

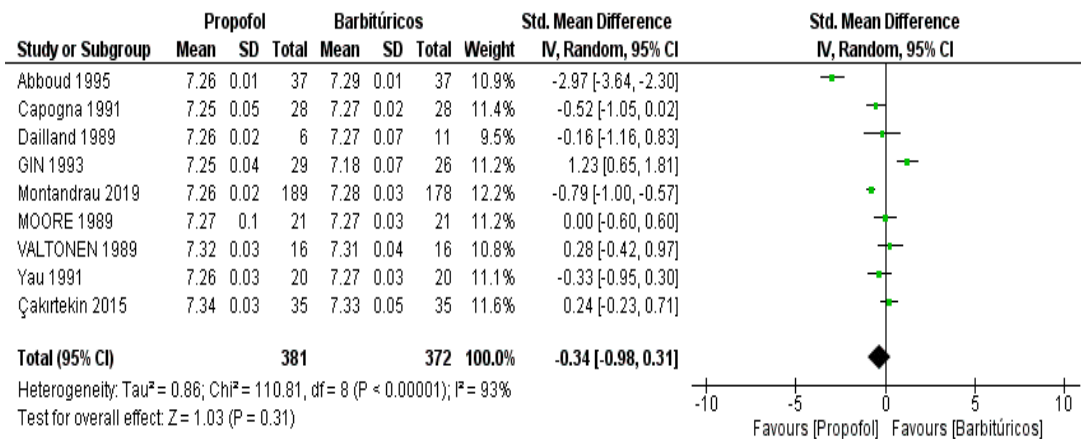


Figure 14: Forest graph for the neonatal pH analysis

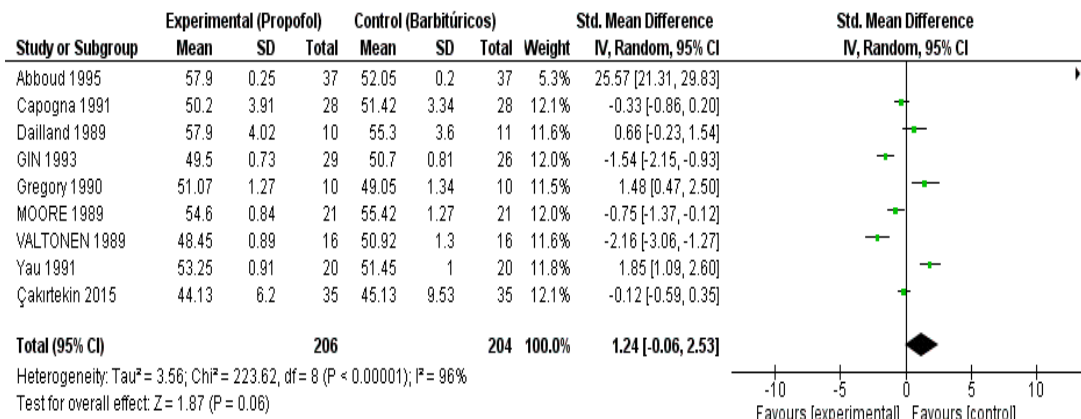


Figure 15: Forest graph for the neonatal pCO₂ analysis

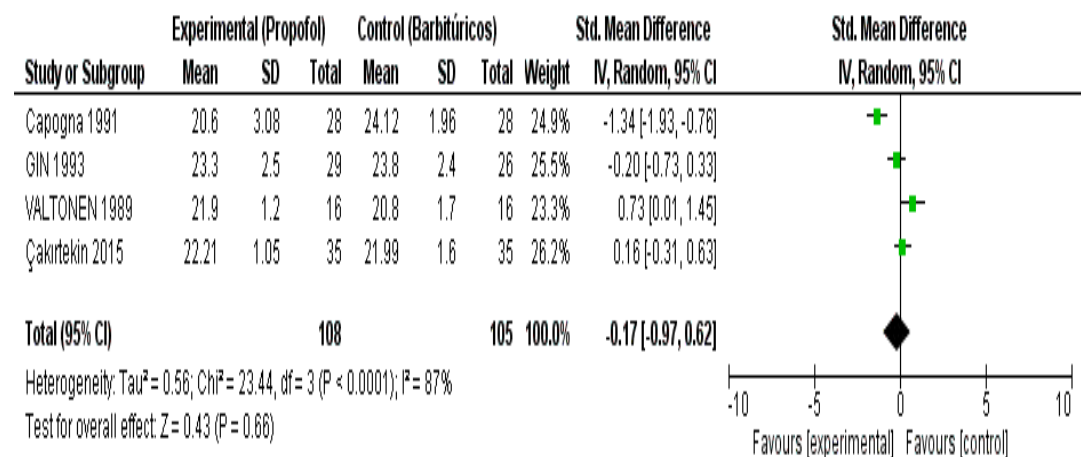


Figure 16: Forest graph for the neonatal HCO₃ analysis

The analysis of heterogeneity included chi² values of 110.81; 51.26; 223.62 and 23.44, with df of 8; 6; 8 and 3 respectively and the I² values were 93% for pH, 88% for BE, 96% for pCO₂ and 87% for HCO₃. (Considerably heterogeneous studies).

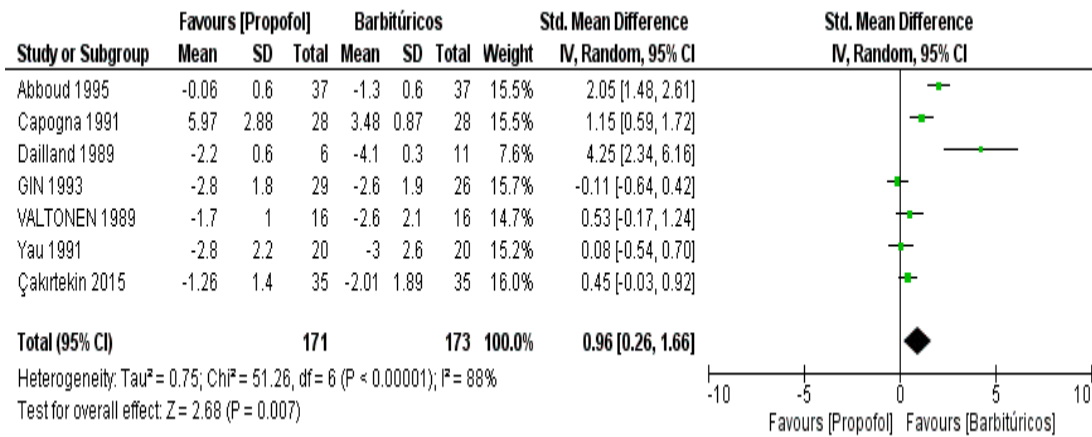


Figure 17: Forest graph for the neonatal BE analysis

The GRADE approach was used to determine the level of evidence. In this case, a moderate level of evidence was obtained, especially due to the number of elements that assess the research risk that were classified as unclear risk. (Table 2)

Neonatal Hypoxia

Nine studies reported data on neonatal depression in the first minute of life (Abboud *et al.*, 1995; Capogna *et al.*, 1991; Dailland *et al.*, 1989; Gin *et al.*, 1993; Montandrou *et al.*, 2019; Moore *et al.*, 1989; Valtonen *et al.*, 1989; Yau *et al.*, 1991; Cakırtekin *et al.*, 2015).

As shown in Fig. 18, there were no statistical differences regarding the pO₂ values of the newborns (SMD: -0.34, 95% CI: -0.98-0.31, p = 0.31; participants: 410 patients). The analysis of heterogeneity included chi² values of 110.81 with df = 8 and the I² value was 93% (considerable heterogeneity).

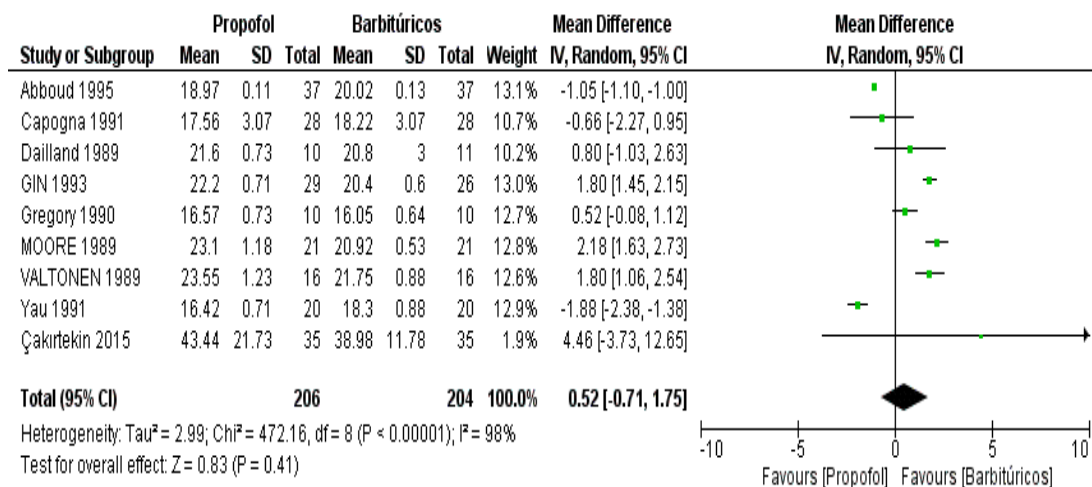


Figure 18: Forest graph for the neonatal pO₂ analysis

The GRADE approach was used to determine the level of evidence. In this case, a moderate level of evidence was obtained, especially due to the number of elements that assess the research risk that were classified as unclear risk. (Table II)

Need for Admission to the NICU

Four studies reported the need for intensive care (Gin *et al.*, 1993; Montandrau *et al.*, 2019; Moore *et al.*, 1989; Tumukunde *et al.*, 2015)

According to the analysis of the need for admission to the neonatal intensive care unit (Fig. 19), it was found that there were no statistical differences between the two comparison groups (RR: 1.11; 95% CI: 0.49-2.54; p = 0.08; participants: 614 patients). The analysis of heterogeneity included chi2 values of 6.78 with df = 3 and the I2 value was 56% (moderate heterogeneity).

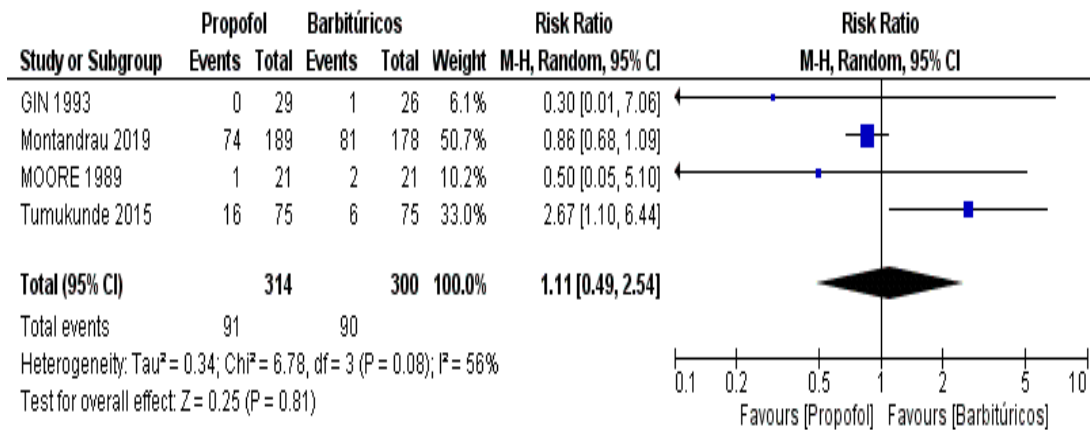


Figure 19: Forest graph according the need of neonatal admission in the Neonatal Intensive Care Unit

Tau2 values are also presented in each figure.

Discussion

The work that was carried out enables the synthesis of the scientific data available and evaluated the results of the use of Propofol as an anesthetic agent for the induction of general anesthesia in cesarean section compared to different barbiturates.

After data analysis, the deduction of fundamental elements in the subject in question is facilitated: that there were statistically significant differences in favor of the use of Barbiturates in the induction of anesthesia for cesarean section in terms of the physical state of the newborn at the first minute of life. There was no statistical difference according to the physical state of the newborn at five minutes, and the adaptive and neurological capacity between 15 and 30 minutes and at 2 and 24 hours. Also, there

was a lack of evidence to support one or another drug with respect to the acid-base status of newborns, although an accurate analysis could not be performed due to the heterogeneity present in the investigations.

The search found that a systematic review was conducted in 2018 that evaluated the results comparing the use of Thiopental against Propofol, Ketamine and benzodiazepines as inducing anesthetic agents for cesarean section. The authors carried out a study of 18 controlled and randomized clinical trials involving 911 patients, where they found that induction resulted in significantly lower pO₂ values than when it was performed with Thiopental (SMD: -11.52 [-17.60, -5.45] ; p = 0.0002). There were no significant differences in the analysis of other blood gases, or in terms of the Apgar score. (Houthoff Khemlani K *et al.*, 2018)

Abboud *et al.*, 1995; Capogna *et al.*, 1991; Mamidi *et al.*, 2011 and Montandrou *et al.*, 2019, to name just a few studies, found no differences between the results of comparing Propofol and Barbiturates in the physical state of newborns, and consider Propofol an excellent alternative for anesthetic induction in this situation.

Regarding the adaptive capacity of newborns, investigations published by authors such as Dailland *et al.*, 1989; Gin *et al.*, 1993 and Yau *et al.*, 1991, reported Propofol as a safe alternative with little impact on the newborn, without contributing differences with statistical significance.

Regarding the production of acidosis, no differences were found between Propofol and the Barbiturates used, according to the publications of Gin *et al.*, 1993; Moore *et al.*, 1989 and Valtonen *et al.*, 1989, although the BE was higher in the group of Barbiturates, which results in the increased risk for this result.

And finally, the need for intensive care showed no difference between the study groups, although there was a slight increase in risk in patients whose mothers received Barbiturates, as shared by Gin *et al.*, 1993; Montandrou *et al.*, 2019; Moore *et al.*, 1989 and Tumukunde *et al.*, 2015.

The authors consider that the heterogeneity they observed between the studies was mainly due to the different types of measurement and evaluation with which the variables that respond to the acid-base status of the patients were analyzed, which made it difficult to combine the scientific evidence.

The sensitivity assessment that subtraction of the research with less weight in terms of quality did not change the primary outcome that was found.

The analysis of publication bias using the funnel plot showed skewness in the results that

assessed the acid base status of the patients, which may be due to the number and small samples of the studies that were included in the review and the presence of heterogeneity. between investigations.

It is valid to note that when reviewing the anesthetic protocol of the studies that were included, the investigations that favored the control group used doses of Propofol higher than those recommended in the literature (Montandrou *et al.*, 2019) or close to the upper limit of the therapeutic window (Celleno *et al.*, 1989; Celleno *et al.*, 1993; Valtonen *et al.*, 1989), while the barbiturate drug doses were in the middle of the suggested dose range.

From a clinical point of view, it is known that Propofol has a greater negative impact than barbiturates, and despite the fact that its effect as a myocardial depressant has not been demonstrated, it does manifest considerable peripheral vasodilation due to a reduction in sympathetic activity and a reduction in blood pressure availability of calcium for contraction of vascular smooth muscle (Vuyk *et al.*, 2020) This hypotension could put at risk the blood perfusion of the uterus, which is completely dependent on the systemic cardiac output, as it is of high flow and low resistance. This relevant aspect could be prevented by reducing the dose to be used of Propofol, with an adequate preoperative vascular filling, increasing the availability of calcium and the preventive use of vasoconstrictors. In addition, performing laryngoscopy triggers a sympathomimetic stimulus, which could counteract the depressant effects of Propofol.

Among the limitations of the current systematic review and meta-analysis, is the exclusion of several studies due to not having the full text, the limitation of the search languages, and the heterogeneity that occurred in several results, without having a sufficient number of studies to carry out meta-regression analysis. It is valid to point out that the databases where the searches were carried out contain most of the scientific publications in the world, and that the quality of the review makes it possible to implement the knowledge in clinical practice. On the other hand, it is believed necessary to carry out a controlled and randomized clinical trial to strengthen this evidence in Cuba.

Conclusion

The use of Propofol for anesthetic induction in cesarean section is a good alternative with little impact on the physical state at five minutes since there was greater depression at one minute of life with the use of this; and the adaptive and neurological capacity of the newborn, the production of acidosis and the need for neonatal intensive care. Therefore, its use is recommended to perform anesthetic induction of patients who arrive for elective cesarean section surgery.

Recommendations

Carry out a clinical trial with the purpose of demonstrating the effectiveness of the use of propofol as an inducing agent in elective caesarean section with respect to neonatal outcomes.

References

- Abboud TK, Zhu J, Richafwsoiv M, Peres da SILVA E, Donovan M. Intravenous propofol vs thiamylal-isoflurane for caesarean section, comparative maternal and neonatal effects. *Acta Anaesthesiol Scand* 1995; 39: 205-209.
- Afolabi BB and Lesi FE. Regional versus general anaesthesia for caesarean section. *Cochrane Database Syst Rev* 2012.
- Baker MT and Naguib M. The Challenges of Formulation. *Anesthesiology* 2005; 113: 860-876.
- Boletín de la Federación Latinoamericana de Sociedades de Obstetricia y Ginecología (FLASOG). 2015; 4.
- Borenstein M, Hedges LV, Higgins JP, Rothstein HR. Random-effects model. En: Borenstein M, Hedges LV, Higgins JP (editors). *Introduction to meta-analysis*. New York: John Wiley & Sons, Ltd.; 2011.
- Çakırtekin V, Yıldırım A, Bakan N, Çelebi N, Bozkurt O. Comparison of the Effects of Thiopental Sodium and Propofol on Haemodynamics, Awareness and Newborns During Caesarean Section Under General Anaesthesia. *Turk J Anaesth Reanim* 2015; 43: 106-112.
- Capogna G, Celleno D, Sebastiani M, Muratori F, Costantino P, Cipriani G, Passarelli F, Varrassi G. Propofol and thiopentone for caesarean section revisited: maternal effects and neonatal outcome. *Int J Obstet Anesth* 1991; 1: 19-23.
- Celleno D, Capogna G, Emanuelli M, Varrassi G, Muratori F, Costantino P, Sebastiani M. Which induction drug for cesarean section? Comparison of Thiopental sodium, Propofol, and Midazolam. *J Clin Anesth* 1993; 5: 284-288.
- Celleno D, Capogna G, Tomassetti M, Costantino P, Di Feo G, Nisini R. Neurobehavioral effects of Propofol on the neonate following elective caesarean section. *Br J Anaesth* 1990; 62: 649-654.
- Centro Cochrane Iberoamericano, traductores. *Manual Cochrane de Revisiones Sistemáticas de Intervenciones*, versión 5.1.0. Barcelona: Centro Cochrane Iberoamericano; 2011.
- Chen I, Opiyo N, Tavender E, Mortazhejri S, Rader T, Petkovic J, Yogasingam S, Taljaard M, Agarwal S, Laopaiboon M, Wasiak J. Non-clinical interventions for reducing unnecessary caesarean section. *Cochrane Database Syst Rev* 2018; 9(CD005528).
- Dailland P, Cockshott ID, Lirzin JD, Jacquinet P, Jorrot JC, Devery J, Harmey JL, Conseiller C. Intravenous Propofol during cesarean section: Placental transfer, concentrations in breast milk, and neonatal effects. A preliminary study. *Anesthesiology* 1989; 71: 827-834.
- Delgado C, Ring L, Mushambi MC. General anesthesia in obstetric. *BJA education* 2020 20: 201-207.
- Fleming PS, Seehra J, Polychronopoulou A, Fedorowicz Z, Pandis N. A PRISMA assessment of the reporting quality of systematic reviews in orthodontics. *Angle Orthod* 2013; 83: 158-163.
- Fonseca Pérez JE. Cesárea por solicitud materna (CPSM). *Rev Colomb Obstet Ginecol* 2017; 68: 7-11.
- García Alamino JM and Lopez Cano M. Revisiones sistemáticas con metaanálisis de ensayos clínicos: ¿es evidencia suficiente?. *Cirugía Española* 2020; 98: 4-8.

Gin T, Gregory MA, Chan K, Oh TE. Maternal and Fetal Levels of Propofol at Caesarean Section. *Anaesth Intens Care* 1990; 318: 181-184.

Gin T, O'Meara ME, Kan AF, Leung RQW, Tan P, Yau G. Plasma catecholamines and neonatal condition after induction of anaesthesia with Propofol or Thiopentone at caesarean section. *B J Anaesth* 1993; 70: 311-316.

Gregory MA, Gin T, Yau G, Leung RK, Chan K, TE Oh. Propofol infusion anaesthesia for Caesarean section. *Can J Anaesth* 1990; 37: 514-520.

Houthoff Khemlani K, Weibel S, Kranke P, Schreiber JU. Hypnotic agents for induction of general anesthesia in cesarean section patients: A systematic review and meta-analysis of randomized controlled trials. *J Clin Anesthesia* 2018; 48: 73-80.

Madkour NM, Ibrahim SA, Ezz GF. General versus spinal anesthesia during elective cesarean section in term low-risk pregnancy as regards maternal and neonatal outcomes: a prospective, controlled clinical trial. *Res Opin Anesth Intensive Care* 2019; 6: 119-124.

Mamidi DM, Mahjoobifard M, Panahipoor A, Dadras MA. Comparing Propofol with Sodium Thiopental on Neonatal Apgar Score after Elective Cesarean Section. *Zahedan J Res Med Sci* 2011; 15: 21-24.

Martínez Segura RT. ¿Cómo hacer anestesia total intravenosa en obstetricia? *Rev Mex Anestesiología* 2014; 37: 275-283.

Mekonen S, Eshete A, Desta K, Molla Y. Maternal and Neonatal outcomes in mothers who undergo caesarean section under General and spinal Anesthesia in Gandhi Memorial Hospital, Addis Ababa. *Adv Tech Biol Med* 2015; 3: 1-5.

Miranda AF, Kyi W, Sivalingam N. Propofol and Methohexitone for Elective Caesarean ~ A Comparative Study. *Med J Malaysia* 1992; 47: 280-286.

Montandrou O, Espitalier F, Bouyou J, Laffon M, Remérand F. Thiopental versus propofol on the outcome of the newborn after caesarean section: An impact study. *Anaesth Crit Care Pain Med* 2019; 38: 631-635.

Moore J, Bill KM, Flynn RJ, McKeating KT, Howard PJ. A comparison between propofol and thiopentone as induction agents in obstetric anaesthesia. *Anaesthesia* 1989; 44: 753-757.

Nápoles Méndez D and Couto Núñez D. Análisis de la cesárea como fuente de costo. *Rev Cub Obstet Ginecol* 2017; 21: 1008- 1017.

Sahraei R, Ghanei M, Radmehr M, Jahromi AS. The effect of propofol and thiopental on neonate Apgar in induction of cesarean section Anesthesia: A comparative study. *Life Sci J* 2014; 11: 93-95.

Salud Perinatal. El nacimiento por cesárea hoy. *Boletín del Centro Latinoamericano de Perinatología y Desarrollo Humano (CLAP)*. 1989; 3(9).

Santos AC, Epstein JN, Chaudhuri K. Obstetric anesthesia. *Clinical anesthesiology guide*. New York : Editorial Mc Graw Hill Education 2015; p. 589-637.

Sarduy Nápoles MR, Molina Peñate LL, Tapia Llody G, Medina Arencibia C, Chiong Hernández D. La cesárea como la más antigua de las operaciones obstétricas. *Rev Cuba Obstet Ginecol* 2018; 44: 1-18.

Siles Levy OY. Indicaciones y complicaciones inmediatas de cesáreas realizadas a pacientes que acuden al servicio de Ginecoobstetricia del Hospital Nuevo Amanecer del municipio de Bilwi durante el período de Febrero a Julio del año 2016. Managua: Faculta de Ciencias Médicas de la Universidad Nacional Autónoma de Nicaragua; 2018.

Soens M, Tsen LC. Fetal physiology. En: Chestnut DH, Wong CA, Tsen LC, Ngan Kee WD, Beilin Y, Mhyre JM, *et al.* *Obstetric anesthesia. Principles and Practice*. 6ta ed. Philadelphia: editorial Elsevier. 2020; p: 77-95.

Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, Carpenter J, Rücker G, Harbord RM, Schmid CH, Tetzlaff J. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011; 342: 1-8.

Tolyat M, Zanguoie M, Zanguoie R. Comparative study of the effect of general anesthesia with Propofol, Sodium Thiopental and the combination of Propofol-Thiopental on Apgar score of newborn babies in the cesarean delivery. *International Journal of Advanced Biotechnology and Research* 2016; 7: 979-983.

Tumukunde J, Lomangisi DD, Davidson O, Kintu A, Joseph E, Kwizera A. Effects of propofol versus thiopental on Apgar scores in newborns and peri-operative outcomes of women undergoing emergency cesarean section: a randomized clinical trial. *BMC Anesthesiol* 2015; 15: 63-69.

Valtonen M, Kanto J, Rosenberg P. Comparison of propofol and thiopentone for induction of anaesthesia for elective Caesarean section. *Anaesthesia* 1989; 44: 758-762.

Vanegas Saavedra A. *Anestesia intavenosa 3era ed.* Colombia: Editorial Panamericana 2014; p: 182-263.

Vuyk J, Sitsen E, Reekers M. Intravenous anesthesia. En: Miller RD, Eriksson LI, Fleisher LA, Wiener- Kronish JP, Young WL. *Miller's Anesthesia*. 9th ed; Philadelphia: Editorial Elsevier 2020; p: 638-679.

Yau G, Gin T, Ewart MC, Kotur CF, Leung RKW, Oh TE. Propofol for induction and maintenance of anaesthesia at Caesarean section. *Anaesthesia* 1991; 46: 20-23.

links:

1. GHO | By category | Health service coverage - Data by WHO region. WHO. World Health Organization; Disponible en: <https://apps.who.int/gho/data/view.main.1610?lang=en>
2. M19010N01 PROPOFOL 1%.pdf. 2019. Disponible en: <https://www.cecmecmed.cu/sites/default/files/adjuntos/rcp/M19010N01%20%20PROPOFOL%201%20pdf>
3. WHO_RHR_15.02_spa.pdf [citado 2 de septiembre de 2020]. Disponible en: https://apps.who.int/iris/bitstream/handle/10665/161444/WHO_RHR_15.02_spa.pdf;jsessionid=584A3455250A89184B06D33D66D6C4C3?sequence=1