



## Review Article

# A Comparative Study on the Effects of Propofol and Thiopental on the Apgar score of Neonates Undergoing Cesarean Section under General Anesthesia: A Systematic Review Study

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## ARTICLE INFO

## Article history

Receive: 2022-03-19

Received in revised: 2022-04-28

Accepted: 2022-05-10

Manuscript ID: JMCS-2204-1479

Checked for Plagiarism: Yes

Language Editor:

Dr. Fatimah Ramezani

Editor who approved publication:

Dr. Khosro Khajeh

DOI:10.26655/JMCHMSCI.2022.6.14

## KEYWORDS

Propofol

Thiopental

General anesthesia

Apgar score

Cesarean section

## ABSTRACT

**Introduction:** Apgar score of neonates at birth is one of the determinants of postnatal mortality and one of the effective factors in Apgar score of cesarean section neonates that is the type of drug used for maternal anesthesia. Owing to the disagreement on the benefits and possible side effects of anesthetics, the present study was an attempt to evaluate and compare the effects of propofol and thiopental on the Apgar score of neonates undergoing cesarean section under the general anesthesia.

**Methods:** The present study is a systematic review. Persian articles were searched in databases such as SID, Iranmedex, Magiran, and English articles were searched in databases such as Science Direct, PubMed, ProQuest, Cochrane Library, Embase, Scopus, and Google Scholar search engine without any time limitation. To access the full text of articles, the keywords of propofol, thiopental, general anesthesia, neonatal Apgar score, cesarean section, and their combination, the Boolean search methods, and conjunctions of "And" and "Or" were used. The information of reviewed articles included the first author, year of publication, the country of study, the sample size, and the outcome of the study.

**Results:** A total of 27 articles were included to the study. In 22 studies, no statistically significant difference was found between thiopental and propofol effects on neonatal Apgar score at minutes 1 and 5. Also, in 4 studies, Apgar scores at minutes 1 and 5 were reported higher in the propofol group than the thiopental group. Furthermore, in one study, Apgar score at minute 1 was reported higher in the propofol group than the thiopental group. In three studies, Apgar score of neonates at the minute 1 in thiopental group was reported higher than the propofol group.

**Conclusion:** It seems that neonates whose mothers underwent the general anesthesia with propofol for cesarean section have better Apgar scores than those who received thiopental. One of the effects of propofol is its shorter duration of action, and if the patient has a problem with difficult intubation, the effect of the drug ends sooner and the patient's breathe returns as soon as possible. Likewise in this regard, compared to thiopental, which has a longer effect, Propofol is a more effective drug in cesarean section women under the general anesthesia.

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## GRAPHICAL ABSTRACT



### Introduction

Cesarean section is a common method of termination of pregnancy which increases every year. Its major causes are delivery at an old age, the reduced number of deliveries, the increasing use of the electronic fetal monitoring, and the selection of cesarean section in breech deliveries [1]. The proper management of delivery and proper anesthesia method to cause analgesia and maintaining the health of mother and fetus during cesarean section are crucial [2]. An increase in the number of neonates born with cesarean section technique in the recent years has led to pay more attention to maternal and fetal complications of this delivery method [3]. The selection of type of anesthesia for cesarean section depends on factors such as the urgency of the cesarean section and the patient's intention and willingness. The selected method in cesarean section is the spinal anesthesia; however, the general anesthesia is further selected in some cases (i.e. the patient dissatisfaction, coagulation problems, increased intracranial pressure, etc.). In developed countries, a total of 17% of cesarean sections are performed under the general anesthesia [4-5]. Pregnant mothers experience complications such as chills, nausea, vomiting, etc. during pregnancy and during cesarean section. In different studies, various pharmacological and non-pharmacological methods have been suggested to control these complications [6-8]. Neonatal Apgar score at birth is one of the determinants of postnatal mortality and one of the effective factors in neonatal Apgar score of cesarean section neonates is the type of drug used for maternal anesthesia [9]. Thiopental sodium is the most commonly used drug for anesthesia induction in

cesarean section, but in cases such as asthma and severe allergies where sodium thiopental is contraindicated and its consumption exacerbates asthma and allergies, a suitable alternative drug should be selected [10]. Several studies have indicated that propofol has no negative effect on neonatal Apgar score [11-12]. By using propofol, induction and continuation of anesthesia in the mother, 100% oxygen during the operation is provided without increasing the risk of the mother's waking up during the operation [13-14]. Due to the pharmacological differences and similarities of the intravenous hypnotics, clarifying their differences at levels of clinical fetal depression, and further comparing and influencing neonatal Apgar scores can be helpful in selecting more appropriate drugs. Thus, the present study aimed to compare propofol and thiopental drugs on the Apgar score of neonates under cesarean section with general anesthesia in a systematic review study.

### Materials and Methods

The systematic review study was conducted to compare the effects of propofol and thiopental drugs on the Apgar score of neonates undergoing cesarean section under the general anesthesia. To review the preliminary studies, the Persian language database of SID, Iranmedex, and Magiran were used, and English language databases of Science Direct, PubMed, ProQuest, Cochrane Library, Embase, Scopus, and Google Scholar search engine were used without any time limitation. To access the full text of articles, the keywords of propofol, thiopental, general anesthesia, neonatal, Apgar score, cesarean section and their combination, Boolean search

methods, and conjunctions of “And” and “Or” were used (Table 1).

**Table 1:** Database search strategy

1	' Propofol ' OR ' Apgar score ' OR ' Cesarean section OR ' Thiopental ' OR ' Neonatal'
2	' Thiopental ' AND ' Propofol ' AND ' Apgar score' AND ' Apgar score ' AND ' Neonatal'

#### *Inclusion criteria and evaluating the quality of articles*

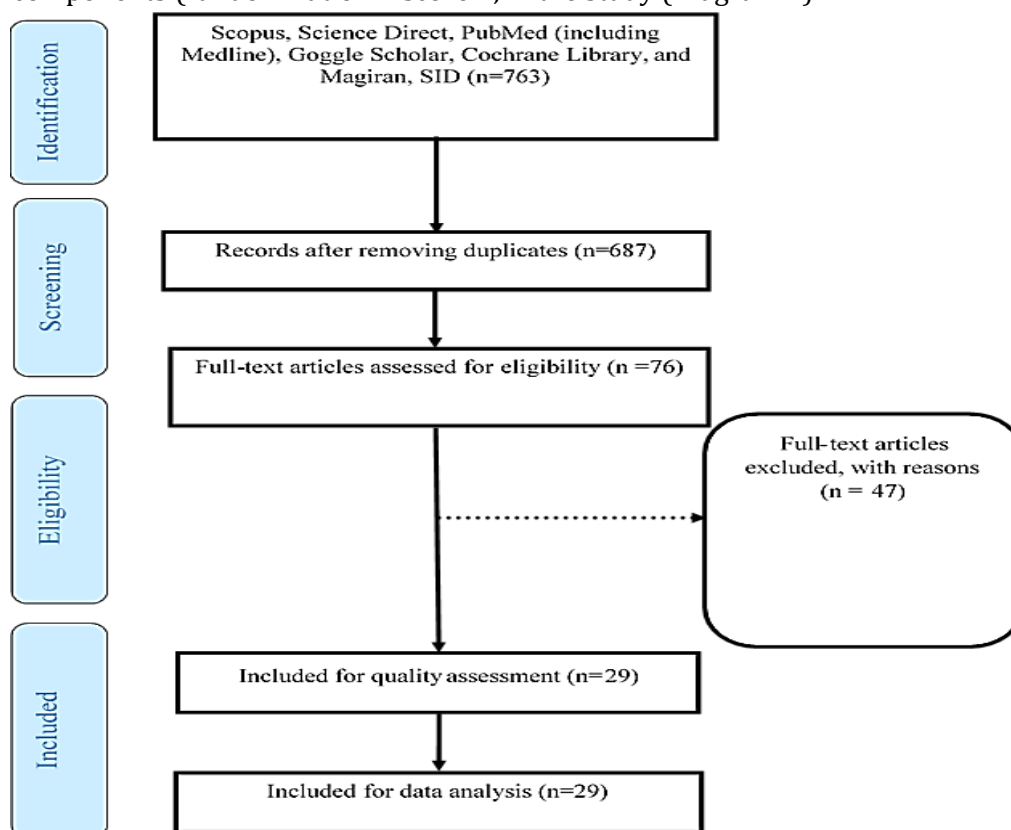
First, a list of titles and abstracts of all articles in the mentioned databases were prepared by the researchers and were reviewed independently to determine and select the relevant titles. By reviewing the studies, the duplicate ones were excluded and after careful reviewing of the full text of the articles, the relevant articles were selected. Inclusion criteria included the minimum score required based on the checklist for inclusion in the study and the articles related to neonatal Apgar in cesarean section under the general anesthesia. Exclusion criteria included the studies performed by spinal anesthesia, duplicate articles, review or meta-analysis articles, short articles, conference papers, and letters to the editor.

The quality of the articles was evaluated using the Jadad standard checklist [15]. This checklist includes 3 components (randomization = score 2,

blinding = score 2, and patient exclusion fate = score 1). The total score of this checklist is between 0 and 5. If the score is 3 or higher, the articles will be included in the study. To prevent bias, the articles were extracted and evaluated by two independent researchers. In cases in which there was disagreement between the two researchers, the article was reviewed by a third researcher. The information of the articles reviewed in the study (Table 2) includes first author, year of publication, the country of study, sample size, and the outcome of the study.

#### **Results**

In the initial stage of article search, 763 studies were reviewed. Then, the researchers reviewed the searched articles and 734 articles were excluded due to the irrelevance to the subject of the study, duplication, and lack of access to the full article text. Finally, 29 studies were included to the study (Diagram 1).



**Diagram 1:** The PRISMA flow diagram

The study period ranged from 1989 to 2021. In 22 studies, no statistically significant difference was found between thiopental and propofol effects on neonatal Apgar score at minutes 1 and 5. Furthermore, in 4 studies, Apgar scores at minutes 1 and 5 were reported higher in the propofol group than the thiopental group. Moreover, in one study, Apgar score at minute 1 was reported

higher in the propofol group than the thiopental group. In three studies, the neonatal Apgar score at the minute 1 in thiopental group was reported higher than the propofol group. The minimum sample size was 20 and the maximum sample size was 392. Table 2 presents a summary of the important findings.

**Table 2:** Studies included in the systematic review

Author	Year of study	Country	Outcome
Yusefi Moghadam, <i>et al.</i>	2021	Iran	Apgar score in minutes one and five in propofol group was significantly higher than thiopental group [16].
Ota, <i>et al.</i>	2019	Japan	The Apgar score was higher in the thiopental group at one minute. But at 5 minutes, there was no significant difference between the two groups [17].
Hadavi, <i>et al.</i>	2019	Iran	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [18].
Montandrou, <i>et al.</i>	2018	France	Apgar score was higher in the propofol group at one minute. But at 5 minutes, there was no significant difference between the two groups [19].
Tumukunde, <i>et al.</i>	2015	Uganda	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [20].
Cakirtekin, <i>et al.</i>	2015	Turkey	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [21].
Sahraei, <i>et al.</i>	2014	Iran	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [22].
Dadras, <i>et al.</i>	2013	Iran	Apgar score in minutes one and five in propofol group was significantly higher than thiopental group [23].
Lotfalizade, <i>et al.</i>	2012	Iran	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [24].
Rabiee, <i>et al.</i>	2012	Iran	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [25].
Mercan, <i>et al.</i>	2012	Saudi Arabia	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [26].
Mahjoobifard, <i>et al.</i>	2011	Iran	Apgar score in minutes one and five in propofol group was significantly higher than thiopental group [27].
Akhavan Akbari, <i>et al.</i>	2010	Iran	General anesthesia with sodium thiopental and propofol did not have a significant effect on neonatal Apgar score [28].
Golfam, <i>et al.</i>	2009	Iran	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [29].
Lee, <i>et al.</i>	2007	Korea	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [30].
Badrkhahan, <i>et al.</i>	2007	Iran	General anesthesia with sodium thiopental and propofol did not have a significant effect on neonatal Apgar score [31].
Lak, <i>et al.</i>	2006	Iran	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [32].
Beigom Khezri, <i>et al.</i>	2005	Iran	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [33].
Ghodrati, <i>et al.</i>	2003	Iran	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [34].

Djordjević, <i>et al.</i>	1998	Serbian	Apgar score in minutes one and five in propofol group was significantly higher than thiopental group [35].
Seong-Bae KIM, <i>et al.</i>	1995	Korea	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [36].
Zamora, <i>et al.</i>	1994	Spain	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [37].
Celleno, <i>et al.</i>	1993	Italy	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [38].
Gin, <i>et al.</i>	1993	Chinese	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [39].
Siafaka, <i>et al.</i>	1992	Greece	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [40].
Capogna, <i>et al.</i>	1991	Italy	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [41].
Yau, <i>et al.</i>	1992	Chinese	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [42].
Gin, <i>et al.</i>	1990	Chinese	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [43].
Valtonen, <i>et al.</i>	1989	Finland	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [44].
Moore, <i>et al.</i>	1989	Northern Ireland	Apgar score of one and five minutes in the two groups of propofol and thiopental was not statistically significant [45].

## Discussion

The rate of cesarean section has increased dramatically over the past decade in the United States and other parts of the world. This rate has increased from less than 5% in the United States in 1965 to 30.2% in 2005, and is currently the most common surgery in the United States [46]. The rate of cesarean section is 50-60% in Iran [47]. The best method of anesthesia for cesarean section is the spinal anesthesia, but if it is contraindicated for the mother, general anesthesia will inevitably be used. Some of the disadvantages and problems of general anesthesia are aspiration of the gastric secretions by the patient, failure in intubation, over ventilation of the mother, suppression of the neonate breathing, maternal anesthesia during childbirth, reduced uterine muscle strength after delivery, and bleeding [48- 49].

Examining the neonate condition after birth can be helpful in selecting the best method to create the best technique for anesthesia of mothers undergoing cesarean section. One of the methods used to evaluate the neonate condition after birth is the Apgar score, which is determined at minutes 1 and 5 after delivery. Minute 5 Apgar score and especially the change in the score between

minutes 1 and 5 are useful criteria for the effect of resuscitation. The type of drugs used during cesarean section is among the factors affecting neonatal Apgar score [50]. There is much disagreement about the effect of drugs used in general anesthesia on neonatal Apgar scores in cesarean section. However, there is still no definitive theory about the preference of drugs used in cesarean section. Nowadays, cesarean section is one of the most common procedures performed around the world. Likewise, the drug used for anesthesia in these operations should have the least effect on the fetus since a change or drop in Apgar of neonates is one of the causes of increased mortality among them [42]. In the present study, we compared the two drugs of propofol and thiopental on the Apgar score of neonates undergoing cesarean section under the general anesthesia.

Studies have indicated that recovery from anesthesia using propofol is short and is of great importance for mothers who are still at risk of aspiration of acidic gastric contents (after cesarean section) [51]. Furthermore, the placental transfer of propofol is rapid and high, and fetal contact with a sufficient amount of drug may cause a reduction in neural function after birth.

Moreover, it might reduce fetal bloodstream and cause complications by affecting maternal blood pressure [52-55]. Another drug used for induction of anesthesia is thiopental, which passes rapidly through the placenta [56] and has known and controllable effects and complications [42]. Based on the results of present study, 22 studies reported no statistically significant difference between thiopental and propofol effects on neonatal Apgar score at minutes 1 and 5 [18, 20-22, 24-26, 28-34, 36-37, 39-40, 42-45]. Also, in 4 studies, Apgar scores at minutes 1 and 5 were reported higher in the propofol group than the thiopental group [16, 23, 27, 35]. Likewise, in one study, Apgar score at minute 1 was reported higher in the propofol group than the thiopental group [19]. In three studies, Apgar score of neonates at the minute 1 in thiopental group was reported higher than the propofol group [17, 38, 41].

The conflicting results regarding the effect of propofol and thiopental sodium on neonatal Apgar score may be due to the very small difference between the two drugs, which sometimes propofol and sometimes thiopental revealed a better effect in different conditions. The slight difference between the two drugs may be due to pharmacological similarities and consequently similar concentrations of drugs in the fetal bloodstream. Propofol and thiopental are both fat-soluble and have similar placental penetration. Due to the proven clearance of propofol faster than thiopental and based on the similarity of neonatal Apgar scores (Apgar scores at minutes 1 and 5) in the two groups in the proposed study, it can be concluded that the drugs are very diluted in the fetal bloodstream and a small amounts of them reaches CNS, which the depression resulting from it is not clinically obvious.

### Conclusions

It seems that neonates whose mothers underwent the general anesthesia with propofol for cesarean section have better Apgar scores than those who received thiopental. One of the effects of propofol is its shorter duration of action, and if the patient has a problem with difficult intubation, the effect of the drug ends sooner and the patient's breathe returns, as soon as possible. Likewise in this

regard, compared to thiopental, which has a longer effect, Propofol is a more effective drug in cesarean section women under the general anesthesia.

**Limitation:** There were no limitations on this study

### Acknowledgments

We would like to thank the Clinical Research Development Unit of Peymanieh Educational and Research and Therapeutic Center of Jahrom University of Medical Sciences for providing facilities to this work.

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to responsible for all the aspects of this work.

### Conflict of Interest

There are no conflicts of interest in this study.

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#### HOW TO CITE THIS ARTICLE

Seyed Ebrahim Sadeghi, Mehrdad Malekshoar, Majid Vatankhah, Pourya Adibi, Elham Rahmanian, Mohammad Sadegh Sanie Jahromi, Maryam Nemati. A Comparative Study on the Effects of Propofol and Thiopental on the Apgar score of Neonates Undergoing Cesarean Section under General Anesthesia: A Systematic Review Study, *J. Med. Chem. Sci.*, 2022, 5(6) 1008-1017

<https://dx.doi.org/10.26655/JMCHEMSCI.2022.6.14>

URL: [http://www.jmchemsci.com/article\\_149685.html](http://www.jmchemsci.com/article_149685.html)