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INVITED REVIEW ARTICLE

Rethinking general anesthesia for cesarean section

Hiroyiki Sumikura[1] · Hidetomo Niwa[2] · Masaki Sato[3] · Tatsuo Nakamoto[4] · Takashi Asai[5] · Satoshi Hagihira[6]

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Abstract In this review, we describe the current consensus surrounding general anesthetic management for cesarean section. For induction of anesthesia, rapid-sequence induction using thiopental and suxamethonium has been the recommended standard for a long time. In recent years, induction of anesthesia using propofol, rocuronium, and remifentanil have been gaining popularity. To prevent aspiration pneumonia, a prolonged preoperative fasting and an application of cricoid pressure during induction of anesthesia have been recommended, but these practices may require revision. Guidelines for difficult airway management were developed first in obstetric anesthesia, and the use of a supraglottic airway is now recognized as an effective rescue device. After the delivery of a fetus, switching from volatile anesthetics to intravenous anesthetics has been recommended to avoid uterine atony. At the same time, intraoperative awareness should be avoided. The rate of persistent wound pain is higher when only general anesthesia was used during cesarean section than with regional anesthesia, and thus it is necessary to provide a sufficient postoperative analgesia using multimodal analgesia, including intravenous patient-controlled analgesia (IV-PCA), transversus abdominis plane (TAP) block, nonsteroidal inflammatory drugs, and acetaminophen.

Keywords Cesarean section · Rapid-sequence induction · Airway management · Intraoperative awareness

✉ Hiroyiki Sumikura
hiroyuki.sumikura@gmail.com

[1] Department of Anesthesiology and Pain Medicine, Juntendo University, 3-1-3 Hongo Bunkyo-ku, Tokyo 113-8421, Japan

[2] Department of Anesthesiology, Hirosaki University Graduate School of Medicine, 5 Zaifu-cho, Hirosaki, Aomori 036-8562, Japan

[3] Department of Anesthesiology, National Center for Child Health and Development, 2-10-1 Okura, Setagaya-ku, Tokyo 157-8535, Japan

[4] Department of Anesthesiology, Kansai Medical University, 2-3-1 Shin-machi, Hirakata, Osaka 573-1191, Japan

[5] Department of Anesthesiology, Dokkyo Medical University Koshigaya Hospital, 2-1-50 Minamikoshigaya, Koshigaya, Saitama 343-8555, Japan

[6] Department of Anesthesiology, Osaka University, 2-15 Yamadaoka, Suita, Osaka 565-0871, Japan

Introduction

Based on national statistics of the United States between 1985 and 1990, Hawkins et al. reported in 1997 that the mortality rate of cesarean section under general anesthesia was 16.7 times higher than that with regional anesthesia (95 % CI 12.9–21.8) [1]. Recently, the same group evaluated the data from 1997 to 2002, and demonstrated that the risk of general anesthesia decreased to 1.7-fold (95 % CI 0.6–4.6) and differences in anesthetic methods were shown to no longer influence mortality rates [2]. Is it possible to interpret their result that general anesthesia for cesarean section has become as safe as regional anesthesia?

It seems to be true that the overall safety of anesthesia for cesarean section has been improved, as anesthetic-related maternal mortality decreased nearly 60 % when data from 1979 to 1990 were compared with data from 1991 to 2002 [2]. However, it should be noted that maternal mortality with regional anesthesia increased from 2.5 (per 1 million parturitions) between 1991 and 1996 to 3.8 (per 1 million parturitions) between 1997 and 2002, although maternal mortality with general anesthesia reduced from 16.8 to 6.5 in the same period. These findings can be explained by a

trend that regional anesthesia has been selected in high-risk cases in which general anesthesia would have been selected in the past. Therefore, the reduced maternal mortality related to general anesthesia may be simply explained by the different indication of general anesthesia between these two periods.

It is also true that the overall safety of general anesthesia improved dramatically in the past two decades, because of newly developed drugs, instruments, and monitors. These developments, along with practical knowledge of how to use them, have led to a major transformation in anesthetic management methods across various types of surgery. For cesarean section, however, precedence has been given to the avoidance of general anesthesia during this period; consequently, insufficient effort has been made to incorporate and optimize new techniques and findings in general anesthetic management methods [3, 4].

In this review, we describe the current consensus surrounding general anesthetic management methods for cesarean section and discuss future direction.

1. Drugs for induction of general anesthesia.

   Rapid-sequence induction and intubation using thiopental and suxamethonium has been the standard for cesarean section for a long time. However, in recent years, induction of anesthesia using propofol, rocuronium, and remifentanil has also been discussed.

   (a) *Induction agents* Induction agents administered to the mother are transferred to the fetus through the placenta; this can occasionally result in babies being born anesthetized "sleeping baby". When a neonatologist is not present at delivery, it would be prudent to reduce doses of induction agents as low as possible, and to shorten the time from administration of anesthetics to delivery of a baby.

   Owing to their extensive use and established safety [5], short-acting barbiturates (thiopental and thiamylal) have maintained their status as the standard drugs for inducing anesthesia [6]. However, initiating surgery without providing sufficient anesthesia increases the risk of the mother being aware [7] and developing tachycardia and hypertension. Therefore, when a neonatologist is present at delivery, providing sufficient anesthesia to the mother is a greater priority than avoiding a "sleeping baby". From this perspective, propofol is expected to be superior to barbiturates [8]. Unfortunately, in some countries (including Japan), propofol has not been approved for pregnant women [9–11]. However, in the future, with a reduction in the use of thiopental, the supply of thiopental may be terminated, or its price may be increased. The safety of propofol for parturients and fetuses is expected to be authorized, which would thereby allow its approved application to parturients.

   (b) *Neuromuscular blocking agents* Suxamethonium, a depolarizing neuromuscular blocking agent, has started to become phased out in operations other than cesarean section, owing to fatal, although rare, side effects such as malignant hyperthermia and hyperkalemia. However, for cesarean section, the risk of complications associated with airway management (such as aspiration pneumonia and hypoxia) is greater; therefore, suxamethonium remains the first choice for cesarean section. Theoretically, short-acting suxamethonium is convenient for parturients, who are at high risk of rapid hypoxia after respiratory arrest. In addition, the short duration of action of suxamethonium enables rapid resumption of spontaneous breathing, in cases of difficult airway management. Non-depolarizing neuromuscular blocking agents were in the past considered unsuitable for cesarean section due to their slow onset time and long effect. An attempt was made to shorten the onset time by administering a small dose of a non-depolarizing neuromuscular blocking agent before administration of main dose (so-called priming principle). However, this attempt was generally unsuccessful in parturients because even a small dose of neuromuscular blocking agent frequently produced clinical motor block [12], and did not shorten the onset time.

   Rocuronium, a new-generational non-depolarizing neuromuscular blocking agent, may replace suxamethonium as the first choice [13]. A large dose (1.0–1.2 $mg.kg^{-1}$) of rocuronium can produce neuromuscular blockade as rapidly as suxamethonium [14], and if resumption of spontaneous breathing is required when airway management has failed after induction of anesthesia, sugammadex can shorten the effect of rocuronium as short as the effect of suxamethonium [15]. In addition, a high dose of rocuronium given after the use of sugammadex can produce enough motor blockade for re-intubation seems to justify their use for cesarean section [16].

   Currently, sugammadex is not commercially available in North America. In countries where the clinical use of sugammadex has already been

approved, it is desirable to conduct studies on the proper use of rocuronium and sugammadex.

(c) *Opioids* Debate continues as to whether opioids should be administered when inducing anesthesia for cesarean section [17]. There is a strong opinion that opioids should not be given to mothers until delivery, to avoid the side effects (particularly respiratory depression) occurring in the fetus. However, fentanyl used for labor epidural analgesia, which can diffuse freely from the epidural space into the maternal circulation [18], has been known not to cause respiratory depression. Therefore, small doses of opioids administered to the mother undergoing cesarean section would exert only limited effects on neonate. Recent predominant opinion is that opioids should be given during induction of anesthesia, to prevent hemodynamic changes by tracheal intubation [19]. Until recently, fentanyl has been administered for this purpose, and remifentanil has now begun to be used [20–24]. Nevertheless, it should be noted that muscle rigidity [25] and respiratory depression [26] in neonates has been reported. Further research into the safe use of remifentanil in parturients is warranted.

2. Airway management.

(a) *Aspiration pneumonia* In parturients, aspiration pneumonia, once was widely known as Mendelson syndrome [27], is still the major problem [28]. Although strict fasting before cesarean section had been recommended to prevent aspiration [29, 30], instructions to preoperative fast have been revised following the widespread implementation of the enhanced recovery after surgery program [31, 32]. For the next step, a specific instruction to fast for parturient undergoing elective cesarean section with general anesthesia should be discussed.

(b) *Difficult airway algorithms* Parturients were previously considered to be at high risk of difficult intubation [33], but this has recently been challenged [34]. Nevertheless, in parturients, complications that develop during difficult intubation are more serious. Therefore specific difficult airway protocols for parturient have been proposed [35, 36].

(c) *Supraglottic airway devices* To prevent aspiration in parturients, the recommended method of airway management is to intubate the trachea and to inflate the cuff to seal the airway. Currently, there is a strong opposition to use a supraglottic airway device as a first line for scheduled cesarean section [37, 38], although its usefulness in cases of difficult intubation in parturients is well recognized [39].

(d) *Cricoid pressure* Since Sellick proposed applying pressure to the cricoid cartilage to prevent aspiration in 1961, cricoid pressure has become widely adopted in the induction of general anesthesia in parturients [40]. However, some studies indicated that cricoid pressure may make tracheal intubation more difficult, and may increase the risk of "cannot ventilate, cannot intubate" situation [41]. Until recently, there has been extensive research into reliable methods for preventing aspiration and numerous studies have focused on education relating to the application of cricoid pressure [42]. Recently, however, doubts have been raised to the efficacy of cricoid pressure in preventing aspiration [43, 44]. Details about this topic are described in an accompanying review [45].

3. Maintenance of anesthesia.

For parturients undergoing cesarean section under general anesthesia, it is essential to achieve sufficient uterine contraction and prevent intraoperative awareness.

(a) *Uterine contraction* It has been known that volatile anesthetics inhibit uterine contraction in a dose-dependent manner, and discontinuation of volatile anesthetics and conversion to intravenous anesthesia have been recommended after delivery. However, volatile anesthetics can be used with careful caution as utero-tonic effect is limited when a low concentration is administered [46]. In addition, at 0.5 minimum alveolar concentration (MAC) of volatile anesthetic, the effect of oxytocin is not attenuated [47]. Furthermore, prostaglandins can effectively prevent volatile anesthetic-induced uterine atony [48]. On the other hand, it should be noted that clinical concentration of propofol may also inhibit uterine contractility [49]. Recently, an optimal dosage of oxytocin during cesarean section with regional anesthesia has been discussed [50–52]. Further studies on the efficient use of uterotonics in general anesthesia are desirable [53].

(b) *Intraoperative awareness* Along with heart surgery, cesarean section is considered to be one of the surgeries in which patients are the most prone to be aware during anesthesia [54]. Although intraoperative awareness is considered less likely with volatile anesthesia than with intravenous anesthesia, reducing the concentration of volatile anesthetics to avoid postpartum uterine atony would increase the risk of intraoperative aware-

ness. However, the minimum concentration of a volatile anesthetic required to prevent intraoperative awareness has not been sufficiently investigated. Although it has been reported that the MAC is lower for parturients than non-parturients, a recent electroencephalographic analysis study demonstrated that there is no difference in sensitivity to anesthetics between parturients and non-parturients of similar ages [55]. Further studies are needed to establish optimal concentration of volatile anesthetics after the delivery.

4. Postoperative analgesia.
After cesarean section, it is necessary for the mother to have physical contact with the neonate and to get out of bed as soon as soon as possible, to improve the bond with the child and prevent thrombosis. Achieving these objectives requires more effective analgesia.

   (a) *Intravenous patient-controlled analgesia* Due to the development of precise devices, intravenous patient-controlled analgesia (IV-PCA) is now recognized as an effective method of postoperative analgesia, as an alternative to patient-controlled epidural anesthesia. Opioids given by IV-PCA may increase the incidence of nausea and vomiting, and thus the use of antiemetics should be considered.

   (b) *Transversus abdominis plane block* When morphine is administered intrathecally, the addition of a transversus abdominis plane (TAP) block is unlikely to increase the analgesic effect [56]. However, a TAP block is an effective method in cesarean section managed with general anesthesia and in which a neuraxial block is not an option for postoperative analgesia [57]. Further research is necessary to determine the optimal approach for achieving more effective postoperative analgesia with a TAP block [58].

   (c) *Multimodal analgesia* The rate of persistent wound pain is higher in parturients undergoing cesarean section managed with general anesthesia than with regional anesthesia [59]. Patient-controlled epidural anesthesia, intrathecal morphine, and other forms of neuraxial anesthesia provide high-quality analgesia and involve little transfer of analgesics to breast milk, thereby making them suitable options for analgesia after cesarean section. Therefore, when general anesthesia is selected for cesarean section, whenever possible, postoperative analgesia should be provided by neuraxial block, IV-PCA, or TAP block. In addition, the combinational use of analgesics, such as non-steroidal inflammatory drugs and acetaminophen, is expected to lead to the development of a mode of anesthesia similar to neuraxial block.

Conclusions

We described the current consensus and the future direction surrounding general anesthetic management methods for cesarean section. The safety of general anesthesia has been improved in the past two decades. However, due to the reduction in education opportunities regarding general anesthesia, in addition to the increase in older and obese parturients, the safety of general anesthesia may decline again. Therefore, continuous efforts to improve the safety and management quality of general anesthesia are necessary.

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