The Minimum Alveolar Concentration of Isoflurane in Patients Undergoing Bilateral Tubal Ligation in the Postpartum Period

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Background: The minimum alveolar concentration (MAC) of volatile anesthetics is decreased during pregnancy, but MAC in the early postpartum period has not been reported. The aim of this study was to determine the MAC of isoflurane and to evaluate the relation between MAC and serum progesterone and β-endorphin concentrations after delivery.

Methods: Eight patients undergoing elective bilateral tubal ligation during general anesthesia in the early postpartum period (12 h postpartum) and eight patients undergoing this procedure in the late postpartum period (12-25 h postpartum) were studied. Eight patients undergoing bilateral tubal ligation more than 6 weeks after delivery served as control subjects. Anesthesia was induced with propofol and maintained with isoflurane in oxygen to a steady end-tidal concentration of 0.8-1.0 vol% for 10 min. Reaction to a standardized electric stimulation applied to the forearm was graded as positive (gross or delayed movement) or negative. By using the bracketing technique, the concentration of isoflurane was increased or decreased by 0.1 vol%, depending on the positive or negative responses.

Results: The MAC (mean ± SD) in patients in the early postpartum period was significantly less (0.75 ± 0.17 vol%) than that in control subjects (1.04 ± 0.12 vol%; P < 0.01) and that in patients in the late postpartum period (0.95 ± 0.2 vol%; P < 0.05). The difference in MAC values between late and control was not significant (P > 0.05). There was an inverse correlation between progesterone concentration postpartum and time after delivery (r = −0.52; P = 0.036), but no relation between β-endorphin and time after delivery (r = 0.089; P = 0.744). There was no correlation between plasma progesterone or β-endorphin and MAC by multiple regression (r = 0.166; P = 0.950).

Conclusions: Isoflurane MAC remains 28% less than normal within the 1st 12 h postpartum and then returns to normal 12–25 h after delivery. (Key words: Anesthesia, obstetric: postpartum. Anesthetics, intravenous: propofol. Anesthetics, volatile: isoflurane. Hormones: β-endorphin; progesterone. Potency, anesthetic: minimum alveolar concentration.)

MANY women undergo tubal ligation during general anesthesia within 24-36 h after delivery. The interval between delivery and surgery may even be decreasing with new discharge policies of 24-36 h after normal delivery in healthy patients. However, the anesthetic requirement of inhalation agents for this population of patients has not yet been studied.

Minimum alveolar concentration (MAC), defined as the alveolar concentration of an anesthetic preventing purposeful movement in 50% of patients in response to a painful stimulus, is recognized as a standard for anesthetic potency and anesthetic requirement. Many physiologic and pharmacologic variables, including pregnancy, alter MAC. During pregnancy, MAC for isoflurane decreases by 40% in ewes, whereas MAC for halothane decreases by 16-19% in rats. Recently, it has been shown that isoflurane MAC is decreased by 28% in pregnant women at 8-12 weeks' gestation. The mechanism underlying the decrease in MAC during pregnancy remains unknown. However, it has been suggested that this decrease in anesthetic requirement may be associated with progressive increases in progesterone and β-endorphin during gestation.

This study was designed to determine the MAC of isoflurane in patients undergoing bilateral tubal ligation by the tetanic stimulation method after delivery and to evaluate the relation between MAC and serum concentrations of progesterone and β-endorphin in the early postpartum period.

Materials and Methods

This study was approved by the Mississippi Medicine Institutional Review Board. Twenty-four healthy nulliparous volunteers (American Society of Anesthesiologists' (ASA) Class I) undergoing elective tubal ligation under general anesthesia, with written informed consent. The ASA physical status of all patients was I according toASA criteria. One patient received an epidural before the study began. The study group consisted of 10 women, aged 20-31 yr, weighing 60-114 kg, with a body mass index of 20-28 kg/m², 8 of whom were in the early postpartum period (12 h postpartum); and 8 patients in the late postpartum group (more than 6 weeks postpartum). All patients were not taking any medications, except for 1 using a contraceptive patch, 1 taking a birth control pill, 1 using an intrauterine device, and 1 using a hormone-releasing intrauterine system. All patients smoked less than 1 cigarette per day, and none had a history of chronic illness, including cardiovascular, pulmonary, or psychiatric disorders. All patients were premedicated with midazolam 2.5-3 mg intravenously 15 min before induction of anesthesia.

After tracheal intubation and placement of a nasogastric tube, the patient was ventilated with air and 2.0 vol% for 12 ml/kg at a fractional inspired oxygen concentration of 0.3. Ventilation was adjusted to maintain a normal end-tidal isoflurane concentration (2.0-2.5 vol%). However, the concentration of isoflurane in the late postpartum patients in the early postpartum group was not significantly different from that in the late postpartum group. Respiratory rate, tidal volume, and end-expiratory carbon dioxide tension were measured with a mass spectrometer (INADA Medical Instruments, Tokyo, Japan) during anesthesia.

A painful stimulus was delivered with a tetanic stimulation method, 0.20-ms square wave for 30 s, every 10 s, with 10 stimuli at a rate of 10 Hz. The painful stimulus was delivered to the left lower leg, using a 1-cm electrode, with the patient in the supine position. The response was graded on a scale of 1 (no response) to 5 (complete muscle relaxation) and recorded at each level of isoflurane anesthesia. The dose-effect relationship was determined by the MAC.

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POSTPARTUM ISOFURANE MAC

Materials and Methods

This study was approved by the University of Mississippi Medical Center Institutional Review Board. Twenty-four patients, American Society of Anesthesiologists (ASA) physical status 1 or 2, aged 21–38 yr, undergoing elective bilateral tubal ligation during general anesthesia were studied after written informed consent. The patients were divided into three groups according to the duration between delivery and surgery: control group (n = 8): at least 6 weeks postpartum; early postpartum group (n = 8): less than 12 h postpartum; and late postpartum group (n = 8): 12–25 h postpartum. Exclusion criteria were a history of alcohol or drug abuse; severe anemia (hematocrit < 10%); abnormal body temperature (< 36°C or > 38°C); hypotension (mean blood pressure < 50 mmHg); abnormal serum electrolyte concentrations; impaired renal or liver function; cardiopulmonary disease; or exposure to clonidine, methyldopa, reserpine, verapamil, lithium, benzodiazepines, or progesterone for the preceding 3 weeks.

All patients received ranitidine (150 mg, oral) and metoclopramide (10 mg, oral) 60–90 min before surgery. Anesthesia was induced with lidocaine (20 mg, intravenous) and propofol (2 mg/kg, intravenous), and the trachea was intubated after administration of succinylcholine (1.5 mg/kg, intravenous). After tracheal intubation, isoflurane in oxygen was administered to achieve an end-tidal concentration of 2.0 vol% for 10 min with a total gas flow of 10 l/1 min. Ventilation was controlled with tidal volume of 8–10 ml/kg at a rate of 8–12 breaths/min to keep end-tidal carbon dioxide tension between 26 and 32 mmHg. The end-tidal isoflurane concentration was decreased to 0.7 vol% and then was adjusted to maintain a steady concentration of 1.0 vol% in control subjects and patients in the late postpartum period and of 0.8 vol% in patients in the early postpartum period for 10 min. The difference between inspiratory and end-tidal concentration of isoflurane was maintained at about 0.1 vol%.

Respiratory gases were continuously monitored by an infrared gas analyzer (Ohmeda 5250 RGM, British Oxygen Company Health Care, Louisville, CO) in all patients.

A painful electric stimulus (60 mA, 50 Hz, 5 s, in 0.20-ms square-wave pulses) was delivered by a peripheral nerve stimulator (750 digital, DAKKomed, Buffalo, NY) though two electrocardiographic electrodes placed on the volar surface of the predominant forearm, 5 and 13 cm below the skin fold in the cubital fossa and 1 cm to the ulnar side from the midline of the forearm, with the positive electrode placed proximally. A positive response was considered to be gross movement of head or extremity. A delayed movement of extremity within 1 min after stimulation also was considered a positive result. However, the movement of the arm on the stimulated side during the tetanic stimulation and the movement caused by endotracheal tube, including coughing and swallowing, were not considered as positive reactions. If a positive response was observed, the concentration of isoflurane was increased by 0.10 vol%. If no response to stimulation occurred, the concentration was decreased by 0.10 vol%. The stimulation was repeated after at least 10 min of establishing a steady end-tidal concentration.

The bracketing technique was used to achieve a pattern of positive–negative–positive or negative–positive–negative responses. The anesthetic concentration midway between that allowing and that preventing movement was the individual MAC value. In each patient the surgical procedure began after determination of isoflurane MAC. Each patient was interviewed within 24 h after surgery for awareness of intraoperative events.

In patients in the early or late postpartum period, 15 min after induction, a venous blood sample (3 ml) was collected from each patient. The plasma concentrations of progesterone were assayed with a radioimmunoassay technique with a sensitivity of 0.1 ng/ml and assay coefficients of variation of 11.8% at 1.1 ng/ml and 15.9% at 19.9 ng/ml. The plasma concentrations of β-endorphin were assayed by a radioimmunoassay technique with a sensitivity of 14 pg/ml and assay coefficients of variation of 9% at 190 pg/ml and 7.7% at 892 pg/ml.

Data were analyzed with a statistical program (Systat, Evanston, IL). Student’s unpaired t test and Dunnnett’s test were used for analysis of variance among the groups. The effects of independent variables (progesterone or β-endorphin) on a dependent variable (MAC) and the effect of progesterone or β-endorphin versus MAC were analyzed with linear regression. P values less than 0.05 were considered significant.

Results

The demographic data were not significantly different between the three groups (table 1). The durations.

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(mean ± SD) between induction and MAC determination in the control, early postpartum, and late postpartum groups were 63.8 ± 13.0, 64.4 ± 7.8, and 75.0 ± 17.3 min respectively. The body temperature (mean ± SD) at MAC determination in these groups were 36.1 ± 0.6, 36.6 ± 0.5, and 35.6 ± 0.1 degrees, respectively. They were not significantly different from each other (table 1).

The MAC (mean ± SD) of isoflurane in patients in the early postpartum period (0.75 ± 0.17 vol%) was significantly different from MAC values in control subjects (P < 0.01) and in patients in the late postpartum period (P < 0.05), whereas the MAC in the late postpartum period (0.95 ± 0.20 vol%) was not significantly different from that in the control group (1.04 ± 0.12 vol%) by Student’s unpaired t test and Dunnett’s test. The MAC value in the early postpartum period at 7.3 h (range 4.5–11 h) after delivery was 28% less than that in the control group. Seven (88%) of eight patients in the early postpartum period and four (50%) of eight patients in the late postpartum period had MAC values less than the mean value of the control group. The lowest MAC value was 0.45 vol%, which was 57% less than the MAC in control patients.

By linear regression, there was an inverse correlation (fig. 1A) between progesterone concentration postpartum and time after delivery (r = −0.527; P = 0.036) but no relation between β-endorphin concentration and time after delivery (fig. 1B) (r = 0.089; P = 0.744). Linear regression analysis of plasma progesterone (r = 0.005; P = 0.985) or β-endorphin (r = 0.154; P = 0.568) against MAC showed no correlation (fig. 1C and 1D), a result confirmed by multiple regression (r = 0.166; P = 0.950).

**Discussion**

Previous studies have demonstrated that MAC during pregnancy is decreased by 28% (isoﬂurane) in humans, by 40% (isoﬂurane) in ewes, and by 19% (halothane) in rats. In this study the MAC of isoﬂurane was decreased by 28% in the 1st 12 h of the postpartum period.

Traditionally, MAC determination in humans involves inhalation anesthetics to eliminate the synergistic effect of intravenous anesthetic agents given during induction of anesthesia. However, in the postpartum period, the risk of aspiration of gastric contents is well recognized, prompting us to use propofol, a short-acting induction agent, with application of Sellick’s maneuver to intubate the trachea rapidly. After a single bolus injection of 2 mg/kg propofol, the concentration in blood at 1 h decreases to 0.28 μg/ml in patients postpartum and 0.5 μg/ml in pregnant patients, comparable with those in nonpregnant women (0.34 μg/ml). These blood propofol concentrations are less than the concentration (0.7 μg/ml) at the time of awakening, suggesting that the residual concentration of propofol 1 h after induction may have minimal effects on the central nervous system. Furthermore, the MAC of isoﬂurane in our control group (64 min after propofol injection) was similar to the isoﬂurane MAC in control patients after delivery, and an induction dose of propofol (1.15 mg/kg) provided a minimal concentration of propofol.

Patients’ expired carbon dioxide was measured in the room that would be occupied by the control, early postpartum, and late postpartum groups. However, no carbon dioxide was present when arterial blood gases were obtained (2.7 to 4.2 mm Hg).

Recently, there have been increases in the use of cutting-edge local anesthetic techniques for surgery with a new method to determine the MAC in individual patients. This new method would provide a period of time before the contribution of the MAC (e.g., 0.5 vol%) is identified as a threshold (adjusted for individual variability) and verified in an individual patient. The MAC in this new method is the concentration at which anesthesia is verified in an individual patient.

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The anesthetic-sparing effect of opioids is well known. Large doses of butorphanol (≥0.1 mg/kg, intravenous) decrease the MAC for enflurane by 11%, but smaller doses of butorphanol (22 μg and 44 μg/kg, intravenous) have no significant effect on MAC. In our study, even smaller doses of intravenous butorphanol (about 13 μg/kg) were administered for pain control 5–28 h before induction of anesthesia. Five hours after a single intravenous injection (2 mg), the plasma concentration of butorphanol decreases 29 times (from 20 to 0.7 ng/ml); therefore, the MAC value in this study is unlikely to have been affected by residual serum butorphanol.

The mechanism explaining the decrease in MAC during pregnancy and early postpartum period is unclear. Selye was the first to report that steroids such as progesterone possessed anesthetic activity. Intravenous progesterone can induce sleep in women and decrease halothane MAC in nonpregnant rabbits. The increase in β-endorphin during pregnancy may decrease anesthetic requirements. However, a recent study shows no correlation between serum progesterone and MAC in pregnant women at 8–12 weeks' gestation. Similarly, our study shows no correlation between serum progesterone or β-endorphin and isoflurane MAC in the postpartum period. Alternatively, MAC may be affected by other factors. Putative candidates
as 5α-dehydroprogesterone and 3α-hydroxy-allopregnan-20-one (metabolites of progesterone), potent inhibitors of the central nervous system, β-lipoprotein, the precursor of β-endorphin, and serotonin. In addition, whether MAC is directly influenced by the substance in the plasma or in the cerebrospinal fluid has not been determined. It is recognized that plasma concentrations of β-endorphin do not correlate with the concentrations in the cerebrospinal fluid.

In conclusion, our study demonstrates that the MAC of isoflurane is 28% less than normal within the 1st 12 h postpartum and returns to normal at 12-24 h after delivery. Further studies are required to elucidate the mechanism responsible for the decrease in isoflurane MAC during early postpartum period.

References


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Clinical

I. Severe Hypertension

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Background

Hypertensive emergency and hypertensive crisis (HIFP) is a dangerous and potentially life-threatening condition. Although the definition of HIFP varies, most agree that hypertensive emergencies are acute increases in blood pressure that occur within hours and that the increase is >150/100 mm Hg. The differential diagnosis for HIFP includes preeclampsia, eclampsia, and postpartum hemorrhage.

Methods:

The management of HIFP is complex and requires a multidisciplinary approach. The initial management involves stabilization of the patient, control of blood pressure, and treatment of any associated conditions. Medical management includes the use of antihypertensive medications, such as calcium channel blockers, β-blockers, and angiotensin-converting enzyme inhibitors. Surgical management, such as nephrectomy or renal artery stenting, may be necessary in certain cases.

Results:

Successful treatment of HIFP requires a combination of multidisciplinary care, including anesthesiologists, intensivists, and nephrologists. The key to success is early recognition, rapid diagnosis, and prompt intervention. The goal is to achieve a gradual reduction in blood pressure to prevent complications such as end-organ damage and stroke.

Conclusions:

Hypertensive emergencies and crises are serious conditions that require prompt and appropriate management. Anesthesiologists play a vital role in the care of these patients, providing expert care and ensuring the best possible outcomes.

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