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Original research article

The effect of sevoflurane on interventions for blood loss during dilation and evacuation procedures at 18–24 weeks of gestation: a randomized controlled trial☆,☆☆,★

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Abstract

Objective: The objective was to evaluate whether the use of sevoflurane during general anesthesia for dilation and evacuation (D&E) procedures increases the frequency of interventions to treat excess bleeding.
Study design: A randomized, double-blinded, placebo-controlled trial of a standardized general anesthesia protocol with or without inhaled sevoflurane for D&Es between 18 and 24 weeks' gestation was performed. The primary outcome was need for any intervention to treat blood loss. Secondary outcomes included measured blood loss, procedure time, complications, side effects, patient satisfaction and provider ease of procedure.
Results: One hundred sixty subjects were randomized. Those in the sevoflurane group were slightly more likely to have interventions for bleeding as compared to those subjects who did not receive sevoflurane (25% versus 16.3%, p=.17) or a measured blood loss above 300 mL (15% versus 7.5%, p=.13); however, these differences could have arisen by chance. Most cases of excess bleeding required only minor interventions, including uterine massage and/or uterotonic agents. Procedure time, complications, side effects, satisfaction and ease of procedure were similar between groups.
Conclusion: Addition of sevoflurane to general anesthesia during a D&E between 18 and 24 weeks' gestation did not increase the risk of intervention for bleeding; however, this study was underpowered to detect clinically important differences.
Implications: In this randomized, double-blinded, placebo-controlled trial, sevoflurane did not significantly increase the risk of intervention for bleeding during D&Es. However, this agent should be used with caution as an anesthetic for surgical abortions.

Keywords: Abortion; Pregnancy termination; General anesthesia; Sedation; Volatile anesthetics

1. Introduction

Halogenated agents used in general anesthesia such as halothane and isoflurane are associated with decreased uterine contractility resulting in increased procedural blood loss during obstetric care and abortion [1–7]. In recent years, newer halogenated volatile anesthetics such as desflurane and sevoflurane have been replacing the older agents.

Although not well studied in abortion care, anesthesia providers commonly use sevoflurane because of its more rapid onset time, faster washout time for improved postoperative recovery and less irritation to mucous membranes [8]. It is appropriate for induction and maintenance of anesthesia, and is particularly common in shorter duration procedures and in procedures that require rapid changes in anesthesia concentration [9,10]. The available data are conflicting in regard to whether sevoflurane acts similarly on the uterus as compared to older halogenated agents. In vitro studies have shown that sevoflurane decreases the contractility of gravid human and rat myometrium similarly to halothane and isoflurane [11,12].

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In many clinics, abortion providers routinely perform second-trimester abortions under general anesthesia. A 2001 survey of National Abortion Federation members found that 25% of facilities used general anesthesia for 80% to 100% of patients [13]. While only 1 respondent out of 49 reported use of halogenated agents (personal communication with author), this survey represented mostly outpatient clinics.

Several professional organizations currently recommend against the use of inhaled anesthesia for second-trimester abortion due to the potential for uterine atony and excessive bleeding [14–16]. However, these recommendations are based mostly on studies showing increased blood loss with older halogenated agents such as isoflurane [7,17,18]. Only one previous study has evaluated the use of sevoflurane for surgical abortion. A small randomized trial by Nathan et al. found that subjects who received sevoflurane had significantly greater blood loss compared to those who received only propofol [blood loss measured by weight of aspirate; 230 g (range 110–800 g), $n=13$, compared to 110 g (range 60–160), $n=12$; p=.004] [19]. The authors report that they terminated the study due to the "unacceptable increase in bleeding observed in the sevoflurane group." Gestational age range was not reported in the study.

Given that sevoflurane is included in anesthetic regimens for dilation and evacuation (D&E) procedures, more information is needed to understand its impact on safety. Therefore, we designed a prospective, randomized, double-blinded, placebo-controlled trial comparing use of inhaled sevoflurane to inhaled oxygen alone as part of an established general anesthesia protocol during D&E procedures between 18 and 24 weeks' gestation. This study aimed to evaluate whether the use of sevoflurane during D&E procedures increases the frequency of interventions to treat increased blood loss.

2. Materials and methods

This randomized controlled trial was designed to address the hypothesis that sevoflurane increases interventions for blood loss when administered with an established general anesthesia protocol of intravenous (IV) propofol, IV midazolam, IV fentanyl and inhaled nitrous oxide during D&E procedures between 18 and 24 weeks' gestation. Surgical procedures were performed at a private community outpatient surgical center (Lovejoy Surgicenter) and in the hospital main operating room at Oregon Health and Science University (OHSU) in Portland, OR. Study procedures were initiated after approval by the Institutional Review Board at OHSU.

Research coordinators approached potential study participants after they had consented to surgical termination of pregnancy between 18 and 24 weeks' gestation as determined by ultrasound dating (biparietal diameter). Additional eligibility criteria included age 16 years or older, voluntarily requesting termination of pregnancy, and willing and able to sign an informed consent. Women were excluded if they had known severe maternal respiratory disease or upper respiratory infection or sinus blockage; were currently anticoagulated; and had a known multiple pregnancy fetal demise for greater than 2 weeks and known allergy/sensitivity to sevoflurane or any other inhaled anesthetic agents.

Participants were randomized to treatment group using a predetermined computer-generated randomization scheme and were allocated using sequentially numbered, opaque, sealed envelopes. Study staff not involved with enrollment of subjects pre-prepared the randomization sequence and the envelopes. The surgeons and subjects were blinded to the randomization allocation, but for safety reasons, the anesthesia providers were not blinded. The anesthesia providers were not involved in data collection or analysis. At the outpatient clinic, two experienced certified registered nurse anesthetists administered anesthesia. Four board-certified anesthesiologists administered anesthesia for study subjects at the hospital.

Experienced D&E providers performed procedures according to the local standard of care which included cervical preparation utilizing a combination of overnight laminaria and, per provider preference, 400 mcg buccal misoprostol approximately 90 min prior to the D&E. Providers included two Family Planning specialists, three Maternal Fetal Medicine specialists and two Family Planning fellows under the supervision of an attending provider. Patients over 22 weeks' gestation at the outpatient site received an intraamniotic or intrafetal digoxin injection. All subjects received perioperative doxycycline prior to the procedure. Upon entry into the operating room, the anesthesia provider opened the randomization envelope and administered the appropriate gas (treatment arm: sevoflurane as dosed for the patient as a mixture with oxygen, control: supplemental oxygen only). Both oxygen and sevoflurane were delivered by the same clear facemask and tubing. No subjects were intubated. The anesthesia provider positioned a drape to prevent visibility between the anesthesia equipment with the gas dials and the surgeon. All subjects received IV fluids with oxytocin intraoperatively, but no other uterotonic medications were routinely provided during or after the procedure. Subjects did not receive cervical anesthetic injection with vasopressin.

All patients received IV propofol, IV midazolam, IV fentanyl and inhaled nitrous oxide, and either sevoflurane (Halocarbon Products Corporation, P.O. Box 661, River Edge, NJ 07661) or no additional inhalational agent based upon the randomization. The anesthesia provider recorded the rate that sevoflurane was given and the timing of administration.

The primary outcome was need for any intervention to treat blood loss. Secondary outcomes were measured blood loss, procedure time (time from speculum placement to speculum removal), complications (e.g., need for transfer to another facility, uterine perforation, need for further surgery, transfusion and inpatient hospitalization), medication side effects, patient satisfaction with anesthesia and provider ease of procedure.