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Contraception xx (2017) xxx – xxx

Contraception

Original research article

Nitrous oxide versus oral sedation for pain management of first-trimester surgical abortion — a randomized study☆

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Received 29 December 2016; revised 3 June 2017; accepted 7 June 2017

Abstract

Objective: The objective of the study was to compare nitrous oxide with oxygen (N_2O/O_2) to oral hydrocodone/acetaminophen and lorazepam for analgesia during first-trimester surgical abortion.
Study design: This double-blind randomized trial assigned women undergoing first-trimester surgical abortion at<11 weeks' gestation to inhaled N_2O/O_2 vs. oral sedation for pain management. The N_2O/O_2 group received up to 70:30 ratio during the procedure and placebo pills preprocedure; the oral group received inhaled oxygen during the procedure and oral hydrocodone/acetaminophen 5 mg/325 mg and lorazepam 1 mg preprocedure. The primary outcome was maximum procedural pain, assessed on a 100-mm visual analog scale (VAS; anchors 0=*no pain* and 100=*worst pain*) at 2 min postprocedure. A difference of 13 mm on the VAS was considered clinically significant. Satisfaction with pain management was measured on a 100-mm VAS (anchors 0=*very unsatisfied*, 100=*very satisfied)*.
Results: We randomized 140 women, 70 per study arm. Mean age of participants was 26±6.6 years; mean gestational age was 7.3±1.5 weeks. Mean maximum procedure pain scores were 52.5±26.7 and 60.8±24.4 for N_2O/O_2 and oral groups, respectively (p=.09). Satisfaction with pain management was 69.3±28.4 and 61.5±30.4 for N_2O/O_2 and oral groups. respectively (p=.15).
Conclusion: We found no difference in mean procedural pain scores between women assigned to N_2O/O_2 vs. those assigned to oral sedation for first-trimester surgical abortion. Satisfaction with both options was high.
Implications: Women undergoing early surgical abortion experienced no differences in pain and satisfaction between those who used inhaled nitrous oxide and oral sedation. Nitrous oxide, with side effects limited to the duration of inhalation and no need for a ride home, is a viable alternative to oral sedation for first-trimester abortion pain management.

Keywords: Nitrous oxide; Surgical abortion; Pain; Oral analgesia; First trimester

1. Introduction

Approximately 700,000 abortions occurred in the United States in 2012; 91.4% were at ≤13 weeks' gestational age [1]. Many first-trimester surgical abortions take place in outpatient clinics under a paracervical block (PCB) with or without oral medication or under PCB with our without intravenous sedation. Surgical abortion is painful; up to 97% of patients report at least moderate procedural pain [2]. Outpatient pain management measures — preoperative nonsteroidal anti-inflammatory drugs (NSAID), oral and intravenous narcotics, and anxiolytics — show varying efficacy in reducing the pain of surgical abortion. Use of narcotics and anxiolytics requires a ride home, can prolong postoperative recovery and has side effects [3]. Offering intravenous sedation requires compliance with local and state facility guidelines; clinical staff must receive and maintain competency in specialized training/skills including advanced cardiac life support, and certification for moderate sedation.

Nitrous oxide is an inhaled gas delivered with oxygen (N_2O/O_2) in a fixed ratio which can be titrated for anesthesia and sedation. Onset of action is rapid, and the gas has analgesic, sedative and anxiolytic effects. It is ultra-short-acting; effects dissipate rapidly after use is stopped. N_2O/O_2 is safely used in a variety of settings

☆ Clinical trial registration: ClinicalTrials.gov, www.clinicaltrials.gov, NCT02096575

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http://dx.doi.org/10.1016/j.contraception.2017.06.003
0010-7824/

including reduction of fractures or joint dislocations, suturing of pediatric lacerations, dental procedures and labor analgesia [4–6].

Three prior publications have examined N_2O/O_2 use for first-trimester abortion, two of which did not find reduced pain compared to either intravenous sedation [7] or local anesthesia plus intravenous paracetamol [8]. Additionally, these studies used a relatively low concentration (50:50) of nitrous oxide. A small feasibility study found that higher concentrations of N_2O/O_2 (70:30) resulted in higher satisfaction with pain management compared to oral sedation [9]. We conducted this study to compare pain management with N_2O/O_2 and oral sedation during first-trimester surgical abortion.

2. Materials and methods

This randomized double-blind trial comparing N_2O/O_2 and placebo pills to oral sedation and oxygen (O_2) during first-trimester surgical abortion was conducted at the University of New Mexico Center for Reproductive Health between September 2013 and March 2015. Our primary outcome measure was recall of maximum procedure pain at 2 min postprocedure. Secondary outcome measures were satisfaction with pain management, pre- and postprocedure anxiety levels, and provider and patient assessment of their treatment assignment.

We recruited English-speaking women age ≥18 years desiring and meeting criteria for outpatient surgical abortion at gestational age <11 weeks, and who desired local anesthesia ± oral sedation for pain management and had no contraindications to the use of study medications. Participants were excluded if they had allergies to study medications or contraindications to N_2O/O_2 including active respiratory infection; inability to breathe through the nose; or use of alcohol, opiates, benzodiazepines or stimulants on the day of their procedure. Obstetrics/gynecology family planning faculty or fellows or family medicine family planning faculty performed all aspiration procedures. Participants provided written consent for study participation and received a $25 gift card to a local retailer to compensate for their time.

An investigator not involved with recruitment generated a block randomization scheme using SAS software (version 9.4; SAS Institute, Inc., Cary, NC, USA). Sequence generation with random blocks of four was concealed in sequentially numbered opaque sealed envelopes opened after the participant had signed the consent form and immediately before the procedure. Medications (hydrocodone/acetaminophen and lorazepam) and placebo pills (methylcellulose gel) were concealed in identical gel caps.

All participants received ibuprofen 800 mg and doxycycline 200 mg orally 30 min prior to the procedure. The N_2O/O_2 group received two placebo pills, and the oral group received one hydrocodone/acetaminophen 5/325 mg and lorazepam 1 mg at least 30 min before the procedure. The oral group received oxygen during the procedure. N_2O/O_2 or oxygen was administered via a scented nasal mask to blind participants to the intervention. N_2O/O_2 administration was started at a concentration of 20:80 and titrated up in increments of 5%–10% up to a maximum of 70% N_2O and 30% O_2 based on desired anesthetic effects. Anesthetic effects of N_2O/O_2 include the patient appearing comfortable and relaxed, the patient showing less fear and anxiety, and her eyes appearing less active and glazed. A screen in the procedure room concealed the administration of gas from the participant, physician and research coordinator. A staff member trained in the administration of N_2O/O_2 and not involved in other aspects of the patient's care administered the gasses for 1 min before we initiated the procedure, defined as placement of the speculum.

Participants completed a demographic questionnaire and were instructed on completion of the visual analog scale (VAS) after providing informed consent for the study. Our primary outcome measure was recall of maximum procedural pain assessed on a 100-mm VAS (anchors 0=*no pain*, 100=*worst pain*) 2 min after procedure completion including intrauterine device (IUD) placement. Removal of the speculum defined procedure completion. Secondary outcomes, also assessed by VAS, included baseline pain, expected pain, pain at 5 min after procedure completion and pain prior to discharge from the clinic. All data were collected by a research coordinator blinded to the group assignment. VAS scores for each outcome were placed on separate sheets of paper which the research coordinator held in front of the participant, allowing her to mark the VAS line with a pen. We collected baseline anxiety levels prior to the procedure using the short-form Spielberger State–Trait Anxiety Inventory (STAI), in which women rate five statements (I feel calm, I am tense, I feel upset, I am relaxed, I am worried) on a Likert scale of 1 to 4 (not at all, somewhat, moderately, very much) [13,14]. Postprocedure, we assessed satisfaction with pain management using a 100-mm VAS and postprocedural anxiety with the short-form STAI.

All participants received a standardized PCB of 18 mL 1% lidocaine buffered with 2 mL 8.4% sodium bicarbonate and 0.2 mL of 4 U of vasopressin (20.2 mL total). The PCB was injected with a 22-gauge spinal needle: 2 mL at the 12 o'clock tenaculum site and 18 mL over 60 s at the cervicovaginal junction in four equal aliquots at 2, 4, 8 and 10 o'clock [15]. The provider began dilation immediately after application of the PCB. Technique of the aspiration procedure, source of vacuum, and cannula type was at provider discretion. No participants received preprocedure misoprostol.

Sample size was based on mean procedure pain scores from current evidence. Previous studies of first-trimester abortion under local anesthesia with or without ibuprofen demonstrate mean VAS between 51 and 62 mm with standard deviations (SDs) of 22–25 mm [10–12]. Clinically