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Contraception 72 (2005) 358–361

Contraception

Original research article

A randomized clinical trial of the addition of laminaria to misoprostol and hypertonic saline for second-trimester induction abortion

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Received 10 May 2004; revised 22 April 2005; accepted 27 April 2005

Abstract

Objective: To compare the outcomes of second-trimester induction abortion with misoprostol and hypertonic saline, with and without use of laminaria.

Method: Fifty-eight women, between 17.5 and 22.5 weeks' gestation, were randomly assigned to receive or omit laminaria in conjunction with other procedures for induction abortion. All women received a fetocidal dose of 60 cc intra-amniotic hypertonic saline. If the woman was to receive laminaria, they were inserted next. This was followed by vaginal misoprostol 200 μg, which was repeated every 6 h.

Result: Women with laminaria inserted before misoprostol administration had longer intervals from start of misoprostol to delivery of the fetus (induction times) than women without laminaria. Induction time was 14.4 vs. 11.4 h, respectively ($p=.04$, Wilcoxon rank sum test). Total misoprostol use was higher in the laminaria group, 628 μg (95% CI, 516–738) vs. 496 μg (95% CI, 419–573) ($p=.05$). Total analgesic use was also higher in the laminaria group, 41 mg of morphine (95% CI, 32–50) vs. 26 mg of morphine (95% CI, 18–32) ($p=.02$).

Conclusion: Laminaria use, in conjunction with misoprostol and hypertonic saline, significantly prolongs induction time and increases narcotic analgesia usage.

Keywords: Abortion; Second trimester; Laminaria; Osmotic dilators; Misoprostol

1. Introduction

Women seek second-trimester abortion for a variety of reasons, including antenatal detection of fetal defects and social and personal changes during pregnancy. Both medical and surgical techniques can be used; the choice of technique may depend on the woman's preference, but is frequently determined by the facilities available to her. Second-trimester abortion by medical induction technique has been accomplished with several agents; the earliest agents were supplanted in most practices by use of prostaglandins E_2 or $F_{2\alpha}$ and analogues [1]. Misoprostol, a prostaglandin E_1 analogue, has largely replaced prostaglandins E_2 and $F_{2\alpha}$ as it is equally effective, more stable, less expensive and has fewer gastrointestinal side effects [1,2]. Osmotic dilators, such as laminaria, have been used with several prostaglandin analogues as an adjunct for induction of abortion [1,3–11]; however, there has been little evaluation of the use of osmotic dilators with misoprostol. One randomized trial of laminaria in conjunction with misoprostol induction at 12–22 weeks concluded that laminaria did not improve efficacy; however, the majority of patients in that study had spontaneous intrauterine fetal death [3].

At the Boston Medical Center, a combination of procedures to induce abortion had been in use for several years. After admission, three procedures were performed in succession. First, an amnio-injection of 60 cc of hypertonic (23.4%) saline was routinely used as a fetocidal agent. Laminaria were then inserted, followed by misoprostol 200 μg vaginally. Misoprostol was repeated every 6 h. We aimed to evaluate whether our practice of using laminaria with misoprostol and hypertonic saline abortion was beneficial.

2. Materials and methods

This study was approved by the Institutional Review Board at the Boston University School of Medicine. Women who had already requested and consented to an induction abortion were eligible if they had a live pregnancy between

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0010-7824/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.contraception.2005.04.016

17.5 and 23.5 menstrual weeks, were able to understand English and had no medical contraindications to osmotic dilators. Contraindications to the other agents used, hypertonic saline, misoprostol and morphine, were not explicitly stated. Study consent was obtained by one of the investigators at the time of the clinic visit prior to admission.

Women were admitted to the gynecology service at the Boston Medical Center on the morning of induction. All women were given a patient-controlled intravenous analgesia pump; the pump would administer 1 mg morphine sulfate doses on demand, with a minimum of 6 min between doses. Randomization occurred after admission, but before any procedures were performed. An investigator opened the next numbered opaque envelope containing the group assignment. Both the physician and the woman were blinded until that point, after which blinding was not possible. After randomization, for the control group, there was a series of three procedures, First, an intra-amniotic injection of 60 cc of hypertonic (23.4%) saline was used as a fetocidal agent. Second, laminaria were inserted; the operator placed as many as tolerable to the woman. If laminaria were used, a sponge with povidone iodine might be left in the vaginal vault at the discretion of the operator. Third, a 200-μg misoprostol tablet was placed in the vaginal vault. For women in the no-laminaria group, the laminaria step was omitted and sponges were never used.

After the initial procedures, women continued analgesia as needed. Additional doses of 200 μg misoprostol were placed vaginally every 6 h until abortion occurred or until 24 h had elapsed. After 24 h, the agent used was at the discretion of the woman's doctor. After delivery of the fetus, the placenta was generally allowed to deliver spontaneously unless bleeding occurred. There were no restrictions on operative intervention. The usual practice was to intervene if the woman's discharge would be delayed by waiting further. Generally, removal was performed the morning after induction start (20–24 h after the start of induction), regardless of the time of delivery, as the procedure room was only available during the day.

The primary outcome was the time from the start of misoprostol to delivery of the fetus (induction time), with the expectation of a null result. To have a power of 80% to detect a 3-h time difference between the two treatment groups at $p<.05$, 30 women in each group were needed. A randomization of 1:1 was achieved with permuted blocks of random length, using a random table generator (Statools, GE Dallal, Tufts University). The envelopes with the randomization assignments were prepared by a study staff member with no clinical contact. Data were analyzed as intent-to-treat. Time to abortion was analyzed with a survival (time-to-event) model. Survival curves were plotted using Kaplan–Meier estimation. Survival times were

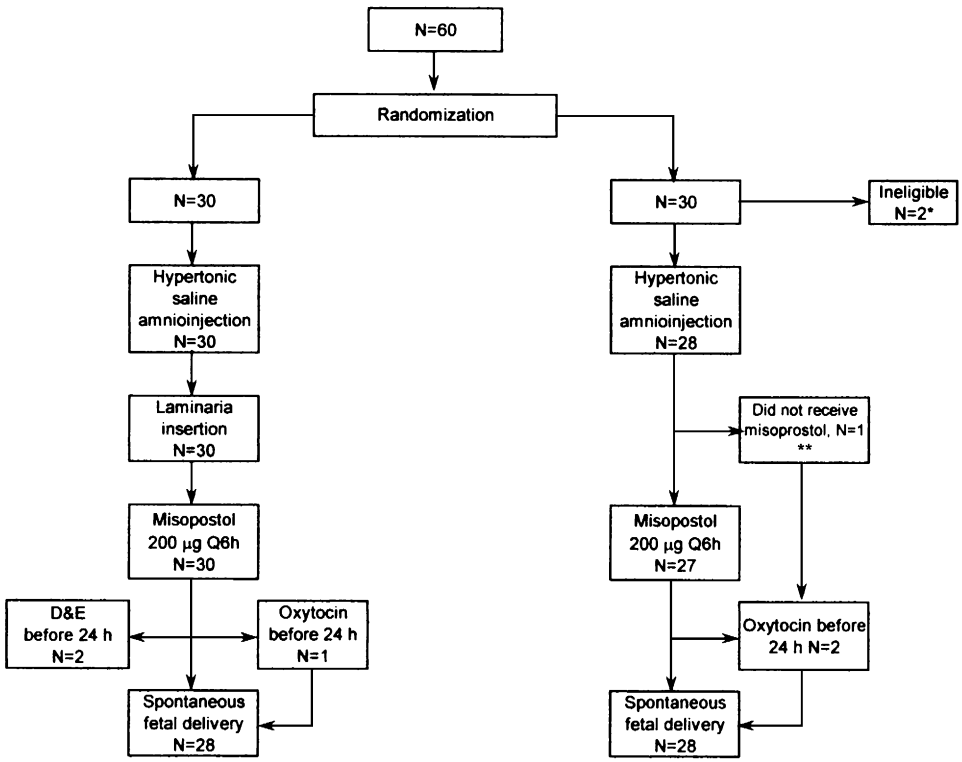

Fig. 1. Study procedures. All women had an intra-amniotic injection of 60 cc (23.4%) saline. Women in Group 1 had laminaria inserted immediately afterward. After the preceding procedures were concluded, women in both groups received misoprostol 200 μg vaginally. Misoprostol was continued every 6 h until delivery occurred or until 24 h elapsed from the first misoprostol dose. *Two women were uncertain about participating at the time that study procedures were ready to begin. **One women did not receive any misoprostol at all; her physician felt it was contraindicated in the presence of inflammatory bowel disease.