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Original research - Orijinal araştırma

Use of cervical dilators is not necessary during curettage after combined oral and vaginal administration of misoprostol from five to ten weeks of pregnancy

Beş ile on hafta arasındaki gebeliklerde oral ve vajinal misoprostol uygulamasından sonra küretaj sırasında servikal buji kullanımı gerekli değildir

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Abstract

Aim. The aim of this study was to determine the efficacy of oral and vaginal misoprostol administered for cervical priming in nullipar women before first-trimester surgical abortion. **Methods.** Medical records of 84 nulliparous women, aged 18-42 years, who admitted for pregnancy termination request were reviewed retrospectively. The pregnancies were between 5 and 10 weeks of gestation. 100 µg misoprostol was administered by oral and vaginal route in 84 patients. The doses repeated 4 hours later. Exclusion criteria were systemic disease, a history of cervical operations, bleeding or spotting during the current pregnancy and basal cervical dilation greater than 4mm. **Results.** Targeted cervical dilatation for pregnancy termination was determined according to gestational age of every patient (for gestations at 5, 6, 7, 8, 9, and 10 weeks, required cervical dilatations from 5, 6, 7, 8, 9, and 10 mm, respectively). A significant correlation was found between gestational ages and achieved cervical dilatation after misoprostol use. **Conclusions.** Suggested administration of misoprostol provides adequate cervical dilatation. Use of cervical dilators is not necessary during curettage after administration 100 µg misoprostol oral and vaginal two times four hours apart from five to ten weeks of pregnancy.

Key words: Misoprostol; first trimester abortion; cervical priming

Özet

Amaç. Bu çalışmanın amacı birinci trimester cerrahi abortus öncesi nullipar kadınlara servikal olgunlaşma için uygulanan oral ve vajinal misoprostolün etkinliğinin belirlenmesidir. **Yöntem.** Gebelik sonlandırması istemiyle başvuran, 18-42 yaş arası toplam 84 nullipar kadının medikal kayıtları geriye dönük olarak değerlendirilmiştir. Gebelikler 5-10. gebelik hafaları arasında idi. 84 hastaya oral ve vajinal yolla 100 µg misoprostol uygulanmıştır. Dozlar 4 saat sonra tekrarlanmıştır. Dışlama kriterleri sistemik hastalık, servikal operasyon hikayesi, mevcut gebelik süresince kanama veya lekelenme ve bazal servikal dilatasyon düzeyinin 4 mm'den fazla olmasıydı. **Bulgular.** Her hastada gebelik terminasyonu için hedeflenen servikal dilatasyon gestasyonel yaşa göre belirlenmiştir (5, 6, 7, 8, 9 ve 10 haftalık gebelikler için gerekli görülen servikal dilatasyon sırasıyla 5, 6, 7, 8, 9 ve 10 mm). **Sonuçlar.** Misoprostolün önerilen uygulama şekli yeterli servikal dilatasyon sağlar. Beş ile on hafta arasındaki gebeliklerde dört saat ara ile iki kez oral ve vajinal 100 µg misoprostol uygulamasından sonra küretaj esnasında servikal bujiye gerek kalmamaktadır.

Anahtar sözcükler: Misoprostol, ilk trimester abortus, servikal olgunlaşma

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Introduction

Misoprostol (15-deoxy-16-hydroxy-16-methyl PGE1) is a synthetic prostaglandin E1 analog that has been widely used for treatment and prophylaxis of gastric ulcers. Subsequently, the effectiveness of the drug for many obstetric and gynecological conditions including postpartum hemorrhage, intra-uterine fetal death, labor induction, first and second trimester abortion, and incomplete and missed abortion was discovered [1]. Misoprostol induces uterine contractions that empty uterine content. In addition, the drug allows greater dilation for intrauterine procedures by softening the cervix [2, 3]. Wide availability, inexpensiveness and easy administration make the drug preferable for the treatment of these clinical conditions. Misoprostol can be administered by oral, vaginal, sublingual, buccal and rectal routes. In spite of its extensive use in many obstetric and gynecologic conditions, no standard or labeled regimens have been established so far.

The aim of this study was to determine the efficacy of oral and vaginal misoprostol administered for cervical priming in nullipar women before first-trimester surgical abortion.

Materials and methods

A retrospective review of medical charts of 84 nullipar women, aged 18-42 years, between 5 and 10 weeks of gestation, who had requested therapeutic and legal termination of pregnancy, was performed. The study protocol was approved by human ethics committee of our school (09/167). Gestational age of each pregnancy was confirmed by transvaginal ultrasonography. All patients had a vaginal exam and evaluation of basal cervical dilation using a Hegar dilator before evacuation. The routine dose regimen of our clinic, 100 μg of misoprostol were given by oral and vaginal route for the termination of the pregnancies. The doses were repeated 4 hours later. Misoprostol tablets were placed into the posterior vaginal fornix. Aspiration was performed two hours after the last doses given. The outcome measures were cervical dilation before surgery and surgical time needed for aspiration. The incidence of side effects, such as nausea, vomiting, diarrhea, fever/chills and paresthesia was evaluated. Exclusion criteria were systemic disease, a history of cervical operations, bleeding or spotting during the current pregnancy, basal cervical dilation greater than 4mm and a preoperative hemoglobin level less than 11 g/dl.

Results

Table 1 shows the age, gravidity, parity, gestational age, and basal and achieved cervical dilatations.

Table 1. Selected clinical data.

Age	26.1+6.3
Gravidity	1.9+1.4
Parity	0 (0-3)
Gestational age	6.5+1.1
Basal cervical dilatation (mm)	2.4+0.8
Cervical dilatation achieved (mm)	6.6+1.2

Targeted cervical dilatation for pregnancy termination was determined due to gestational age of individual patient. A significant correlation was found between gestational age and achieved cervical dilatation after misoprostol use (p=0.001; r=0.759).

Mild and moderate gastrointestinal side effects were reported by six patients of whom two had nausea, two had vomiting and two had diarrhea.

Discussion

In this retrospective study, we aimed to determine the efficacy of oral and vaginal 100-µg misoprostol administered for cervical priming in nullipar women before first-trimester pegnancy termination. We concluded that the use of cervical dilators are not necessary during curettage after administration of 100-µg misoprostol used orally and vaginally two times four hours apart from five to ten weeks of pregnancy. Misoprostol is a synthetic prostaglandin E1 analogue that was firstly used for the treatment of peptic ulcers due to its inhibitor effect on gastric acid secretion and mucosal protective properties [4]. In obstetrics, misoprostol has been administered for induction of first and second trimester abortion, for induction of labor in the third trimester, and to control postpartum hemorrhage [5]. Food and Drug Administration has not approved the use of misoprostol for obstetric indications. However, the drug is widely used throughout the world. The drug reduces the rate of cesareans, shortens the time from induction to birth, also, it is inexpensive and many administration routes are possible. On the other hand, the drug may lead uterine hyperstimulation that rarely causes uterine rupture and death. Clark et al. [1] reported that ‘‘considerable variations in the regimens used; moreover, the regimens commonly used in clinical practice often differ from those recommended in the medical literature’ regarding misoprostol use in Brazil, Jamaica, and the United States.

Misoprostol tablets were developed for oral use, however, other routes of administration including vaginal, sublingual, buccal and rectal have also been used extensively in obstetric and gynecological practice [6]. Misoprostol has a rapid and almost complete absorption from the gastrointestinal tract after oral administration. The rectal route of administration has been studied recently for the management of postpartum hemorrhage [7]. This route of administration is less commonly used for other applications.

After a dose of 400 µg orally administered misoprostol, the drug plasma level increases rapidly and peaks at 30 minutes, declines by 120 minutes and remains low after that [7, 8]. Clinical studies showed that administration by vaginal route was more effective than oral route in medical abortion [9]. Vaginal absorption of misoprostol is variable and may be incomplete in some cases, possibly due to pH of the vaginal discharge. Although the mixture of misoprostol with water before vaginal administration is a common practice, this method has been shown to be ineffective to increase the bioavailability of the drug [7]. The administration of misoprostol by sublingual route has been studied for medical abortion and cervical priming. The misoprostol tablet is very soluble and can be dissolved in 20 minutes when it is put under the tongue [6]. It was shown that sublingual misoprostol has the shortest time to peak concentration, the highest peak concentration and the greatest bioavailability among all routes [7]. The drug also may be administered by buccal route, however, clinical studies dealing this route of administration are lacking.

For regular uterine contractions, sustained serum level, rather than high level, is required indeed, a very low serum level of misoprostol is enough for regular uterine contractions.

The uterine cervix is essentially a connective tissue organ. Smooth muscle cells account for less that 8% of the distal part of the cervix [7]. The mechanism of physiological cervical ripening is not known. The action mechanism of misoprostol in pregnant cervix have been shown to be mainly on the connective tissue stroma with evidence of disintegration and dissolution of collagen [10]. Taşcı et al compared the complete evacuation rate of two different single dose misoprostol regimens in termination of missed abortion within 24 hours. One hundred and one women with a diagnosis of missed abortion were randomized into two groups. Women in group 1 received four tablets of misoprostol vaginally, in group 2 two tablet misoprostol were administered vaginally at the same time two tablets taken orally. Women were evaluated by sonography after initiation of vaginal bleeding (primary visit) or in cases with no bleeding within 24 hours after the administration. They concluded that with a single dose misoprostol regimen regardless of the route of administration, overall complete evacuation rate was low at the first follow up visit [11].

Misoprostol is a safe and well-tolerated drug. Toxicological studies indicate a safety margin of at least 500-1000 fold between lethal doses in animals and therapeutic doses in humans [12]. The toxic dose of misoprostol is unknown, a woman who died of multi-organ failure following an overdose of misoprostol has been reported (60 tablets over 2 days) [13]. No clinically significant adverse effects including hematological, endocrine, biochemical, immunological, respiratory, ophthalmologic, or cardiovascular side effects have been associated with misoprostol so far. Diarrhea, usually mild in severity and self-limiting, is the commonest adverse reaction that has been reported consistently with misoprostol. Nausea and vomiting may also occur and resolve in hours [7].
We suggest that misoprostol 100 µg used orally and vaginally two times four hours apart from five to ten weeks of pregnancy provides adequate cervical dilatation for surgical termination and after its use, there is no need to use mechanical cervical dilators.

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