The use of misoprostol for pre-operative cervical dilatation prior to vacuum aspiration: a randomized trial

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Misoprostol is effective for cervical priming prior to vacuum aspiration for first trimester termination of pregnancy. Previous studies showed that the oral route was more acceptable to patients but there were higher incidences of side-effects when compared with the vaginal route. This study is to determine the optimal dosage and route of administration of misoprostol for pre-operative cervical dilatation. A double-blind, randomized trial was undertaken for 225 nulliparous women with 8–12 weeks amenorrhoea. They were randomly assigned to groups given 0 (placebo), 200 or 400 µg oral or vaginal misoprostol 3 h prior to vacuum aspiration. In misoprostol-treated groups the baseline cervical dilatation was significantly increased when compared with the placebo group; the effect was dose-related in the oral but not in the vaginal group. The cumulative force and blood loss was significantly decreased in the misoprostol-treated groups. The incidences of side-effects were more frequent in misoprostol groups but were not related to the route and dosage of medication. The duration of procedure, incidences of post-operative complications, the duration of post-operative bleeding and the interval to the first period were similar in the five treatment groups. We conclude that a 3 h pre-treatment interval is effective for both oral and vaginal routes. When given orally, 400 µg is more effective than 200 µg. The efficacy was otherwise similar when compared with the vaginal route. We recommend 400 µg oral misoprostol 3 h prior to vacuum aspiration for cervical dilatation.

Key words: cervical priming/misoprostol/oral/vaginal

Introduction

In recent years, significant advances have been made in the development of non-invasive methods for termination of pregnancy. The use of mifepristone in combination with misoprostol is effective for termination of early pregnancy (Norman et al., 1991). However, the rate of incomplete abortion and treatment failure increases as gestation advances. Therefore, the surgical method, i.e. vacuum aspiration, still plays a major role in termination of pregnancy.

It is well known that vacuum aspiration is associated with complications such as excessive haemorrhage, incomplete abortion, cervical tear and uterine perforation. The risk is increased when difficulty is encountered during cervical dilatation at vacuum aspiration, especially in nulliparous patients. Therefore, a lot of cervical priming agents had been studied in an attempt to reduce the operative morbidity.

Laminaria tents, synthetic prostaglandin analogues and mifepristone have been shown to be effective in cervical priming prior to vacuum aspiration. Laminaria tents are not expensive and are widely available. However, a trained member of staff is needed for insertion of the tent. Complications such as displacement of the tent causing cervical tear, have been reported (Liang et al., 1983). Patients need to be admitted 1 day before the operation for the tent to be effective and this increases the hospital cost.

Mifepristone has been reported to be effective for cervical priming prior to vacuum aspiration (WHO, 1990). However, the drug is only available in China, France, Sweden and the UK. To be effective, the drug has to be given 36–48 h before the procedure. Women may change their mind after ingestion of the drug. Also, mifepristone is expensive. Since vacuum aspiration is one of the most common gynaecological procedures, this may pose a significant burden on hospital budgets.

Gemeprost, a prostaglandin analogue, has been shown to be as effective as mifepristone when used as a cervical priming agent prior to termination of pregnancy (Henshaw and Templeton, 1991), but side-effects such as excessive haemorrhage, nausea and vomiting are common. Recently, misoprostol, a synthetic prostaglandin analogue that was initially used for peptic ulcer, has also been shown to be effective for cervical priming prior to vacuum aspiration (Ngai et al., 1995a). When given 12 h before the operation, oral misoprostol was more effective than vaginal gemeprost given 3 h before operation (Ngai et al., 1995b), and was as effective as mifepristone (Ngai et al., 1996). Both the oral and vaginal routes have been demonstrated to be effective for cervical priming prior to vacuum aspiration (Lawrie et al., 1996). Women prefer the oral route (Ho et al., 1997) but a recent study showed that they might abort and suffer from excessive bleeding when oral misoprostol was given 12 h prior to vacuum aspiration (Lawrie et al., 1996). It is possible that the incidence of these side-effects may be reduced by a shorter treatment interval. Therefore, we conducted a randomized comparative study to determine (i) whether oral misoprostol is also effective when it is given 3 h before the operation and (ii) to determine the optimal dosage and route of administration of misoprostol for pre-operative cervical dilatation.

Materials and methods

Ethical approval for the study was granted by the Ethics Committee, Faculty of Medicine, University of Hong Kong. Pregnant women
They were nulliparous, with age ranging from 16–42 years. All gave informed consent after the study had been explained, including their right to withdraw from the trial at any time without prejudice to their further medical care. Criteria for inclusion were a normal general and gynaecological history and examination. The gestational age was established by a reliable menstrual history and confirmed by either physical examination or ultrasound. The study involved a randomized, double-blind comparison of five treatment regimens: 0 (placebo), 200 or 400 µg misoprostol given by oral or vaginal route. The randomization schedule for allocation was produced as described by Meinert (1986). The five treatment groups were: group 1, 200 µg oral misoprostol and vaginal placebo; group 2, 400 µg oral misoprostol and vaginal placebo; group 3, oral placebo and 200 µg vaginal misoprostol; group 4, oral placebo and 400 µg vaginal misoprostol; group 5, oral and vaginal placebo. Both oral and vaginal medications were given 3 h prior to the operation. Vitamin B6 was chosen to be the placebo because it was known to have no cervical priming effect. The consistency and colour were the same as misoprostol.

The women were admitted in the morning on the day of operation. Vacuum aspirations were performed by one of the two investigators (Drs C.Ngai or Y.M.Chan) to reduce individual variability. Before the operation, blood pressure, pulse rate, temperature and the development of side-effects were recorded. The procedures were performed under general anaesthesia by administration of intravenous propofol (1.5–2.0 mg/kg) and fentanyl (0.5 µg/kg). The randomization schedules were unknown to the surgeon. A cervical tonometer (West of Scotland Health Board, Department of Clinical Physics and Bio-engineering, UK) was used to measure the peak force required to enter the cervical os with successive dilators from 3–8 mm. The resistance of the cervix to dilatation was objectively assessed using a series of tapered dilators attached to a force-sensing handle as described by Hazem et al. (1994). Baseline dilatation was defined as the first dilator requiring a peak force of 5 N to enter the internal os. The cumulative force required to dilate the cervix was calculated by adding the peak forces needed for each dilator up to 8 mm. Other parameters such as passage of tissue mass, nausea, vomiting, diarrhoea and abdominal pain were compared. The intra-operative blood loss was taken as the volume of the uterine aspirate after sieving away the products of conception. Following termination of pregnancy, women were kept in hospital for a further 6 h and attended a follow-up visit at 6 weeks after the operation.

The difference in pre-operative cervical dilatation was used as the main outcome indicator in the calculation of sample size. The sample size was estimated initially to be 200 using the method described by Meinert (1986), with the assumptions of type 1 error of 0.05 and power of 0.80; and a 2 mm difference in baseline cervical dilatation between placebo and misoprostol groups. Assuming 10% of the data was retrospectively excluded either due to incomplete data entry or violation of protocol, the number chosen was 45 in each group. Therefore, the total sample size was 225.

All data were recorded on standardized forms. Comparisons between treatment groups were made by using analysis of variance (ANOVA; Kruskal–Wallis) and post-hoc (Dunn’s) tests for non-parametric multiple comparisons as appropriate.

Results
A total of 225 nulliparous women were entered into the trial but 21 were excluded from analysis because they had some characteristics which deviated from the inclusion criteria specify-
120 min, and remained low for the remainder of the study. In contrast, plasma concentration of misoprostol acid in all women receiving vaginal doses rose gradually, reached maximum values between 60 and 120 min, and declined slowly, to an average of 61% of the peak value at 240 min after administration. Therefore, the onset of action should be faster when misoprostol is given orally rather than vaginally. Recently, vaginal misoprostol given 3 h prior to vacuum aspiration has been shown to be sufficient for pre-operative cervical dilatation (Fong et al., 1998). With this information, we believed that misoprostol given 3 h before surgery would be adequate in both oral and vaginal routes. Second, the incidence of pre-operative side-effects should be lower when the pre-treatment interval is shortened. This is the first study showing that oral misoprostol is effective for cervical priming when given 3 h prior to the procedure. We showed that oral misoprostol 400 μg is more effective than 200 μg without increase in pre-operative side-effects when given 3 h prior to vacuum aspiration. The 400 μg oral misoprostol is of similar efficacy when compared with the 200 and 400 μg vaginal route. No significant difference was detected between the two dosages in the vaginal route. Other peri-operative findings including the amount of blood loss, the incidence of side-effects and duration of the procedure were similar among the four misoprostol-treated groups. No
patients suffered from excessive blood loss or major complications.

Our data were different from Lawrie et al. (1996) who showed that women taking misoprostol by the oral route experienced more severe pain and heavier pre-operative bleeding when compared with the vaginal group. They gave 400 µg misoprostol orally, 12 h prior to surgery and compared with patients receiving 800 µg misoprostol vaginally, 2–4 h prior to surgery. The dosage of misoprostol and the pre-treatment interval was different between the two groups. Here, we adopted a shorter pre-treatment interval in the oral group which may account for the lower incidence of side-effects.

In a day care setting, oral misoprostol administered in the morning of the procedure may reduce the workload of the staff and gain higher acceptability by patients. We suggest that 400 µg oral misoprostol should be given 3 h prior to vacuum aspiration for cervical priming in nulliparous women. We conclude that either oral or vaginal misoprostol given at dosages of 400 µg is effective for cervical dilatation when administered 3 h prior to vacuum aspiration. We recommend a 400 µg oral regimen in view of patients’ acceptance and efficacy of the medication.

Acknowledgements
This study was supported by the Task Force on Postovulatory Methods of Fertility Regulation, Special Programme of Research, Development and Research Training in Human Reproduction, World Health Organization.

References


Received on February 11, 1999; accepted on May 6, 1999.