Comparative Evaluation of 50 Microgram Oral Misoprostol and 25 Microgram Intravaginal Misoprostol for Induction of Labour at Term: A Randomized Trial

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Abstract

Objectives: To assess and compare the efficacy and safety of 50 µg oral misoprostol and 25 µg intravaginal misoprostol for induction of labour at term.

Methods: This non-blinded, randomized clinical trial included 228 pregnant women at term with obstetric or medical indications for induction of labour. Women either took 50 µg misoprostol orally (two 25 µg tablets) or had one 25 µg tablet of misoprostol inserted in the posterior vaginal fornix. In each group, misoprostol administration was repeated every four hours in the same dose until regular uterine contractions were established or to a maximum of five doses. Time to delivery and outcome data for each group were compared.

Results: Of the 228 women, eight (3.5%) were excluded from the analysis as they withdrew their consent after randomization. Mean induction-to-delivery interval was similar in both groups (21.22 hours in the oral group vs. 20.15 hours in the vaginal group; $P = 0.58$). There was no significant difference between the groups with respect to the number of women who delivered within 24 hours or who required oxytocin augmentation of labour, the mode of delivery, and neonatal outcomes ($P > 0.05$). Uterine hyperstimulation occurred in two women who received misoprostol vaginally, but not in any of the women in the oral misoprostol group.

Conclusion: Oral misoprostol in a dose of 50 µg every four hours, to a maximum of five doses, has the potential to induce labour as safely and effectively as 25 µg misoprostol administered vaginally every four hours.

Key Words: Cervical ripening, labour induction, oral misoprostol, prostaglandin, vaginal misoprostol

Competing Interests: None declared.

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Résumé

Objectifs : Évaluer et comparer l'efficacité et l'innocuité de 50 µg de misoprostol par voie orale et de 25 µg de misoprostol par voie intravaginale pour le déclenchement du travail à terme.

Méthodes : Cet essai clinique randomisé n'ayant pas été mené à l'insu portait sur 228 femmes enceintes à terme qui présentaient des indications obstétricales ou médicales en ce qui concerne le déclenchement du travail. Ces femmes ont été affectées au hasard à un groupe devant prendre 50 µg de misoprostol par voie orale (deux comprimés de 25 µg) ou à un groupe devant se faire insérer un comprimé de 25 µg de misoprostol dans le cul-de-sac postérieur du vagin. Dans chacun de ces groupes, l'administration de la même dose de misoprostol a été répétée toutes les quatre heures jusqu'à ce que des contractions utérines régulières aient été établies ou jusqu'à l'administration d'un maximum de cinq doses. Le délai jusqu'à l'accouchement et les données quant aux issues ont été comparés chez ces groupes.

Résultats : Huit (3,5 %) de ces 228 femmes ont été exclues de l'analyse puisqu'elles ont révoqué leur consentement à la suite de la randomisation. L'intervalle déclenchement-accouchement moyen était semblable dans les deux groupes (21,22 heures au sein du groupe « oral » vs 20,15 heures au sein du groupe « vaginal »; P = 0,58). Aucune différence significative n'a été constatée entre les deux groupes en ce qui concerne le nombre de femmes ayant accouché dans les 24 heures ou ayant nécessité une accélération du travail à l'oxytocine, le mode d'accouchement et les issues néonatales (P > 0,05). Une hyperstimulation utérine s'est manifestée chez deux des femmes

qui avaient reçu du misoprostol par voie vaginale; toutefois, aucune des femmes ayant reçu du misoprostol par voie orale n'a été affectée par un tel phénomène.

Conclusion : Le misoprostol administré par voie orale à raison de 50 µg toutes les quatre heures, jusqu'à un maximum de cinq doses, présente le potentiel de déclencher le travail de façon tout aussi sûre et efficace que le misoprostol administré par voie vaginale à raison de 25 µg toutes les quatre heures.

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INTRODUCTION

Induction of labour is widely performed when continuation of pregnancy is hazardous to the mother or fetus.[1] Prostaglandin E_2 has been the agent of choice for pre-induction cervical ripening for several decades and is one of the pharmacologic agents approved by the United States Food and Drug Administration for this indication. However, it has several disadvantages: it is expensive, it requires continuous refrigeration, and it is not widely available.[2]

Misoprostol (a prostaglandin E_1 analogue) is a comparatively new agent for pre-induction cervical ripening and labour induction. It has excellent cervical ripening and uterotonic properties,[3] and is on the WHO essential drug list for labour induction.[4] In 2003, the Food and Drug Administration in the United States revised the contraindication to use of this drug in pregnant women and created a new section of labelling for labour and delivery, providing safety information related to that use.[5]

Misoprostol has been extensively investigated in the past few years for use in cervical ripening and labour induction.[6–13] It has several potential advantages: it is stable at room temperature, is relatively inexpensive, and can be administered by several routes (oral, vaginal, sublingual, and buccal). These properties make misoprostol a useful agent for induction of labour, particularly in settings in which the use of prostaglandin E_2 is not possible because of a lack of availability, a lack of facilities for storage, or financial constraints.

The ideal dose, route, and frequency of administration of misoprostol are still under investigation. Most clinical trials[6–15] have used doses ranging from 25 µg to 100 µg, prepared from 200 µg oral tablets and inserted intravaginally into the posterior fornix. The most common vaginal dose used has been 50 µg, inserted once or administered every four to six hours; inserting 25 µg every six hours intravaginally has been associated with the fewest side effects.[2,14,15]

Although vaginal application of misoprostol has been validated as a reasonable means of induction,[2] there is patient resistance to repeated digital examination necessary for placement of the agent. There is also a risk of ascending infection because of repeated vaginal examinations.[16] Oral misoprostol is well tolerated when used for the management of upper gastrointestinal tract dysfunction.[2] For these reasons, oral administration of misoprostol has been introduced for cervical ripening and labour induction.[17,18]

There have been few trials assessing the efficacy and tolerability of oral misoprostol for induction of labour. Oral misoprostol in a dose of 50 µg was found by Windrim et al. to be as effective as other conventionally used methods of labour induction.[18] Bennett et al.[19] and Shetty et al.[20] found oral misoprostol in a dose of 50 µg to be less effective than the equivalent dose of vaginal misoprostol but found an increasing trend of uterine hyperstimulation in the vaginal misoprostol group. Seyfettin et al.[21] found 100 µg oral misoprostol to be as effective as 50 µg vaginal misoprostol. These were all multiple dose trials. However, although the efficacy was high at higher doses, there was a significantly higher incidence of abnormal uterine activity, non-reassuring fetal heart rate tracings, and meconium-stained amniotic fluid. [9,19,22] There have been few randomized trials conducted comparing 50 µg oral misoprostol with 25 µg intravaginal misoprostol for labour induction.[23]

In view of the uncertainty regarding the preferred dose and route of administration of misoprostol for induction of labour, we designed this study to assess and compare the efficacy and safety of 50 µg oral misoprostol with 25 µg intravaginal misoprostol for induction of labour at term. We chose the oral dose of 50 µg because of our experience with this dose and the experience of other investigators with oral doses up to 200 µg.[17] We chose the vaginal dose of 25 µg because this dose has been shown to be effective with the least complications.[2] The advantages of the oral route include ease of administration and the ability to administer repeated doses without internal examinations and without increasing the risk of bacterial contamination in women with ruptured membranes.[22] An advantage of the vaginal route is that the bioavailability of vaginally administered misoprostol is more than twice that of orally administered misoprostol.[24]

ABBREVIATIONS

FHR	fetal heart rate
PGE_2	prostaglandin E_2
RR	relative risk