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# Initial clinical experience with a misoprostol vaginal insert in comparison with a dinoprostone insert for inducing labor

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ABSTRACT

*Objective:* Only one phase III trial has been published to date on the efficacy and safety of misoprostol vaginal inserts for inducing labor. The aim of this study was to compare misoprostol inserts with dinoprostone inserts.

*Study design:* This retrospective cohort study evaluated the reduction in time to vaginal delivery and delivery within 24 h, in routine clinical work, in 119 labor inductions using a 200-μg misoprostol vaginal insert (Misodel®; June–October 2014) in comparison with 124 inductions using a 10-mg dinoprostone insert (Propess®; December 2013–April 2014).

*Results:* Vaginal delivery within 24 h occurred in 77.3% ($n = 92$) of the misoprostol cohort and 74.2% ($n = 92$) of the dinoprostone cohort ($P = 0.654$). Time from insert application to vaginal delivery (min) was 761.76 (±409.44, cohort M) versus 805.17 (±473.00, cohort D) ($P = 0.817$). Cesarean delivery was performed in 10.1% ($n = 12$) versus 10.5% ($n = 13$) in the misoprostol and dinoprostone cohorts, respectively ($P \geq 0.999$). The modified Bishop scores were 2.0 versus 3.0 ($P = 0.001$), mean body mass index (BMI) was 24.72 versus 23.95 ($P = 0.033$), and fetal scalp blood testing was required in 12.6% ($n = 15$) versus 3.2% ($n = 4$; $P = 0.008$). No differences were observed with regard to the rates of transfer to the neonatal unit or any type of fetal acidosis.

*Conclusions:* The groups thus had similar results for rates of vaginal delivery within 24 h, cesarean delivery and fetal outcomes. The misoprostol group had lower modified Bishop scores, higher BMIs, and a higher rate of fetal scalp blood testing.



## Introduction

Iatrogenic induction of labor has been a matter of debate for several decades now. Women undergo induction of labor as part of everyday routine work in obstetrics, and the procedure is preferable to expectant management in an increasing number of situations such as management of large-for-date-fetuses, gestational hypertension or mild pre-eclampsia [1–3].

Labor can be induced using a variety of techniques, including mechanical methods or administration of oxytocin or prostaglandins. Prostaglandins have been shown to increase the rate of vaginal delivery within 24 h and to decrease the need for oxytocin, and they appear to have no effect on the rate of cesarean delivery in women with an unscarred uterus [4]. Prostaglandins are available in different forms, such as prostaglandin $E_2$ analogs (dinoprostone) or $E_1$ analogs (misoprostol). Misoprostol appears to be the more effective drug. It can be administered orally or vaginally—preferably orally—but it has still not yet been approved for induction of labor [5,6]. However, it can also be administered using a vaginal insert, which has received approval in Europe, and a phase III trial reported that this was associated with a favorable outcome in comparison with a dinoprostone vaginal insert [7].

The aim of the present retrospective cohort study was to reassess the favorable outcomes reported in that trial by comparing a misoprostol vaginal insert with a dinoprostone vaginal insert in routine clinical work. The main target parameter in the study was the rate of vaginal delivery within 24 h. Among the patients treated at Kepler University Hospital in Linz, Austria, a wide range of indications for labor induction are used in everyday routine work in obstetrics, including premature rupture of the

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membranes. The study was approved by the local ethics committee for Upper Austria.

## Materials and methods

This retrospective cohort study conducted at Kepler University Hospital, Linz, Austria, included women in whom labor was induced at ≥36 + 0 gestational weeks. Following the approval of the misoprostol vaginal insert in April 2014, an interval of 1 month was set between the two cohorts included, in order to allow time for the new agent to have been fully integrated into everyday routine work. The analysis periods were therefore set as 1 December 2013 to 30 April 2014 for the dinoprostone cohort (the D group) and 1 June 2014 to 31 October 2014 for the misoprostol cohort (the M group). The patients were selected by searching the hospital's electronic database using the Medical Process Assistant program (MPA®; Systema Human Information Systems Ltd., Steyr, Austria) for cases involving 'induction of labour'.

Patients were excluded in cases of fetal malpresentation; previous cesarean delivery or a history including other causes of uterine scarring; premature rupture of the membranes 24 h or more before the start of treatment or <36 + 0 gestational weeks; severe preeclampsia; body mass index >50; and if the dataset was incomplete. Gestational age was assessed on the basis of the last menstrual bleeding and was corrected in accordance with the crown–rump length if necessary.

Patients received vaginal inserts either with 10 mg dinoprostone or 200 μg misoprostol, which were placed in the posterior vaginal fornix, with a water-soluble gel being used if needed. Following Wing et al. [7], the vaginal insert was removed having three or more contractions within 10 min, lasting 45 s or longer, and of moderate or better quality, resulting in cervical change or leading to a dilation of 4 cm with any frequency of contractions, or after completion of the 24-h dosage period. If there was premature rupture of the membranes, labor was induced if there were no contractions within 12 h. Intravenous antibiotics were started 12 h after premature rupture of the membranes, or immediately if a group B streptococcal smear test was positive or had not been carried out before 37 gestational weeks. In both groups, an interval of at least 30 min was set between the removal of the vaginal insert and the start of intravenous oxytocin administration according to the prescribing information. Cervical balloons for cervical ripening were not used in this study.

The baseline demographic data and characteristics collected included maternal age, body mass index, parity, membrane status, gestational age, gestational diabetes and the modified Bishop score ([8], Fig. 1), evaluated at the time of vaginal insert placement. Each patient underwent at least 20 min of cardiotocographic assessment to record the fetal status and confirm that there was no uterine pattern of active labor. The time and mode of delivery (vaginal, cesarean, instrumented vaginal) were recorded.

The primary target parameter was the rate of vaginal delivery within 24 h. Further target parameters were: the time from placement of the vaginal insert to vaginal delivery; the time from placement of the vaginal insert to delivery; the time from placement of the vaginal insert to the onset of labor; the rate of emergency cesarean deliveries due to an abnormal fetal heart rate pattern (non-reassuring fetal status) within 24 h of placement of the insert; the proportion of women requiring predelivery oxytocin; the rate of fetal scalp blood sampling; the rate of tocolysis to treat fetal heart rate abnormalities and/or tachysystole; and the rate of peridural anesthesia. Tachysystole was defined, following Wing et al. [7], as five or more contractions within 10 min, averaged over three consecutive 10-min periods.

To assess the outcome for the neonate, the rates of 5-min Apgar score <7, umbilical artery pH <7.1, and umbilical artery base excess ≤12 mmol/L were obtained.

### *Statistical analysis*

All datasets for quantitative variables were checked for normal distribution (using the Kolmogorov–Smirnov test with Lilliefors significance correction, type I error = 10%). Variables with normally distributed datasets were compared between the two cohorts (dinoprostone versus misoprostol) using the *t*-test for independent samples; otherwise, the exact Mann–Whitney *U* test was used. Categorical variables were compared using either Fisher's exact test or the exact chi-squared test (with provision of adjusted residuals).

To investigate predictive factors for benefit in terms of a favorable result after the induction of labor, logistic regression analysis (stepwise forward and backward, based on the likelihood ratio approach) was carried out using any of the following dependent variables: medication (dinoprostone or misoprostol), age, BMI, gestational week, parity, modified Bishop score and premature rupture of the membranes.

The type I error was not adjusted for multiple testing. The results of the inferential statistics are therefore only descriptive.

| Points | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| Effacement (cm) | 2 | 1 | ½ | 0 |
| Consistency | Firm | Medium | Soft | |
| Position | Posterior | Mid | Anterior | |
| Dilatation (cm) | 0 | 1 | 2 | 3 |
| Station | -2 | -1 | +1 | |

According to Uhl [8]

**Fig. 1.** Modified Bishop-score.