

Rectal misoprostol vs 15-methyl prostaglandin F_{2α} for retained placenta after second-trimester delivery

Subha Sundaram, MD; John P. Diaz, MD; Víctor Hugo González-Quintero, MD, MPH; Usha Verma, MD

OBJECTIVE: The purpose of this study was to compare rectal misoprostol (RM) with 15-methyl prostaglandin F_{2α} (PGF_{2α}) for the management of retained placenta after second-trimester deliveries.

STUDY DESIGN: A retrospective study of all second-trimester deliveries between the years 2000 and 2005 was performed. Women were divided into 2 groups, depending on whether they received RM or PGF_{2α} after the delivery.

RESULTS: Three hundred three second-trimester deliveries were analyzed. The time from the administration of medications to the placental

delivery was significantly shorter in women who received PGF_{2α}, compared with the RM group (49.5 vs 89 minutes; $P < .01$). Women who received PGF_{2α} had lower rates of retained placenta (4.9% vs 12.4%; $P = .02$).

CONCLUSION: The use of PGF_{2α} after second-trimester deliveries results in shorter third stage of labor and lower rates of retained placenta compared with RM.

Key words: misoprostol, prostaglandin F_{2α}, retained placenta, second-trimester delivery

Retained placenta is a significant cause of maternal morbidity after second-trimester deliveries. Traditionally, this complication has been managed by instrumental removal and curettage with general anesthesia, which may be associated with hemorrhage, infection, and uterine perforation. Medical management to facilitate the delivery of the retained placenta is a safe alternative that avoids surgical intervention.

Prostaglandins and prostaglandin analogues (PGs) in various routes have been investigated for use in the control of postpartum hemorrhage. However, most literature that involves PGs in the

third stage of labor have focused on term pregnancies.^{1,2}

Only a limited number of studies have described the use of PGs after second-trimester deliveries.³⁻⁵

The purpose of our study was to compare the efficacy of RM and 15-methyl prostaglandin F_{2α} (PGF_{2α}) in the management of retained placenta after the delivery of the fetus in women with second-trimester deliveries.

MATERIALS AND METHODS

This retrospective study was done at Jackson Memorial Hospital/University of Miami and was approved by our institutional review board. All women between 13 and 28 weeks of gestation who had been admitted between January 2000 and January 2006 were identified and included women in spontaneous labor, preterm premature rupture of membranes, fetal death, serious fetal anomaly, and advanced cervical dilation. Maternal demographic parameters, gestational age at the time of induction, parity, indication and mode of induction, and duration of induction were abstracted. Labor for all women was induced with 200 μg of misoprostol every 6 hours for 24 hours, which was repeated if delivery had not occurred to a maximum period of 48 hours.

After the fetus was delivered, spontaneous expulsion of the placenta was

awaited for 30 minutes. At the attending physician's discretion, if the placenta did not deliver within 30 minutes, either 800 μg of misoprostol was placed rectally or 250 μg of PGF_{2α} was given intramuscularly. In patients who received PGF_{2α}, if placenta did not deliver spontaneously within the next 20 minutes after the first injection, the medication was repeated up to 2 more injections at 20-minute intervals. The RM was not repeated in any of the patients. If the placenta was undelivered up to 2 hours after the delivery of the fetus, the retained placenta was diagnosed, and instrumented removal or curettage with anesthesia was performed. Women were divided into 2 groups, depending on whether they received rectal misoprostol (RM) or PGF_{2α}.

The primary outcomes that were measured included the time from the delivery of the fetus to the administration of medication, the duration of third stage of labor, and the rates of retained placenta that required intervention. The *duration of induction* was defined as the time from the administration of the misoprostol to the delivery of the fetus. The *third stage of labor* was defined as the time from the delivery of the fetus to the time of placental delivery, either spontaneously or by instrumental removal. *Instrumental removal* was defined as the removal of the placenta with a ring forceps

From the Department of Obstetrics and Gynecology, University of Miami, Miller School of Medicine, Miami, FL.

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Reprints: Usha Verma, MD, Department of Obstetrics and Gynecology, University of Miami, Miller School of Medicine, PO Box 016960, Miami, FL 33136.
uverma@med.miami.edu.

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TABLE 1
Maternal demographics

Variable	RM (n = 161)	15-methyl PGF _{2α} (n = 142)	P value
Age (y) ^a	29.8 ± 4.5	29.0 ± 5.3	.189
Gestational age (wk) ^a	19.6 ± 2.8	19.0 ± 3.2	.104
Nulliparity (%)	74	72	.867
Previous cesarean delivery (%)	5.2	4.6	.816
Twins (%)	2.4	3.1	.702

^a Data are presented as mean ± SD.

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or curettage with general or regional anesthesia.

Descriptive statistics were obtained for all variables. Continuous variables were analyzed with the Student's *t*-test. Categorical variables were analyzed with the χ^2 test. Statistical analysis was done by means of the Statistical Packages for the Social Sciences (SPSS-PC, version 13.0; SPSS Inc, Chicago, IL). A probability value of < .05 was considered to be statistically significant.

RESULTS

A total of 335 second-trimester deliveries were available for study: 161 women received RM, and 142 women received PGF_{2α} in the third stage. Thirty-two women were excluded from analysis for the following reasons: failed induction, delivery of the fetus and placenta together, delivery of the placenta 30 minutes within expulsion of the fetus, and missing data. Twelve of the 32 women had delivered

the placenta within 30 minutes of the delivery of the fetus and were not eligible for treatment.

Table 1 shows the demographic features of the study population. There were no significant differences between the RM and PGF_{2α} groups, respectively, in indications for delivery: fetal death (59% vs 61%), fetal anomaly (26% vs 24%), preterm premature rupture of membranes at < 24 weeks of gestation (10% vs 11%), advanced cervical dilation (4% vs 3%), and maternal indication (1% vs 1%). All of the pregnancies between 24 and 28 weeks of gestation were terminations of pregnancy for fetal deaths.

Table 2 shows the outcome measures. Although the duration of induction and the time from delivery of the fetus to medication were similar, women in the PGF_{2α} group had a shorter third stage of labor and lower rates of instrumental removal of placenta.

TABLE 2
Outcome measures

Variable	RM (n = 161)	15-methyl PGF _{2α} (n = 142)	P value
Duration of induction (h) ^a	16.1 ± 3.2	16.5 ± 3.5	.629
Time from delivery of fetus to medication (min) ^a	34.5 ± 4.3	35 ± 4.1	.533
Time from initiation of medication to placental delivery (min) ^a	89.1 ± 17.8	49.5 ± 17.4	< .01
Retained placenta at 2 hr that required instrumental removal (%)	12.4	4.9	.02

^a Data are presented as mean ± SD.

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COMMENT

Our study found that the PGF_{2α} group delivered, on average, 14 minutes after the drug was administered; the RM group required, on average, 54 minutes until the delivery of the placenta. Carlan et al⁴ reported a reduction in the third stage of labor with PGF_{2α} compared with placebo. Leader et al⁵ reported that serial oral misoprostol of 200 μ g every hour for a maximum of 2 doses did not reduce the time to spontaneous placental delivery. Li and Yin³ reported 100% success with the use of 800 μ g of RM in the delivery of the placenta. However, their study involved only 8 women who underwent medical termination of pregnancy in their second trimester.

In our study, we noted a significant reduction in the number of women who required instrumental removal of placenta in the PGF_{2α} group. Although the exact mechanism of the superior efficacy of PGF_{2α} over RM is not clear exactly, we speculate that it may be related to pharmacokinetics of rectal administration. Meckstroth et al,⁶ in their study on drug absorption of misoprostol that was administered by various routes found that, after rectal administration, the serum levels peaked earlier, then dropped more abruptly, and that the peak tone and peak uterine activity were lower than other routes. Also, our rates of retained placenta after second-trimester deliveries were lower (4% in the PGF_{2α} group and 12% in the RM group), compared with the rates quoted by other authors. Leader et al⁵ had reported a higher incidence (26%) of curettage in their study.

There is no consensus about the optimal time for instrumental removal in a woman with retained placenta who does not experience bleeding complications. Kirz and Hang⁷ have suggested that expectant management of the third stage of labor beyond 30 minutes may produce increased complication rates, such as hemorrhage. However, we did not notice an increase in complications with expectant management up to 2 hours.

In summary, we conclude that use of PGF_{2α} for retained placenta after second-

trimester deliveries results in shorter third stage of labor and reduced rates of instrumented removal, compared with RM. ■

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