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Dinoprostone priming of the cervix prior to termination of midgestation pregnancy with sulprostone

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Abstract

Objective: To determine if cervical ripening with the prostaglandin E_2 analogue dinoprostone effectively shortens the induction-to-delivery interval in midpregnancy terminations with sulprostone. *Study design:* We retrospectively studied 100 women admitted for pregnancy termination at midgestation because of fetal anomalies between September 1989 and January 1993. Three regimens were used: 27 women received intramuscular sulprostone only, 29 women received intravenous sulprostone only, and 44 women received intravenous sulprostone after cervical priming with dinoprostone. Wilcoxon's rank sum test was used for statistical analysis. *Results:* Dinoprostone priming did not significantly reduce the induction-to-delivery interval in either parous or nulliparous women. However, when divided into first and subsequent pregnancies, we found that primigravidae, but not multigravidae, had an induction-to-delivery interval that was significantly shorter by approximately 10.5 h when pretreated with dinoprostone. *Conclusion:* Dinoprostone priming of the cervix prior to termination of midgestation pregnancy with sulprostone (Nalador) effectively shortens the induction-to-delivery interval in women in their first pregnancy.

Keywords: Sulprostone; Prostaglandin; Second trimester abortion; Pregnancy termination; Dinoprostone; Midgestation termination

1. Introduction

Termination of second trimester pregnancy for fetal anomalies is commonly carried out in Europe with the use of the prostaglandin analogue, 16-phenoxy-17,18, 19,20 tetranor PGE_2 methylsulphonamide (sulprostone, Nalador®). Sulprostone can either be given as continuous intravenous infusion or by repeated intramuscular injections. Because continuous intravenous infusion is easier to control, produces less side effects and requires a lower total dose, continuous intravenous infusion has replaced intramuscular injections in recent years [1].

Cervical application of prostaglandin E_2 (dinoprostone, Cerviprost®) has been used both for ripening of the cervix prior to induction of labour at term [2] and prior to first trimester termination of pregnancy [3]. Based on the idea that intracervical dinoprostone might facilitate termination of second trimester pregnancy with the use of sulprostone, and some encouraging earlier reports [4–6], patients who were admitted for termination of midgestation pregnancy with sulprostone were routinely pretreated with dinoprostone at our Department of Gynaecology from July 1991 onwards.

To evaluate if priming of the cervix with dinoprostone indeed effectively shortens the time to delivery of the fetus after the initiation of sulprostone administration, we retrospectively analysed the data of women admitted for termination of pregnancy.

2. Materials and methods

In a retrospective study we analysed the data of 100 consecutive women who were admitted for termination of pregnancy on the basis of structural and chromo-

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somal fetal anomalies at the University Hospital, Rotterdam. In the period from September 1989 to January 1993, three different regimens were used in a more or less chronological order: (1) Repeated intramuscular injections of sulprostone, at the rate of one injection of 500 μg every 4 h for 24 h, followed by a sulprostone-free interval of 24 h. This regimen was repeated until delivery; (2) Continuous intravenous infusion of sulprostone at the rate of 2 μg/min for 24 h, followed by a sulprostone-free interval of 24 h. This regimen was repeated until delivery; (3) Continuous intravenous infusion of sulprostone identical to Regimen 2 was initiated 12–16 h after a single intracervical dose of 0.5 mg dinoprostone, if the patient had not delivered within that time.

We studied the interval between initiation of sulprostone therapy and the expulsion of the fetus for the three regimen groups. We performed two analyses: one based on a division according to parity and one based on a division into primigravidae vs. multigravidae. We report median values and ranges, and we used the Wilcoxon's rank sum test and the Chi-square test for statistical analysis. A P-value of <0.05 was taken as the level of significance.

3. Results

A total of 100 women were admitted to the University Hospital, Rotterdam, for termination of midgestation pregnancy after diagnosis of a congenital anomaly of the fetus. From September 1989 until July 1991, Regimen 1 or 2 were used in 56 of these patients, 19 nulliparae and 37 parae; from July 1991 until January 1993 Regimen 3 was used in 44 patients, 22 nulliparae and 22 parae. All patients who underwent termination delivered vaginally without major side effects of the medication, or any other major complication.

Table 1 shows the differences in gestational age and interval between the initiation of sulprostone treatment and delivery, according to parity and regimen. There were no significant differences in gestational age between subgroups. The induction-to-delivery interval was lower in parous than in nulliparous women (by approximately 8.5 h). The difference in interval between parous and nulliparous women was significant in the women treated with sulprostone only (approximately 10 h), but not in those women pretreated with dinoprostone (approximately 4.5 h). In the dinoprostone pretreated group two women (one nullipara and one para) delivered before sulprostone induction was initiated. Although the women who were pretreated with dinoprostone tended to have shorter intervals than the women who were treated with sulprostone only (by approximately 8 h for nulliparae and 2 h for parae), these differences were not significant, both compared to sulprostone i.v. only and to sulprostone i.v. and i.m. combined, due to marked variation between individuals.

Of the total group of 41 nulliparae, 31 were primigravida at the time of pregnancy termination and 10 were in their second or subsequent pregnancy. Of these women, one had a spontaneous abortion plus dilatation and curettage, four women had an elective abortion through vacuum curettage, one woman had a previous midgestation termination with sulprostone; the other women had a history of a combination of these.

Table 2 shows the differences in gestational age and induction-to-delivery interval, according to gravidity and regimen. There were no significant differences in gestational age between subgroups. The induction-to-delivery interval was significantly shorter in multigravidae than in primigravidae by approximately 7 h. The difference in interval between multigravidae and primigravidae was significant in the women treated with sulprostone only (approximately 10 h), but not in those

Table 1
Differences in gestational age and the interval between initiation of sulprostone treatment and delivery, for nulliparae and parae

	Sulprostone i.m.	Sulprostone i.v.	Dinoprostone + sulprostone i.v.	Total
Nulliparae				
Number	9	10	22	41
Gestational age (weeks)	18 5/7 (15 6/7–23 0/7)	18 0/7 (14 1/7–22 5/7)	19 2/7 (15 0/7–23 2/7)	19 0/7 (14 1/7–23 2/7)
Interval to delivery (h)	23.25 (9.38–47.08)	23.63 (8.92–70.83)	15.58 (0.00–88.17)	21.00 (0.00–88.17)
Parae				
Number	18	19	22	59
Gestational age (weeks)	18 4/7 (13 4/7–21 0/7)	18 6/7 (15 6/7–23 0/7)	18 4/7 (14 0/7–22 5/7)	18 5/7 (13 4/7–23 0/7)
Interval to delivery (h)	13.92* (3.25–42.58)	12.92* (5.25–62.75)	11.00 (0.00–71.50)	12.55* (0.00–71.50)

Median value with ranges in brackets.
*$P < 0.05$ compared with nulliparae. No significant differences between treatment groups.

Table 2
Differences in gestational age and the interval between initiation of sulprostone treatment and delivery, for primigravidae and multigravidae

	Sulprostone i.m.	Sulprostone i.v.	Dinoprostone + sulprostone i.v.	Total
Primigravidae				
Number	8	8	15	31
Gestational age (weeks)	18 5/7 (15 6/7–23 0/7)	18 5/7 (15 0/7–22 5/7)	19 2/7 (15 0/7–23 2/7)	19 0/7 (15 0/7–23 2/7)
Interval to delivery (h)	23.13 (9.38–47.08)	24.67 (8.92–70.83)	14.00* (0.00–88.17)	19.75 (0.00–88.17)
Multigravidae				
Number	19	21	29	69
Gestational age (weeks)	18 4/7 (13 4/7–21 0/7)	18 5/7 (14 1/7–23 0/7)	18 6/7 (14 0/7–23 0/7)	18 5/7 (13 4/7–23 0/7)
Interval to delivery (h)	14.33** (3.25–42.58)	12.92** (5.25–62.75)	13.00 (0.00–71.50)	13.00** (0.00–71.50)

Median value with ranges in brackets.
*$P < 0.05$ compared with sulprostone only.
**$P < 0.05$ compared with primigravidae.

women pretreated with dinoprostone (approximately 1 h). In the dinoprostone pretreated group, two women (one primigravida and one multigravida) delivered before sulprostone induction was initiated. In primigravidae who received pretreatment with dinoprostone, the induction-to-delivery interval was significantly reduced (by approximately 10.5 h) as compared to women who received sulprostone only, both compared to sulprostone i.v. only and to sulprostone i.v. and i.m. combined. In multigravidae, pretreatment with dinoprostone did not result in a significant reduction of the induction-to-delivery interval.

Seventy-eight women, 28 of 41 nulliparae (68%) and 50 of 59 parae (85%), 21 of 31 primigravidae (68%) and 57 of 69 (83%) multigravidae, delivered within 24 h after initiation of sulprostone treatment. A significantly higher percentage of nulliparous women delivered <24 h after initiation of sulprostone treatment following dinoprostone priming (18/22, 82%) than without priming (10/19, 53%). Similarly, a significantly higher percentage of primigravidae delivered <24 h after initiation of sulprostone priming (13/15, 87%) than without priming (8/16, 50%). Dinoprostone priming had no significant effect on the chance to deliver <24 h after the initiation of sulprostone treatment in parae and multigravidae.

4. Discussion

If it is necessary to terminate a pregnancy in midgestation, it is desirable that the technique of termination is optimally effective, with minimal side effects. Therefore, the duration of hospital admission and the interval from initiation of treatment to delivery should be as short as possible. In addition, a recent study has shown that an infusion rate of sulprostone half that of which was used in the present study is also effective [1]. Although the intramuscular route of sulprostone is no longer used because of the risk of overdosage, our study shows that intramuscularly and intraveneously administered sulprostone are equally effective.

In term pregnancies, ripening of the cervix with locally applied prostaglandin E_2 facilitates induction of labour and reduces the induction-to-delivery interval [2]. It is not well known whether this also applies to midterm pregnancy. Several investigators have attempted to improve upon the technique of midgestation termination with the use of prostaglandins, and report a favorable effect of pretreatment either through vaginal application of prostaglandin E_2 tablets [4] or cervical application of sulprostone gel, prostaglandin E_2 or $F_{2\alpha}$ gel [5,6]. However, these studies all lack a control group, which limits their importance.

We found that the induction-to-delivery interval after sulprostone in midgestation is much shorter in multigravidae and parae compared to primigravidae and nulliparae. Apparently, the cervix dilates more easily after it has been previously dilated. Given the already short induction-to-delivery interval in multigravidae and parae it may not be surprising that the interval is not significantly shortened any further by pretreatment of the cervix with a locally applied, but weaker, prostaglandin analogue.

Our observation that pretreatment with dinoprostone does significantly reduce the induction-to-delivery interval in primigravidae but not in nulliparae suggests that it makes little difference as to how the cervix has previously been artificially dilated. Because all of the 10 multigravidae nulliparae had experienced an artificial type of dilatation, it is uncertain to what extent a previous spontaneous abortion alone, without dilatation,

might affect the response to dinoprostone pretreatment in a subsequent pregnancy.

Although only a prospective, placebo-controlled, randomized trial can answer definitively the question to what extent cervical priming with dinoprostone shortens the induction-to-delivery interval in midpregnancy termination with sulprostone, our retrospective study strongly suggests that pretreatment with dinoprostone is indeed effective in primigravidae. When dinoprostone on this indication is administered on an outpatient basis, in primigravidae the duration of hospitalization for sulprostone termination in midpregnancy can be reduced.

References

[1] Kanhai H, Keirse M. Low-dose sulprostone for pregnancy termination in cases of fetal abnormality. Prenat Diagn 1993; 13: 117–121.

[2] Rayburn W. Prostaglandin E_2 gel for cervical ripening and induction of labor: a critical analysis. Am J Obstet Gynecol 1989; 160: 529–534.

[3] Christensen NJ, Bygdeman M, Green K. Comparison of different prostaglandin analogues and laminaria for preoperative dilatation of the cervix in late trimester abortion. Contraception 1983; 27: 51–61.

[4] Mursch G, Kassowitz C, Arzt W, Frölich H. Prostaglandine zur Schwangerschafsbeendigung im 2. und 3. Trimenon. Geburtsh u Frauenheilk 1988; 48: 893–895.

[5] Grünberger W, Husslein P. Kombinierte perizervikale und intramuskuläre Prostaglandin Medikation zur Schwangerschaftsbeendigung im II. und III. Trimenon. Geburtsh u Frauenheilk 1983; 43: 240–244.

[6] Rath W, Ulbrich R, Kuhn W. Zervixreifung und Wehenindukton beim Schwangerschaftsabbruch im mittleren und späten II. Trimenon mittels intrazervikaler und extraamnialer Prostaglandingel Applikation. Wien Klin Wochenschr 1985; 97: 486–493.