Early induction of labor with PGE_2-intravaginal gel in premature rupture of membranes

E. Sturlese[1], A. Tripodi[1], G. Retto[1], A. Pulia[1], D. A. La Gamba[1], L. Tripodi[2]

[1]Gynecology & Obstetrics Clinic, Department of Medicine & Surgery;
[2]Specialization School of Pharmacology, Dept. of Pharmacology, University of Messina (Italy)

Summary

Results of induction of labor with PGE_2-intravaginal gel in PROM, were evaluated considering the best management.

Key words: PROM; PGE_2-intravaginal gel.

Introduction

Premature rupture of the membranes (PROM) during term pregnancy or near term occurs fairly frequently (10%); nonetheless, management of such event has not been well documented in the literature.

Indeed, there is no agreement between physicians who use rapid induction and those who instead prefer to wait for spontaneous labor, especially in patients with an unfavorable local condition (Bishop score <5) which occurs in about 45% of cases.

There are studies in which waiting is justified in that 60-70% patients with PROM have spontaneous labor within 24 successive hours. In these cases waiting, besides not being correlated with an increased incidence of maternal-neonatal infections, should lead to a reduction in the percentage of cesarean sections due to failure of induction.

In contrast, other authors argue that waiting has no significant effect on the percentage of cesarean sections and involves an increased risk of infective complications. The use of PGE_2-intravaginal gel for the induction of labor in these patients was drastically limited a few years ago, and still today, by the "contra indications" specified by drug manufacturers [1, 2].

However after the publication of the first four randomized studies, PGE_2 has been used increasingly more frequently by those who over the course of years have experience and better familiarity with the usage of such drug. Moreover, the formulation "gel" is better accepted by pregnant women both because it allows the patient to walk within half an hour of application and because contractions, analogous to what happens in spontaneous labor, appear with progressive intensity [3]. Consequently, in the Gynecology and Obstetrics Clinic of the University of Messina, 358 patients with PROM underwent early induction with PGE_2-intravaginal gel. The results of induction were evaluated by taking into consideration patient parity (nulliparous vs. pluriparous) and the more or less favorable local condition (Bishop score > 5 vs. Bishop score < 5).

Revised manuscript accepted for publication April 2, 2001

Materials and Methods

From January 1998 to May 2000, 358 patients with PROM were recovering at the Gynecology and Obstetrics Clinic of the University of Messina; all had reached a gestational age of greater than 35 weeks.

In 75 (20.9%) induction of labor was spontaneous within six hours after rupture of the amnio-chorio membrane; the remaining 283 patients were induced by administration of 1 mg of PGE_2-intravaginal gel after having evaluated the Bishop score, doing a cardiotocography for at least 30 min and giving antibiotic prophylaxis.

In the final phase of labor (birth period) all the patients were able to tolerate the intravenous infusion of oxytocin (5 IU in 500 ml Na Cl solution).

Until regular reliable contractions started, another application of 2 mg of PGE_2 could be given at 4-hour intervals for a maximum of two times.

In our study we did not use oxytocin during the early phase of labor. Patients were excluded from the study if they had compromised cardiovascular, hepatic or renal functions, asthmatic conditions, glaucoma, fetal-pelvic disproportion, prior uterine surgical interventions, previous difficult and/or traumatic labor, were multiparous (5 or more pregnancies at term), had non cephalic presentation of the fetus, prostaglandin hypersensitivity, presence of vaginal hematic loss hidden during pregnancy, twin familiarity or fetal distress.

Statistical analysis was carried out with the Student's t-test and chi-square test.

Results

The clinical characteristics of the patients are reported in Table 1. By looking at Table 2 it can be seen that in 25.5% of treated patients it was necessary to administer a second dose of gel and that the percentage of cesarean sections was on average 5%; in detail five had fetal distress and ten missed outlet engagement. The percentage of cesarean sections was halved – from 6% to 3% – if the number of gel applications is considered (Table 2).

The mean time interval between the first administration of gel and delivery was 4 hrs, 40 mins ± 1 hr, 30 mins. If these data are analyzed more in depth it can be observed that the majority of births (85%) occurred in the first six hours and that the incidence of cesarean section was very

Table 1. — *Clinical characteristics of examined women.*

	No. of patients	%
Pluriparous	90	32
Nulliparous	193	68
Patients with Bishop score < 5 during PROM	168	59
Patients with Bishop score > 5 during PROM	115	41

Table 2. — *Number of applications of PGE_2-gel and type of birth.*

	Patients	Spontaneous births	Cesarean sections
1st application of gel (1 mg)	211 (74.5%)	198 (94%)	13 (6%)
2nd application of gel (2 mg)	72 (25.5%)	70 (97%)	2 (3%)

high (5%) in the group of women who gave birth within six hours while in the second group the decrease is statistically significant (7%, Table 3).

As is known, during PROM the factors that influence the successful induction are patient's parity and local condition (Bishop score). Consequently we have compared nulliparous with pluriparous patients and those with a favorable (> 5) vs. unfavorable Bishop score (< 5).

By examining Table 4, as could be predicted, the majority of the pluriparous women (94%) gave birth after one single application of gel while the nulliparous patients required a second application in 36% of the cases. The mean time interval between induction and delivery was significantly longer in the nulliparous women and in those with an unfavorable Bishop score. This group required a greater number of applications of vaginal gel. Moreover, the mean time interval between induction and birth was also longer in patients with an unfavorable Bishop score with respect to those patients whose general condition was more favorable; indeed, the former group gave birth in a time interval which was much longer with respect to that of women with a more favorable local condition (Table 5).

Table 3. — *Time interval between induction and birth.*

Time	No. of spontaneous births	No. of cesarean sections
< 6	228 (85%)	13 (5%)
> 6 < 12	40 (15%)	2 (7%)

Table 4. — *Type of birth induction in relation to parity.*

	Patients	
	Nulliparous (No. 193)	Pluriparous (No. 90)
1st application of gel (1 mg)	64%	94%
2nd application of gel (2 mg)	36%	6%

Table 5. — *Type of birth induction in relation to the Bishop score.*

	Bishop score < 5 (No. 168)	Bishop score > 5 (No. 115)
1st application of gel (1 mg)	57%	100%
2nd application of gel (2 mg)	43%	–

The incidence of cesarean section was significantly higher in women with a Bishop score < 5. If we consider at the same time both parity and local condition we can see that the incidence of cesarean sections increased in the nulliparous women with an unfavorable bishop score but was not statistically significant. As was expected, the nulliparous women with an unfavorable general condition had a clearly longer mean time interval between induction and delivery. It was a different case for the pluriparous group whose time between induction and birth was not different; this depended on the patient's local condition at the start of induction.

Conclusions

Up to today there is no unequivocal protocol on the management of PROM; randomized studies done for this purpose have led to completely opposite conclusions: in some studies waiting was indicated as the most advantageous procedure with a halving of the percentage of cesarean sections. Other studies instead have shown that a better choice is to induce labor six hours after PROM; according to these authors waiting longer than this can cause a significant increase in the incidence of maternal-neonatal complications without any difference in the number of cesarean sections performed. On the contrary the time interval between PROM and delivery is considerably shorter in women who undergo rapid induction [4].

In our study we collected data on a quite high number of early-induced patients after PROM using exclusively intravaginal PGE_2 gel. From the data in the literature it comes out that with waiting 60.7% of women with PROM give birth within 24 hours however in our study 94% of the patients gave birth within 12 hours [5]. It seems therefore evident that waiting represents a losing tactic with respect to rapid induction with vaginal PGE_2, not only because patient compliance is improved but also because a considerable reduction in health costs can be obtained – rapid induction implies that in 30-40% of cases the hospital stay will be shorter by one day.

Moreover, in our protocol (application of gel every 4 hrs), we observed an incidence of cesarean sections of less than 6% which is half of that reported in the literature [6]. Nonetheless, in agreement with the literature, our study also found pluriparity and a favorable Bishop score during PROM to be positive prognostic factors for successful induction.

We had no infective complications in our study in mothers or babies; this is probably also due to our protocol which already established the immediate use of antibiotic prophylaxis. In our opinion, another important factor was that induction with vaginal PGE_2 allows optimal compliance for patients in that they can walk after 30 minutes of the application of gel. Moreover, possible complications due to a prolonged supine position during labor are reduced to a minimum.

Our experience shows that in cases of PROM early induction with vaginal PGE_2 allows a rapid birth without infective maternal-neonatal complications and with a low

incidence of cesarean sections, especially in pluriparous patients with a favorable local condition. Neonatal outcome has been very satisfactory with an average neonatal weight of 3,165 g ± 400 g with an Apgar score of > 7 at 5 minutes.

References

[1] Mead P. B.: "Management of the patient with premature rupture of the membranes". *Clin. Perinatal.*, 1980, *7*(2), 243.

[2] Harris A. S., Stemberg P., Ulmstein U.: "A study of the in vitro release profile of a new PGE_2 delivery system for local administration in obstetrics". *Acta Obstet. Gynecol. Scand. Supp.*, 1983, *113*, 59.

[3] Grant J. M., Serle E., Mahmood T., Sarmandal P., Conway D. I.: "Management of prelabour rupture of the membranes in term primigravidae: report of a randomized prospective trial". *Br. J. Obstet. Gynaecol.*, 1992, *99*(7), 557.

[4] Duff P., Huff R. W., Gibbs R. S.: "Management of premature rupture of membranes and unfavorable cervix in term pregnancy". *Obstet. Gynecol.*, 1984, *63*(5), 697.

[5] Mahmood T. A., Dick M. J., Smith N. C., Templeton A. A.: "Role of prostaglandin in the management of prelabour rupture of the membranes at term". *Br. J. Obstet. Gynaecol.*, 1992, *99*(2), 112.

[6] Ray D. A., Garite T. J.: "Prostaglandin E2 for induction of labor in patients with premature rupture of membranes at term". *Am. J. Obstet. Gynecol.*, 1992, *166*(3), 836.

Address reprint requests to:
A. TRIPODI, M.D.
Via Carcere Nuovo, 16
89133 Reggio Calabria (Italy)