A Randomized Comparison of Prostaglandin E_2, Oxytocin, and the Double-Balloon Device in Inducing Labor

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Objective: **To compare the efficacy of three methods for ripening and dilating the unfavorable cervix for induction of labor.**

Methods: **Pregnant women having an indication for induction of labor with a singleton vertex fetus, intact membranes, and Bishop score of no more than 4 were randomized to one of three induction methods: intravaginal prostaglandin (PG) E_2 tablets (3 mg) followed by a second dose if labor did not start; continuous intravenous oxytocin drip; or the Atad Ripener Device, with inflation of both balloons and removal after 12 hours. For all patients, the cervix was assessed by the same investigator before induction and 12 hours later.**

Results: **Thirty subjects were included in the PGE_2 group, 30 in the oxytocin group, and 35 in the Atad Ripener Device group. The postpartum course was comparable in all. The change in Bishop score in the PGE_2 and Atad Ripener Device groups was significantly better than in the oxytocin group (median and range of 5 [0–9] and 5 [0–7], respectively, versus 2.5 [0–9]; $P < .01$). Cervical dilation more than 3 cm was more frequent in the Atad Ripener Device group compared with both the PGE_2 and oxytocin groups (85.7 versus 50 and 23.3%, respectively; $P < .01$). The trial of induction failed in only two patients (5.7%) in the Atad Ripener Device group, compared with six (20%) in the PGE_2 and 16 (53.3%) in the oxytocin groups ($P < .001$). Mean (± standard deviation) induction-to-delivery interval was 21.3 ± 7.0 hours in the Atad Ripener Device group, 23.2 ± 12.5 hours in the PGE_2 group, and 28.2 ± 14.7 hours in the oxytocin group. The success rate for vaginal delivery was significantly better in the Atad Ripener Device and PGE_2 groups compared with the oxytocin group (77.1 and 70%, respectively, versus 26.7%; $P < .01$).**

Conclusion: **The Atad Ripener Device had a significantly better success rate for cervical dilation and a lower failure rate than those for PGE_2 and oxytocin. The PGE_2 and Atad Ripener Device groups had better results than the oxytocin group in regard to Bishop score change and induction-to-delivery interval. The Atad Ripener Device may be a superior method for cervical ripening and labor induction in patients with unfavorable cervices.** *(Obstet Gynecol 1996;87: 223–7)*

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Induction of labor remains one of the therapeutic challenges in obstetrics. The success of induction depends on the cervical status at the start of the induction process.[1,2] Induction of labor in the presence of an unripe cervix results in a longer labor and a higher incidence of cesarean delivery and fetal asphyxia.[3] Various methods of cervical ripening have been developed to improve the chance of successful labor induction.[4–10] The use of intravenous (IV) infusion of oxytocin and intravaginal or intracervical administration of prostaglandin (PG) E_2 are considered to be the two acceptable methods for labor induction. However, in the presence of an unripe cervix, oxytocin is associated with a prolonged induction period, a significant failure rate, and considerable patient discomfort.[4,5] At present, the most commonly used method for these patients is intravaginal application of PGE_2.[6] However, systemic absorption of this agent is possible and may result in nausea, vomiting, and initiation of uterine contractions that may last for prolonged periods and lead to uterine hypertonicity, placental abruption, and uterine rupture.[11,12] We believe that this may expose the fetus, which may already be compromised by the original indication for labor induction, to extra risk.

Financial Disclosure

Jack Atad, MD, has a patent-licensing arrangement with Emerand Ltd. of Rehovot, Israel, for the Atad Ripener Device and thus has the potential for financial gain from its sales. Emerand Ltd. provided no financial support for this study, nor did it provide the devices used.

0029-7844/96/$15.00 223
SSDI 0029-7844(95)00389-4

A newly developed double-balloon device (Atad Ripener Device; MR&D, Emerand Ltd., Rehovot, Israel) has been introduced to ripen the cervix by mechanical means without causing uterine contractions. Previously, we reported our experience with 50 cases and found this method of induction of labor to be effective and safe.[13] In the last several years, we have gained more experience using this method and have reported in abstract form on 250 patients (Atad J, Ben-David Y, Hallak M, et al. Ripening and dilation of the unfavorable cervix for induction of labor by a double balloon device: A non-pharmaceutical method [abstract]. Am J Obstet Gynecol 1993;168:429). This additional experience confirmed our previous results. The objective of this randomized study was to compare the efficacy of three methods for ripening and dilating the unfavorable cervix for induction of labor.

Materials and Methods

Ninety-five women with unfavorable cervices (Bishop score 4 or less) were included in this study, based on power analysis (β error = .2). This study was approved by the local institutional review board for human investigations. Indications for labor induction were pregnancy-induced hypertension (43 women), postdates pregnancy (17), diabetes mellitus (seven), elective induction (six), nonreassuring nonstress test (six), fetal growth restriction (FGR) (seven), fetal death (three), and other (six). Inclusion criteria were nonlaboring patients with singleton pregnancy, vertex presentation, and intact membranes. Exclusion criteria were placenta previa, abnormal fetal monitoring, or previous cesarean delivery. When the decision was made to induce labor, we evaluated the cervix and determined the first Bishop score. After giving informed consent, patients were assigned to one of three induction methods according to a computer-generated random list. Those assigned to intravaginal PGE_2 tablets (Upjohn s.a., Puurs, Belgium) received 3 mg; if contractions had not started or the patient did not need analgesic agents 6 hours later, a second dose of 3 mg was administered (22 of 30 patients). Those assigned to IV oxytocin received an initial dose of 1.5 mIU/minute and a constant increase of 1.5 mIU/minute every 20 minutes until three contractions in 10 minutes were achieved (as long as fetal monitoring was reassuring). The Atad Ripener Device was inserted into the cervix and both balloons were inflated with 100 mL of normal saline. The balloons were deflated and the device was removed after 12 hours. In each study arm and in all patients, the cervix was assessed by the same investigator at the start of induction and 12 hours later. Method failure was defined as a second Bishop score of no more than 4. Those subjects were crossed over to another study arm: PGE_2 and oxytocin groups had the double-balloon ripener device inserted, and the ripener device group received PGE_2.

The device was inserted according to a technique published previously.[13] With the patient in the lithotomy position, a speculum is inserted to visualize the cervix (Figure 1). Before insertion, the uterine valve tip of the device is occluded and preloaded with 20 mL of saline. Using long forceps, the ripener device is inserted into the cervix until both balloons enter the cervical canal. With the device in place, the occlusion system is removed to allow inflation of the uterine balloon, either automatically or by applying some pressure on the preloaded uterine valve tip. The device is then pulled out until stopped by the uterine balloon covering the internal cervical os. The cervicovaginal balloon located at the external os is inflated by injecting 20 mL of saline through the cervicovaginal valve. At this stage, the speculum is removed and both the uterine and cervicovaginal balloons are inflated further with alternating increments of 20 mL, up to a total of 100 mL in each balloon. The device is taped to the patient's inner thigh. After complete insertion of the device, external fetal monitoring is performed for 30 minutes, after which time the patient's activity is not restricted.

In all patients for whom the Bishop score was 5 or higher, induction of labor was resumed using artificial rupture of the membranes and/or IV administration of oxytocin. Afterward, labor was managed according to obstetric criteria in all patients.

Statistical analysis of maternal age, gestational age, induction-to-delivery interval, and birth weight were compared among the three groups using analysis of variance and multiple comparison procedure (Scheffé procedure). The analysis of ordinal data, Bishop and Apgar scores, was done using Kruskal-Wallis nonparametric test. The comparison among categorical variables was performed by χ^2 test. $P < .05$ was considered statistically significant.

Results

Ninety-five subjects, 53 primiparas and 42 multiparas, were enrolled in this study. The randomization scheme was successful because there was no significant statistical difference among the three groups in regard to mean maternal age, parity, and gestational age (Table 1). Median (range) Bishop scores before induction in the PGE_2, oxytocin, and Atad Ripener Device groups were 2 (0–4), 2 (0–4), and 2 (0–4), respectively (not significant). The change in Bishop score in the PGE_2 and the Atad Ripener Device groups was significantly higher compared with the oxytocin group ($P < .01$, Table 2).

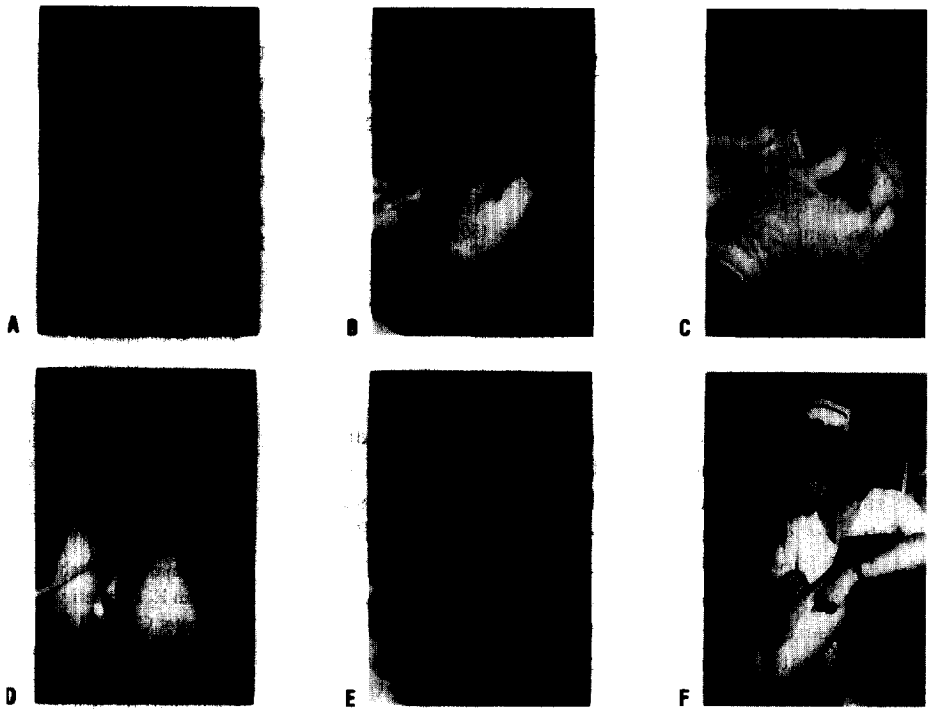

Figure 1. Insertion technique: A) pre-inflation of the uterine valve arm, B) insertion of the device, C) inflation of the uterine balloon, D) inflation of the cervicovaginal balloon, E) additional inflation of the balloons (100 mL each), F) device taped to patient's leg.

Cervical dilation more than 3 cm, as assessed after 12 hours of induction, was significantly higher in the Atad Ripener Device group compared with the oxytocin and PGE_2 groups ($P < .01$). In 20% of the PGE_2 and 53% of the oxytocin subjects, the method used primarily failed and they were crossed over to the Atad Ripener Device, whereas only 5.7% of the Atad Ripener Device group had to be crossed over to PGE_2 ($P < .001$). The induction-to-delivery interval was longer in the oxytocin group compared with the PGE_2 and Atad Ripener Device groups; however, this did not reach statistical significance. The success rate for vaginal delivery (defined as those patients limited to the initially assigned method) was also significantly higher in the Atad Ripener Device and PGE_2 groups compared with the oxytocin group ($P < .01$; Table 2). Twenty-five of all 95 patients (26.3%) underwent cesarean delivery. The distribution of the cesarean rate among the various groups is presented in Table 3. Forty-one (75.9%) of the 54 patients who primarily or finally received the Atad Ripener Device delivered vaginally, whereas 13 (24.1%) underwent cesarean delivery.

Neonatal outcome was the same for all three methods with regard to mean weight and Apgar scores at 1 and 5 minutes. Perinatal morbidity was not significantly different among the three groups.

Table 1. Demographic Data

	PGE_2	Oxytocin	ARD
No. of patients (total)	30	30	35
Primipara (% of total)	17 (56.7%)	17 (56.7%)	19 (54.3%)
Maternal age (y)	28.5 ± 5.2	27.8 ± 5.7	27.3 ± 4.2
Gestational age (wk)	38.8 ± 2.0	39.6 ± 1.7	40.0 ± 1.6

PGE_2 = prostaglandin E_2; ARD = Atad Ripener Device.
Data are presented as mean ± standard deviation.

Discussion

The results of this study demonstrate that PGE_2 and the Atad Ripener Device were significantly better than oxytocin in the induction of labor in patients with unfavorable cervices. The PGE_2 and Atad Ripener De-

Table 2. Comparison Among the Three Labor Induction Methods

Induction method	ΔBishop score: median (range)	Cervical dilation >3 cm	Method failure	Induction-to-delivery (h)	Success rate for vaginal delivery
PGE_2	5 (0–9)*	15/30 (50%)	6/30 (20.0%)	23.2 ± 12.5	21/30 (70.0%)*
Oxytocin	2.5 (0–9)	7/30 (23.3%)	16/30 (53.3%)†	28.2 ± 14.7	8/30 (26.7%)
ARD	5 (0–7)*	30/35 (85.7%)‡	2/35 (5.7%)	21.3 ± 7.0	27/35 (77.1%)*

PGE_2 = prostaglandin E_2; ARD = Atad Ripener Device.
* PGE_2 and ARD < oxytocin, $P < .01$.
† ARD and PGE_2 < oxytocin, $P < .01$.
‡ ARD > PGE_2 and oxytocin, $P < .01$.

Table 3. Cesarean Rates

	PGE_2	Oxytocin	ARD	Total
Cesarean rate in patients with method success	3/24 (12.5%)*	6/14 (42.9%)	6/33 (18.2%)*	15/71 (21.1%)
Cesarean rate in patients with method failure	1/6 (16.7%)	8/16 (50.0%)	1/2 (50%)	10/24 (41.7%)

PGE_2 = prostaglandin E_2; ARD = Atad Ripener Device.
* ARD and PGE_2 < oxytocin, $P < .05$.

vice methods were comparable in regard to the change in Bishop score, induction-to-delivery interval, and success rate for vaginal delivery. The cesarean rate was not statistically significantly different between the PGE_2 and Atad Ripener Device groups, and both rates were lower than that of the oxytocin group. As a result of the higher cesarean rate in the latter group, there was an increased rate of maternal complications, including prolonged hospitalization and febrile morbidity in this group. The Atad Ripener Device was a better method for cervical dilation and had a clinically significant lower failure rate than all other methods.

Induction of labor in patients with unfavorable cervices may be medically indicated or elective. Indicated induction is defined as the initiation of labor due to maternal or fetal indications that outweigh the benefits of continuing the pregnancy. These indications may include pregnancy-induced hypertension, postdates pregnancy, diabetes mellitus, nonreassuring nonstress test, FGR, and fetal death. Elective induction of labor, on the other hand, is defined as the initiation of labor for the convenience of an individual with a term pregnancy and who is free of medical indications.[14] The benefits of elective induction of labor may include a prearranged date of delivery to permit family care arrangements, assure physician attendance, reduce fetal risk from continuation of the pregnancy, and, usually, plan a daytime delivery.[14]

The Atad Ripener Device did not cause the side effects or patient discomfort seen in pharmaceutical methods of labor induction.[13,15] The method is safe and well tolerated by most patients, who can still be mobile while the Atad Ripener Device is in place. Our cesarean rates were low (12.5 and 18.2% for the PGE_2 and Atad Ripener Device groups, respectively) compared with rates reported (more than 30%) for patients induced with an unfavorable cervix.[16,17]

The Atad Ripener Device is a nonpharmaceutical method of labor induction. The mechanism of action can be explained by gradual mechanical cervical dilation achieved by the pressure applied on both the external and internal os by the inflated balloons. This method is especially advantageous for patients in whom prolonged uterine contractions should be avoided, such as those with placental insufficiency, FGR, and oligohydramnios. The Atad Ripener Device may also be effective for a subgroup of patients who prefer planned elective induction rather than waiting for spontaneous labor to start.[18]

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Received April 18, 1995.
Received in revised form September 25, 1995.
Accepted October 6, 1995.

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