Effectiveness of prostaglandin E2 intracervical gel (Prepidil), with immediate oxytocin, versus vaginal insert (Cervidil) for induction of labor


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of prostaglandin E2 (PGE2) to achieve cervical ripening and to shorten the duration of labour. Two regimes were compared. The first was the use of PGE2 as a intracervical gel (Prepidil) immediately followed with oxytocin. The second was the use of PGE2 as a sustained-release insert (Cervidil) with subsequent oxytocin as needed.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women at term requiring induction of labour who presented at the study centre. The criteria for entry to the study were having an unfavourable cervix (Bishops score less than or equal to 6), and being beyond 36 completed weeks' gestation. A range of 11 exclusion criteria were applied, full details of which were given in the paper.

The average age of the patients was 24.4 years. Forty-nine per cent of the patients were white and 51% were nulliparous.

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness, resources and price data all related to April 1996 to July 1997, the period during which the study was conducted.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on a representative sub-sample (approximately 60%) of the sample used for the study.

Study sample
A power calculation was undertaken on the basis of assumptions about differences in the levels of cost, induction-to-delivery time or hospital stay that would be clinically relevant. The sample size was calculated for a power of 0.8 and a significance level of 0.05.

All eligible patients presenting at the centre between April 1996 and July 1997, who were at term, requiring induction and met the entry criteria were selected.

The study sample appears to have been appropriate for the clinical study question posed. A total of 162 women were eligible and consented to enrolment. There were 12 drop-outs following randomisation, 5 from the Prepidil group and 7 from the Cervidil group. This left 77 women in the Prepidil-immediate group and 73 in the Cervidil group.

Women were excluded on the basis of vaginal bleeding, ruptured membranes, noncephalic foetal presentation, frequent contractions, prior uterine surgery, an estimated foetal weight of greater than 4,500 g, known hypersensitivity to prostaglandins, and known foetal anomaly.

**Study design**
The study was a randomised controlled trial. Randomisation was conducted according to a system of randomly mixed, sequentially numbered envelopes prepared by the hospital pharmacy. The study was conducted at a single centre, the Health Sciences Centre, University of Oklahoma, USA. The primary end point was vaginal delivery and there was no loss to follow-up. The clinicians were not blinded to the therapy, as the treatments required different times for the start of oxytocin therapy.

**Analysis of effectiveness**
The analysis was conducted on an intention to treat basis. The primary health outcomes measured were progression through delivery. These included Bishop score change at 12 hours, route of delivery (vaginal, Caesarean) and indication for Caesarean delivery.

The groups were each divided into nulliparous and multiparous sub-groups.

**Effectiveness results**
There were no statistically significant differences between the groups for any of the primary health outcomes. This result applied when the nulliparous and multiparous sub-groups were combined and when they were analysed separately.

**Clinical conclusions**
The Prepidil-immediate oxytocin regime appears to have been as safe and effective as the Cervidil method for the initiation of labour.

**Measure of benefits used in the economic analysis**
The outcome measure used in the economic analysis was the time (hours) between the initiation of therapy to vaginal delivery, the length of stay (hours) in the labour and delivery unit, and the length of hospital stay (days).

**Direct costs**
Discounting was not carried out as the costs were incurred over less than one year. The quantities were not analysed separately from the prices. The costs were estimated from actual hospital charges, which were obtained from the billing data for a sub-sample (approximately 60%) of the patients in the study. The price year was 1997.

**Statistical analysis of costs**
The costs were not treated stochastically.

**Indirect Costs**
The indirect costs were not included

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was conducted

**Estimated benefits used in the economic analysis**
The benefits were measured in terms of reduced time in labour.

The time from the initiation of therapy to vaginal delivery was 9.4 hours with Prepidil and 21.6 hours with Cervidil, (p<0.001).

The proportion of women having a vaginal delivery in 12 hours was 42% with Prepidil and 21% with Cervidil, (p<0.001).

The length of stay in the labour and delivery unit was 18 hours with Prepidil and 17.1 hours with Cervidil, (non significant).

**Cost results**
The delivery costs were $193 in the Prepidil group and $304 in the Cervidil group.

The pharmacy costs were $84 in the Prepidil group and $151 in the Cervidil group.

The total cost-savings was $458.

**Synthesis of costs and benefits**
The benefits of reduced time were translated into costs using hospital-billing information.

**Authors' conclusions**
The Prepidil-immediate oxytocin protocol was as safe and effective as the Cervidil method for inducing labour. In addition, it offered the advantages of earlier vaginal delivery and greater hospital cost-savings, regardless of parity.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparators was justified. Both technologies had approval from the FDA and were being used in favour of the conventional hospital pharmacy preparations. You should decide if the technologies represent valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis used a randomised controlled trial, which was appropriate for the study question. The study sample was representative of women presenting at the Health Sciences Centre, Oklahoma City. The patient groups were shown to be comparable at analysis, thus limiting some of the possible bias and confounding.
Validity of estimate of measure of benefit
The analysis of the benefits was based on the therapeutic equivalence of treatment alternatives. Therefore, the economic analysis only included the costs.

Validity of estimate of costs
All the categories of costs relevant to the perspective of the third-party payer were included in the analysis. The costs of infant care were excluded because the authors assumed that any cost differences would relate to unusual infant health problems, and not to the events at delivery. Time was reported separately to the costs, but the unit prices were not given. The resource use and prices were obtained from the actual hospital billing for a 60% sample of the patients included in the study. The authors acknowledged that the use of hospital charges, rather than the actual costs, might limit the generalisability of their results.

Other issues
The authors compared their results with one other study that showed that a single application of Cervidil ripened the cervix more quickly than did repeated doses of Prepidil. The authors rejected these findings on the grounds that time to delivery was not stratified by parity, that there were widely different risk factors for induction among the study patients, there were no power calculations and the sample size was half of that of their own study. The authors did not address the issue of generalisability to other settings. The results do not appear to have been presented selectively. The authors pointed out one limitation of their study, the lack of clinician blinding to therapy. However, they argued that this was mitigated by the fact that the same team was responsible for the management of all participants, with the same protocols, at the same centre. The study used a particular protocol for Prepidil use. This had been developed at the centre and was aimed at quickening delivery times. In this context, the findings confirm the time advantages of this method of Prepidil use. However, it cannot be assumed that Prepidil has similar advantages over Cervidil in other contexts.

Implications of the study
The authors suggest that, where prompt labour induction and delivery and associated cost-savings are sought, the Prepidil-immediate oxytocin protocol has advantages over Cervidil use.

Source of funding
Supported by J W Records Perinatal Research Fund.

Bibliographic details

PubMedID
9822496

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Intravaginal; Adult; Cervix Uteri; Cost-Benefit Analysis; Dinoprostone /administration & dosage /therapeutic use; Drug Therapy, Combination; Female; Gels; Humans; Labor, Induced /economics /methods; Oxytocin /therapeutic use; Parity /physiology; Pregnancy; Time Factors; Treatment Outcome

AccessionNumber
21998001790