RANDOMIZED CLINICAL TRIAL WITH ORAL PGE_2 TABLETS AND INTRAVENOUS OXYTOCIN FOR INDUCTION OF LABOUR

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By

V. HINGORANI,[1] S. NAIR,[2] D. PATEL,[3] P. MISRA,[4] N. CHOUDHRY,[5] G. I. DHALL,[6] R. V. BHATT,[7] B. PALLIANAPPAN,[8] U. SUTARIA,[9] M. KOCHAR,[10] R. BAVEJA,[11] I. KAMBO,[12] S. GUPTA,[12] A. NAIR,[12] N. C. SAXENA[12] AND *B. N. SAXENA

SUMMARY

Oral tablets of Prostaglandin E_2 (PGE_2) and Intravenous oxytocin (I/V oxytocin) were used to induce labour in 900 pregnant women with gestation of 37 weeks or more. The dose of Oral PGE_2 tab. was 0.5 mg administered hourly up to a maximum period of 18 hrs, and that of Intravenous oxytocin was 2 I.U. (international Units) in 500 ml of 5 per cent glucose. The total dose of oxytocin was not to exceed 4 I.U. No significant difference was noticed in the side effects with these two drugs. The success rate for induction of labour was 74.5 and 78.9 per cent in women treated with Oral PGE_2 tablets and I/V oxytocin respectively. This difference was not statistically significant.

Introduction

Induction of labour with intravenous oxytocin as presently available, although of great clinical usefulness, has been found to be associated with uterine hypertonus and foetal bradycardia. Furthermore there is a possibility of water retention if I/V oxytocin is used for induction of labour in women in whom pregnancy is associated with Eclampsia, Hypertension, Heart and kidney disease. Prostaglandins administered orally, intramuscularly or intravenously has been found to be effective in stimulating the uterus. The efficacy of PGE_2 administered orally either as capsules or liquids has been found to be similar.

[1] *All India Institute of Medical Sciences, New Delhi.*

[2] *SAT Medical College, Trivandrum.*

[3] *Nowrosjee Wadia Maternity Hospital, Bombay.*

[4] *S.P. Medical College, Bikaner.*

[5] *S.S.K.M. Hospital, Deptt. of Obstet. Gynaecology, Calcutta.*

[6] *Postgraduate Institute of Medical Education, and Research Chandigarh.*

[7] *Medical College and S.S.G. Hospital, Baroda*

[8] *Kilpauk Medical College and Hospital, Madras.*

[9] *B.J. Medical College, Pune.*

[10] *Kasturba Gandhi Hospital, Delhi.*

[11] *M.L.N. Medical College and Kamla Nehru Hospital, Allahabad.*

[12] *Central Coordinating Unit, Indian Council of Medical Research, New Delhi.*

[*] *Project co-ordinator.*

From: Division of Human Resource Development Research Indian Council of Medical Research, Ansari Nagar, New Delhi 110 029, India.

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Material and Methods

A multicentre randomised comparative clinical trial with oral PGE_2 tablets and intravenous oxytocin drip for induction of labour was carried out at eleven medical colleges.

The selected women were randomly given either 0.5 mg of Oral tablets of PGE_2 administered hourly upto a maximum period of 18 hours or were induced with 2 IU of I/V oxytocin in 500 ml of 5 per cent glucose at the rate of 8 drops/min. up to a maximum of 40 drops/min. The total dose of oxytocin did not exceed 4 IU.

The criterion for successful induction was taken as initiation of labour within 8 hours followed by vaginal delivery within 18 hours of induction.

Observations

There were a total of 900 patients, 459 were induced with Oral PGE_2 tablets and 441 with I/V oxytocin. The study group matched well with control group with respect to age, weight, height and parity (Table I). The induction was planned in 83.9 per cent of patients, 86.3 per cent in oral PGE_2 tablets group and 81.4 per cent in I/V oxytocin group. The remaining 16.1 per cent women had premature rupture of membranes with no other symptoms of active labour.

TABLE I

Demographic Characteristics

	Oral PGE_2 Tablets Mean ± S.D.	I/V Oxytocin Mean ± S.D.
Age (yrs)	24.8 ± 3.9	24.6 ± 3.9
Weight (kg)	55.3 ± 7.5	54.9 ± 7.4
Height (cms)	152.6 ± 5.6	152.2 ± 5.5
Parity	1.2 ± 1.6	1.0 ± 1.8

Outcome of Trial

The induction of labour was successful in 74.5 per cent of patients in PGE_2 tablets group and in 78.9 per cent of I/V oxytocin group. The difference in the success rate was not statistically significant. There were 30 (6.5%) cases in PGE_2 oral group and 37 (8.4%) in oxytocin group in whom trial had to be interrupted. No response to drug was observed in 87 (19.0%) and 56 (12.7%) women in PGE_2 oral oxytocin group respectively.

Management of Interruptions

The major reason for trial interruption was foetal distress, 15 patients (32.7 per 1000 cases) in oral PGE_2 tablet group and 21 patients (47.6 per 1000 cases) in I/V oxytocin group. Another reason for trial interruption was incoordinate/hypertonic uterine activity, 8 (17.4 per 1000 inductions) with oral PGE_2 tablets and 13 (29.5 per 1000 inductions) with I/V oxytocin. Vomiting was a reason for trial interruption in six women in oral PGE_2 tablet group and fever/rigor in 2 patients in oxytocin group. Trial was interrupted in one patient each of induction with oral PGE_2 tablets and I/V oxytocin group due to low lying placenta, which may not be attributable to any drug regime (Table III).

Of the 67 cases of trial interruptions from both groups. 7 women had vaginal delivery, caesarean section was done in 49 cases and mode of delivery was not recorded in 11 cases.

TABLE II
Outcome of Trial

Outcome of Trial	Oral PGE_2 No.	%	I/V Oxytocin No.	%
Successful	342	74.5	348	78.9
Trial Interrupted	30	6.5	37	8.4
Failure	87	19.0	56	12.7
Total	459		441	

Maternal Side Effects

Gastrointestinal symptoms were the most common side effect with PGE_2 group experienced by 33 women (7.2%) as compared to a single case in I/V oxytocin group. On the whole, the symptoms reported which could be attributed to the drug were 76 women (16.6 per cent) in oral PGE_2 tablets group and 58 (13.2 per cent) in I/V oxytocin group (Table IV. There was no case of maternal death.

Neonatal Side Effects and Mortality

Neonatal side effects included six cases of respiratory depression, 2 following induction with oral PGE_2 and 4 after induction with I/V oxytocin. One baby in each group developed neonatal jaundice and responded to conservative therapy.

There was one case of still birth due to cord around the neck and 2 cases of neonatal deaths in I/V oxytocin group. No still birth or neonatal death was reported in oral PGE_2 tablet group.

TABLE III
Reasons for Trial Interruptions

Reasons for trial interruption	Oral PGE_2 Tablets No.	Rate/1000	I/V Oxytocin No.	Rate/1000
Foetal distress	15	32.7	21	47.6
Incoordinate/Hypertonic uterine activity	8	17.4	13	29.5
Vomiting/diarrhoea	6	13.1	—	—
Fever/rigors/chest pain	—	—	2	4.5
Low lying placenta	1	2.1	1	2.3
Total Trial interruptions	30	65.3	37	83.9
Total cases	459		441	

TABLE IV
Maternal Side Effects

Side Effects	Oral PGE_2 Tablets No.	Per cent	I/V Oxytocin No.	Per cent
Nil	383	83.4	383	86.8
Vomiting/diarrhoea/headache/giddiness	33(6)	7.2	1	0.2
Incoordinate/hypertonic uterine activity	16(8)	3.5	16(13)	3.6
Foetal distress	25(15)	5.5	38(21)	8.7
Fever/Rigors	2	0.4	3(2)	0.7
Total Cases ..	459		441	

(Number in parenthesis indicate cases of trial interruption).

Discussion

Prostaglandins have been successfully used for induction of labour as early as 1971. Karim and Sharma first reported the oxytocin effect of orally administered prostaglandin E_2 and its efficacy for induction of labour. The findings of Craft and Luan *et al* and Elder *et al* have been further confirmed and an improved efficacy demonstrated when amniotomy is combined with oral prostaglandin E_2 therapy.

The high incidence of maternal gastrointestinal side effects is an undesirable feature of using oral prostaglandin E_2 tablets. Earlier in 1973 Tips, *et al* had reported vomiting in 34 pet cent and diarrhoea in 19 per cent of women. In our trial total incidence of gastrointestinal side effects was 7.2 per cent. Similar gastrointestinal side effects with oral prostaglandin E_2 tablets have also been reported by other investigators.

No case of uterine hypertonus with oral prostaglandin E_2 has been reported by Karim and Sharma and others. Similarly Craft and Yip and Co-workers stressed the point that no case of uerine hypertonus with foetal bradycardia was observed when patients were induced with oral prostaglandin E_2 at term. Contrary to this in our study, in-coordinate or hypertonic uterine activity without foetal bradycardia was reported in 3.5 per cent and 3.6 per cent of the inductions with oral PGE_2 tablets and I/V oxytocin respectively. Both drugs were found satisfactory for induction of labour. With respect to the side effects and ease of administration, each method and route has advantages and disadvantages which have to be weighed for individual women and choice made taking into account the medical indications for induction as well.

References

1. Craft, I.: Oral Prostaglandins and amniotomy for induction of labour. Adv. Biosci. 9: 593-598, 1973.
2. Elder, M. G. and Stone, M.: Prostaglandins, 6: 427, 1974.
3. Karim, S. M. and Sharma, S. D.: Brit. Med. J. 1: 260-262, 1971.
4. Luan, Thiam Ang, K. H., Ng. V., Sivanesaratnam, T. A., Sinnathuray and Yusof, K.: Induction of labour with PGE2 tablets. Int. J. Obstet. 15: 15-18, 1978.
5. Yip, S. K., Ma, H. K. and Ng, K. H.: Induction of labour with oral PGE_2. J. Obstet. Gynaec. Brit. Commonwealth, 80: 442, 1973.