Mid-trimester termination of pregnancy — a randomised controlled trial of two prostaglandin regimens

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Abstract ***Objective.*** **To determine the more applicable of two ways of prostaglandin induction currently in use in second trimester induced abortions for congenital or chromosomal abnormalities.**

Design. **A prospective randomised controlled trial.**

Setting. **Department of Obstetrics and Gynaecology, Tygerberg Hospital, CP.**

Study population. **Twenty consecutive patients admitted for termination of pregnancy for congenital or chromosomal abnormalities between 14 and 26 weeks' pregnancy duration.**

Management. **Patients were randomly selected to receive either 1,5 mg prostaglandin E_2 (PGE_2) gel extra-amniotically or 25 mg prostaglandin $F_2\alpha$ ($PGF_2\alpha$) intra-amniotically. Patients in both groups received oxytocin to a maximum dosage of 120 mU per minute if they had not aborted 18 hours after the original administration of either prostaglandin regimen. If abortion had not taken place 36 hours after commencement of treatment, management was considered unsuccessful.**

Main outcome measurements. **Proportion of successful inductions and complications.**

Results. **Complications of management were rare and did not differ between the two management groups. However, there were significantly more failures in the group who received intra-amniotic $PGF_2\alpha$ (7 v. 2 patients) as well as a significantly higher need for oxytocin in this group (10 v. 4 patients).**

Conclusions. **With promising drugs such as prostaglandin analogues and anti-progesterones not universally available, methods of induction suitable to the local situation should be sought. Extra-amniotic PGE_2 seems more suitable than intra-amniotic $PGF_2\alpha$ because of a shorter induction-to-delivery time without increased morbidity.**

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Fetal genetic disorders and congenital abnormalities are mostly diagnosed during the second trimester when termination of pregnancy (TOP) is often the parental choice. Mid-trimester TOP has been complicated by serious maternal morbidity[1] and prolonged, often ineffective, procedures.[2] The use of prostaglandins for mid-trimester TOP has been adequately described,[3] although variations in methods and dosages have precluded definite conclusions as to the best method for second trimester TOP. We examined two methods of prostaglandin induction currently used in our unit to determine which is more appropriate in second-trimester induced abortions for congenital or chromosomal abnormalities.

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Subjects and methods

A randomised controlled trial was performed to evaluate the use of extra-amniotic prostaglandin E_2 (PGE_2) gel compared with intra-amniotic prostaglandin $F_2\alpha$ ($PGF_2\alpha$). Twenty successive patients admitted for TOP at gestational ages between 14 and 26 weeks qualified for the study. Exclusion criteria were a dead fetus on admission, previous uterine scars, a history of asthma, active vaginal or intra-uterine infection and anhydramnios. Patients were randomly allocated to one of two management groups according to the balanced block method. One group received 1,5 mg PGE_2 gel extra-amniotically (Prepidil gel; Upjohn). These patients were examined in the lithotomy position. With the aid of a Cuscoe speculum, the anterior lip of the cervix was visualised and stabilised with a swab holder. Three syringes each containing 0,5 mg PGE_2 gel were used in immediate succession to instil the prostaglandin through the cervix. The other group received intra-amniotic $PGF_2\alpha$. Aspiration of 2 ml of amniotic fluid transabdominally to confirm correct position of the needle was followed by an injection of 5 mg $PGF_2\alpha$. After 5 minutes, a bolus of 20 mg of the drug was administered if no side-effects had occurred. The needle was then removed. After 18 hours, 30 mU oxytocin per minute were administered intravenously if the patient had not yet aborted, irrespective of the original regimen. This dosage was increased every 15 minutes, until a maximum of 120 mU per minute was reached. If the patient had not aborted 36 hours after initiation of treatment, the method was regarded as unsuccessful and the managing physician was free to change over to management of choice. Instructions for initial management were placed in sealed envelopes and the procedures were performed by the registrar rotating through the obstetric special care unit. Informed consent was obtained from patients and the study was approved by the Ethics Committee of Tygerberg Hospital.

Results were analysed by means of Student's *t*-test to compare means of normally distributed data and the signed rank test for data not normally distributed. Ratios were compared by means of Fisher's exact test because of small numbers. *P*-values of less than 0,05 were considered significant.

Results

Patient characteristics were comparable in the two groups (Table I). The difference in the number of primigravidas was not statistically significant. The indications for termination are listed in Table II. Seventeen terminations (85%) were performed either because of genetic disorders or fetal abnormalities of the central nervous system and these were evenly distributed among the two groups. Complications of management were extremely rare. There were no cases of uterine hyperstimulation, excessive haemorrhage before or after abortion or chorio-amnionitis in either group. The 1 case of nausea was managed successfully with antiemetic treatment. Other complications are detailed in Table III. The 2 patients with retained placentas required manual removal thereof under general anaesthesia. Rupture of membranes before abortion occurred more often in patients who had received $PGF_2\alpha$, but the

average duration of rupture before delivery was short (3,44 hours). Oxytocin was needed in all patients receiving $PGF_2\alpha$, but only in 4 of the patients receiving PGE_2 ($P < 0,05$). Induction-to-delivery time was on average almost 14 hours longer in the intra-amniotic group and significantly more failures occurred in this group (Table III). While more analgesics were used on average by the intra-amniotic group, this difference was not statistically significant and was at least partially the result of the longer time that elapsed between induction and delivery in this group.

TABLE I.
Comparison of patient characteristics in the two management groups

	$PGF_2\alpha$ group	PGE_2 group	*P*-value
Maternal age	27,11 (20 - 38)	30,22 (23 - 40)	
Median	27	29,3	NS
Gravidity	2,22 (1 - 4)	2,89 (2 - 4)	
Median	2	3	NS
Parity	0,78 (0 - 3)	1,56 (0 - 3)	
Median	0	1	NS
Nulliparas	5	1	NS
Miscarriages	0,56 (0 - 3)	0	
Median	0	0	NS
Gestational age	22,2 (18 - 26)	22,8 (19 - 26)	
Median	22	22,3	NS
Bishop count < 4 at onset	10	10	NS
Race group			
White	4	4	NS
Coloured	5	5	

NS = not significant.

TABLE II.
Indications for termination of pregnancy in the two management groups

	$PGF_2\alpha$ group	PGE_2 group
Genetic disorders*	3	5
Central nervous system		
Anencephaly	3	1
Hydrocephaly	3	2
Other		
Conjoined twins (cephalothoracophagus)	1	0
Cystic lung tumour	0	1
Multiple pterygium syndrome	0	1

*Excluding multifactorial causes.

TABLE III.
Comparison of outcome of management in the two groups

	$PGF_2\alpha$ group	PGE_2 group	*P* - value
Need for oxytocin	10	4	0,005
Dosage morphine required (mg)	35,63 (0 - 90)	25 (15 - 45)	
Median	30	30	NS
Total time before abortion (h)	39,67 (19 - 61)	25,15 (11 - 54,5)	
Median	38	23	NS
Failures	7	2	< 0,05
Rupture of membranes	4	2	NS
Retained placenta	2	0	NS

Discussion

Procedures for eventual mid-trimester TOP should not be complicated by an unduly long induction process. Given a lack of prostaglandin analogues and anti-progesterones,[4,5] at present prostaglandins seem the most appropriate way of achieving this goal locally. The existence of many methods for TOP emphasises that no particular one is optimal. Furthermore, studies have often been performed on patients at an earlier gestational age than those in our study. This study was undertaken to determine which of two regimens is the most suitable in local circumstances.

The major differences between the two routes of administration was that patients in whom labour was induced by means of extra-amniotic PGE_2 had a significantly better chance of delivering within 36 hours than those induced by means of intra-amniotic $PGF_2\alpha$. They also needed oxytocin augmentation less often and for shorter periods of time. This conclusion might be prejudiced by the higher number of nulliparas in the latter group.[6] However, there was no difference in the initial Bishop scores between the two groups. In addition, oxytocin was needed in all patients receiving intra-amniotic prostaglandin. Furthermore, in this particular group, the difference in induction-to-delivery time was not significantly longer in the nulliparas than in the multiparas.

Both regimens might be adjusted to improve results further. It has been reported that an increase to 2,5 mg in the dosage of PGE_2 given extra-amniotically leads to a shorter induction-to-labour time compared with a dosage of 1,5 mg, without an increase in morbidity.[6] Likewise, some recommend that the dosage of intra-amniotic $PGF_2\alpha$ should be 40 - 50 mg if only a single dose is administered.[7]

This small study, initially intended as a pilot study, confirms that methods of induction suitable to local circumstances should be sought. Extra-amniotic PGE_2 seems more appropriate than intra-amniotic $PGF_2\alpha$ because of a shorter induction-to-delivery time without increased morbidity. The situation with regard to availability of alternative methods should, however, be reviewed constantly and modifications of policy investigated. Continuation of the present study is thus not warranted.

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