

## COMPARATIVE STUDY OF EXTRA-AMNIOTIC PROSTAGLANDIN F2 $\alpha$ AND INCREASING INTRAVENOUS OXYTOCIN INFUSION FOR TERMINATION OF PREGNANCY

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### ABSTRACT

This prospective study was conducted in the Gynaecology & Obstetrics Department of Military Hospital Rawalpindi from January 2000 to December 2000 to investigate the effectiveness of Prostaglandin F2 $\alpha$  by extra amniotic route and to determine its side effects, while comparing it with intra venous Oxytocin infusion. Out of a total of 554 patients, 196 were given PGF2 $\alpha$  extra amniotically (Group A), and 358 patients were given I/V Oxytocin infusion. All patients in Group 'A' aborted within 29 hours, while there were 8.66% (31) failures in the Group 'B' and the remaining 327 patients aborted/ delivered within 36 hours. The mean induction to delivery interval was 11.49  $\pm$  6.11 hours in the PGF2 $\alpha$  and 18.20  $\pm$  8.00 hours in the oxytocin group. Delivery/ abortion within 24 hours was 93.88% Vs 69.55% p<0.0001, complete expulsion rates of 76.53% Vs 68.46% and the complication rates of 7.14% (14) Vs 17.60% (63) in the PGF2 $\alpha$  Vs Oxytocin groups were also significant. Satisfaction with management was much higher in the PGF2 $\alpha$  97.45% (191) Vs 78.21% (280) p<0.0001 in the Oxytocin group. So PGF2 $\alpha$  by this route is superior to Oxytocin in terms of shorter induction to delivery interval, low prevalence of side effects, stronger haemostatic effect, safety and efficacy.

**Keywords:** Prostaglandin, PGF2 $\alpha$ , oxytocin, pregnancy, labour

### INTRODUCTION

Cervical ripening and maturation is of fundamental importance and a pre requisite for successful termination of pregnancy. Extensive researches in the medical methods of induction of labour have proved prostaglandin to be superior effective and safe both for induction before or at term. PGF2 $\alpha$  serves the dual purpose of cervical ripening and initiation of myometrial contractility [1]. Oxytocin was classically used where cervix was favorable. Liberation of PGF2 $\alpha$  from the decidual cells, myometrial cells and cervical tissue at term has a broad spectrum of actions [2] that can generate the observed components of parturition including the biochemical changes in the connective tissue of cervix [3]. Given by the intravenous or intrauterine [4] (extra amniotic or intra amniotic) routes it initiates rhythmic contractions which if continued for sufficient time are capable of expelling the uterine contents. It is also used intra myometrially [5] for control of

primary post partum haemorrhage due to uterine atony and direct injection may be given into the umbilical vein in cases of retained placenta [6]. It also has a luteolytic action [7]. It induces contractions of smooth muscles of the intestinal tract thus leading to vomiting and diarrhea [8]. It is contra indicated in patients with asthma and chronic pulmonary disease [8]. The purpose of this study was to evaluate the effectiveness of PGF2 $\alpha$  by the extra amniotic route in cases of missed abortion, intra uterine fetal death and diagnosed fetal anomalies not compatible with life, while comparing it with the standard method of intravenous Oxytocin infusion. The frequency of side effects of PGF2 $\alpha$  were also studied.

### MATERIALS AND METHODS

It was a quasi experimental study carried out on 554 admitted patients of varying ages and gravidity between 12 and 32 weeks of gestation, selected by purposive non probability sampling from the Gynaecology/Obstetrics ward and

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distributed between the two groups of the study (randomization not done).

All the patients had a foley catheter inserted through the cervix under direct vision and strict antiseptic technique (14 to 18 French sizes according to the gestational age). Balloon was inflated with 10 ml of sterile water and the catheter was strapped to the patient's thigh under slight traction. In group 'A' 196 patients were given PGF2 $\alpha$  extra amniotically. One injection of PGF2 $\alpha$  (5 mg) 1 ml was diluted with 19 ml of sterile water and loading dose of 3 to 5 ml to fill up the dead space was given. Thereafter 1 to 2 ml of this solution was given into the same space after every half to one hour. If labour did not commence within 24 hours, the same procedure was repeated the next day. 358 patients in group 'B' were given intravenous Oxytocin infusion 20 to 25 units in 1000 cc 5% dextrose at 30 drops / min and titrated with contractions. If labour did not commence the induction was repeated the next day. If still no improvement took place the method was considered to have failed, and an alternative method was adopted.

The primary end points of the trial were Induction to delivery interval, 24 hours successful induction rate, type of expulsion of products of conception (complete or incomplete), need for surgical evacuation of uterus, heamorrhage and pelvic infection.

## RESULTS

The ages of our patients ranged from 16 to 45 years (mean  $27.67 \pm 6$  years). Gestational ages ranged between 12 to 32 weeks (mean of  $19.71 \pm 4.68$  weeks). Bishop's score was unfavourable. The parity ranged from 0 to 10 (mean  $3.6 \pm 2.46$ ). There was no significant difference of these demographic variables between the two groups. The reason for pregnancy termination was missed abortion in 64.47% (357), intra uterine death in 25.27% (140) and congenital abnormalities in 10.29% (57) patients. In the PGF2 $\alpha$  group all patients aborted / delivered within 29 hours from the start of the infusion accounting to a successful induction rate of 100%. However, there were 8.66% (31) failures in the Oxytocin group, and the remaining 327 patients aborted / delivered within 36 hours. The mean induction to delivery interval was significantly less in the PGF2 $\alpha$  ( $11.49 \pm 6.11$

hours) than in the Oxytocin group ( $18.20 \pm 8.00$  hours);  $p < 0.0001$ . A significantly greater number of patients in the PGF2 $\alpha$  than in the Oxytocin group were delivered within 24 hours (93.88% vs 69.55%). Complete expulsion took place in 76.53% (150) vs 68.46% (245) patients;  $p < 0.00044$  in the PGF2 $\alpha$  and Oxytocin groups respectively. The remaining patients required surgical evacuation of the uterus. A total of 7.14% (14) patients in PGF2 $\alpha$  group and 17.60% (63) in Oxytocin group developed one or more complications;  $p = 0.001$ , which was a significant result as shown in the table 3. 97.45% (191) of the women were satisfied with management in PGF2 $\alpha$  group as compared to 78.21% (280) in the Oxytocin group (table-3).

## DISCUSSION

The basic method using PGF2 $\alpha$  extra amniotically is inexpensive and safe. Other prostaglandin preparations like PGE2 pessaries, vaginal inserts and intra cervical gels are comparable methods of induction of labour [9,10] but they are relatively costly and not readily available. Since cost is major concern in developing countries therefore, finding an intermediate method that is more effective than the conservative method of Oxytocin infusion and at the same time is less expensive than the fancy PGE2 preparations was of utmost importance.

Our mean induction to delivery interval of PGF2 $\alpha$  was in accordance with the study by Jaschevetzky [11] who reported a mean induction to delivery interval of 12.6 hours with 100% patients delivering within first 24 hours. Another study [12] showed this interval to be  $17.5 \pm 8.6$  hours while using intra amniotic PGF2 $\alpha$ . Comparing with other methods of labour induction e.g using misoprostol [13,14] gave a successful 24 hour evacuation rate between 40% and 62% with the mean abortion time of 22 hours.

Retained products of conception were not found to be increased in the PGF2 $\alpha$  group being 23.47% as compared to 31.56% in the Oxytocin group. These results were much higher than those found by other investigators [12]. The requirement for surgical curettage was much higher the earlier the gestation in both the groups. The overall complication rate was consistent with the complication rate reported in the RCOG survey on

**Table-1: Distribution of patients according to induction delivery interval (n= 554)**

Induction Delivery Interval (Hours)	Group A PGF <sub>2<math>\alpha</math></sub>		Group B Oxytocin		Total (n=554)	
	No	%	No	%	No	%
4-8	76	38.78%	46	12.85%	124	22.38%
9-12	47	23.98%	44	12.29%	91	16.43%
13-16	36	18.37%	57	15.92%	94	16.97%
17-20	14	7.14%	53	14.80%	64	11.55%
21-24	12	6.12%	49	13.69%	60	10.83%
25-28	10	5.10%	32	8.94%	43	7.76%
29-32	1	0.51%	36	10.06%	37	6.68%
33-36	0	0.00%	10	2.79%	10	1.81%
>36	0	0.00%	31	8.66%	31	5.60%
<b>Total</b>	<b>196</b>		<b>358</b>		<b>554</b>	
<i>Pearson Chi Square</i>	=	<b>109.453</b>	<i>Df</i>	=	<b>32</b>	
<i>P-Value</i>	=	<b>0.000</b>	<i>Significance</i>	=	<b>Significant</b>	

**Table-2: Distribution of patients according to success of the induction procedure (n= 554)**

	Group A PGF <sub>2<math>\alpha</math></sub>		Group B Oxytocin		Chi-square (pearson)	Df	P-Value	Significant S /Not Significant NS
	No	%	No	%				
Successful delivery in 24 hrs	184	93.88%	249	69.55%	43.90	1	0.000	S
Successful delivery from 25-36 hrs	12	6.12%	78	21.79%	17.978	1	0.000	S
Failed to deliver in 36 hrs	0	0.00%	31	8.66%	16.376	1	0.000	S

**Table-3: Complications (n= 554)**

	Group A PGF <sub>2<math>\alpha</math></sub>		Group B Oxytocin		Chi-square (pearson)	Df	P-Value	Significant (S) or Not Significant (NS)
	No	%	No	%				
Vomiting	11	5.61%	38	11.17%	5.686	1	0.017	S
Diarrhoea	1	0.51%	4	1.12%	0.522	1	0.470	NS
Pyrexia > 38 °C	2	1.02%	17	4.75%	5.315	1	0.021	S
Hypertonus of uterus	6	3.06%	15	4.19%	0.442	1	0.506	NS
Haemorrhage	1	0.51%	12	3.35%	4.464	1	0.035	S
Coagulation defects	0	0%	2	0.56%	1.099	1	0.294	NS
Hypersensitivity	0	0%	0	0%	-	-	-	NS
Breathlessness	0	0%	0	0%	-	-	-	NS
<b>Total patients with one or more Complications</b>	<b>14</b>	<b>7.14%</b>	<b>63</b>	<b>17.60%</b>	<b>11.569</b>	<b>1</b>	<b>0.001</b>	<b>S</b>

late abortions [15] (> 5%), but was much higher than the Scottish study by Cameron & Baird [16]. Pyrexia > 38 °C occurred in patients who had prolonged induction. No significant increased febrile morbidity was found by the use of cervical foley catheter in our study. Satisfaction with management was much higher in the PGF<sub>2 $\alpha$</sub>  group owing to the shorter induction to delivery interval, greater success rate and shorter period of hospitalization.

## CONCLUSION

We conclude that PGF<sub>2 $\alpha$</sub>  by extra amniotic route is more effective than intravenous Oxytocin

for termination of pregnancy. It is safe, well tolerated and has a stronger haemostatic effect.

## REFERENCES

1. Alastair Harvey MacLennan, Fung Yee Chan, Kerena Eckert. The safety of vaginal Prostaglandin F<sub>2 $\alpha$</sub>  for the stimulation of labour. **Aust NZ J Obstet Gynaecol 1994; 34: 2:154.**
2. Platz Christensen J J, Pernevi P, Bokstrom H, Wiquist N. Prostaglandin E and F<sub>2 $\alpha$</sub>  concentration in the cervical mucus and mechanism of cervical ripening. **Prostaglandins 1997; 53 (4): 253-61.**

3. Olah K S, The cervix in pregnancy and labour. In: Studd J, ed. Progress in obstetrics and Gynaecology. Vol 12 **Churchill Livingstone, 1996: 99- 115.**
4. MacLennan A H, Green R C .Cervical ripening and induction of labour with intra vaginal prostaglandin F 2 alpha. **Lancet 1979; 1: 117-119.**
5. Kupfermanc M J, Gull I, Bar-AmA, Daniel Y, Jaffa A, Shenhav m et al .Intra uterine irrigation with ProstaglandinF2 alpha for management of severe post partum haemorrhage. **Acta Obstet Gynecol Scand. 1998; 77 (5): 548-50.**
6. Bider D, Dulitzky M, Goldenberg M, Lipitz S, Mashlach S. Intra umbilical vein injection of prostaglandin F2 alpha in retained placenta. **Eur J Obstet Gynecol Reprod Biol 1996; 64 (1): 59-61.**
7. Milvae R A. Inter relationships between endothelin and prostaglandin F2 alpha in corpus luteum function. **Rev Reprod 2000; 5(1): 1-5.**
8. Rang H P, Dale M M, Ritter J M. Pharmacology. Fourth edition Edinburgh: **Churchill Livingstone, 1999: 215-217.**
9. Levi J M, Sankpal R. Use of newer prostaglandins in second trimester medical termination of pregnancy. In: Mataliya M V, Jassawalla M J eds. Manual on Medical Termination of Pregnancy: **An update. New Delhi: Jaypee. 1999:74-78.**
10. Rayburn W F. Prostaglandin E2 for cervical ripening. In: Quilligan E J, Zuspan F P eds. Current Therapy in Obstetrics and Gynaecology. 5th edition. **Saunders W B; 2000: 334-337.**
11. Jaschevatzky O E, Rosenberg Ron P, Yitzhak Noy, Shimon Dascalu, Shmuel Anderman and Ballas S. Comparative study of Extra – amniotic Prostaglandin F2 $\alpha$  infusion and increasing intravenous oxytocin for termination of second trimester missed abortion. **J Am Coll Surg 1994; 178: 435-438.**
12. Perry K G, Rinnehart B K, Dom A Terrone, Martin R W, May B L and Roberts W E. Second trimester uterine evacuation: A comparison of intra amniotic (15 S) –15-Methyl prostaglandin F2 $\alpha$  and intra vaginal misoprostol. **Am J Obstet Gynecol 1999; 181: 1057-61.**
13. Nuutila M, Toivonen J, Ylikorkala O, Halmesmaki E. A comparison between two doses of intravaginal misoprostol and gemeprost for induction of second trimester abortion. **Obstet Gynecol 1997; 90: 896-900.**
14. Herabutya Y, O-Prasertsawat P. Second trimester abortion using intravaginal misoprostol. **Int J Gynaecol Obstet 1998; 60: 161-5.**
15. Stanwell-Smith R. Procedures used for legal abortion. In: Late Abortions in England and Wales-Report of a national confidential study (Alberman E & Dennis KJ. eds.), **Royal College of Obstetricians and Gynaecologists. London 1984: 59-65.**
16. Cameron I T, Baird D T Local prostaglandin administration for mid trimester abortion: A retrospective analysis. **J Obstet Gynaecol 1987; 7: 228-232.**