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TERMINATION OF PREGNANCY;
THERAPEUTIC TERMINATION OF PREGNANCY IN SECOND TRIMESTER.

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ABSTRACT… Objectives: To compare efficacy of extra-amniotic Foley's catheter balloon alone versus combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha in therapeutic termination of second trimester pregnancy. **Study Design:** Randomized controlled trial. **Setting:** Department of Obstetrics & Gynecology, Bahawal Victoria Hospital, Bahawalpur. **Period:** Two years. July 2014 to June 2016. **Sample Technique:** Non-probability, consecutive sampling technique. **Patients & Methods:** A total of 256 patients, 16 to 38 years of age with fetal death or missed abortion on ultrasonography in 2nd trimester (14-24 gestational weeks) of pregnancy were included in the study. Patients with previous uterine surgery, multiple pregnancies and parity>3 were excluded. Then selected patients were placed randomly into two groups i.e. Group A (extra-amniotic Foley's catheter balloon alone) & Group B (Foley's catheter balloon along with extra-amniotic instillation of prostaglandin F2-alpha), by using lottery method. Outcome variables like efficacy i.e. expulsion of fetus within 24 hours of induction, were noted. **Results:** The mean age of women in group A was 24.51 ± 4.77 and in group B was 24.29 ± 4.48 years. The mean gestational age in group A was 21.65 ± 2.01 weeks and in group B was 21.28 ± 1.93 weeks. Efficacy was 103 (80.47%) in group A (extra-amniotic Foley's catheter balloon alone) and 119 (92.97%) in group B (combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha) with p-value of 0.003. **Conclusion:** This study concluded that combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha is better and more efficacious than extra-amniotic Foley's catheter balloon alone in therapeutic termination of second trimester pregnancy.

Key words: Medical Abortion, Expulsion of Fetus, Extra-amniotic Instillation.

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INTRODUCTION

Abortion is the termination of pregnancy by the removal or expulsion from the uterus of a fetus or embryo before viability. An abortion can occur spontaneously, in which case it is often called a miscarriage, or it can be purposely induced.[1] The term "termination of pregnancy (TOP)" is used here to describe deliberate removal of an embryo or a fetus (not known to have died before onset of the procedure) from the uterus, thus ending a pregnancy so that it does not progress to birth. This term is often used in the literature and was chosen instead of "induced abortion".[2]

An estimated 44 million abortions are performed globally each year, with slightly under half of those performed unsafely.[3] The worldwide incidence of TOP being performed after 13 weeks of gestation has varied between 5 to 15% of all TOPs.[4] The indications for terminating pregnancy are based on legal constraint. The increasing use of ultra-sonography and serological screening has enhanced the ability of obstetricians to recognize potentially complicated pregnancies early in gestation. After counseling, many of these women elect to take the risks of continuing complicated pregnancy for the risk of a pregnancy termination.[5] The global incidence of spontaneous abortions is around 15% of all pregnancies. Similar figures have been quoted for Pakistan.

It should be kept in mind that the pregnancy-related mortality risk is estimated to be lowest during and after TOP. A live birth is associated

with an intermediate risk of pregnancy-related mortality, while ectopic pregnancy and fetal death are associated with the highest risks of pregnancy-related mortality.[6] Second trimester TOPs constitute one-tenth of all induced abortions worldwide but are responsible for two-thirds of major abortion-related complications.[7] The overall risk of major complications during and after TOP is low, but increasing gestational age is associated with an increased risk of complications. Major complications during second trimester abortion occur in less than 1% to 11% of abortions depending on the site and type of procedure.[8] The increased morbidity in second trimester TOP is likely to be due to increased fetal and placental size, increased blood volume and a distended uterus with decreased resistance.

Medical abortions are those induced by abortifacient pharmaceuticals. Medical abortion became an alternative method of abortion with the availability of prostaglandin analogs in the 1970s and the anti-progestogen mifepristone in the 1980s. Although the idea of using medications to induce a late menses or cause abortion dates back centuries, medically proven regimens have only been found in the last 50 years.

In the 1970s, natural prostaglandins, such as prostaglandin E2 (PGE2) and prostaglandin F2α (PGF2α) were found to be effective at inducing abortion early in pregnancy when administered vaginally.[9] Prostaglandin F2 alpha is a powerful uterotonic given in diluted form parenterally or locally (Intra-myometrially). PGF2α acts by binding to the prostaglandin F2α receptor that mediates luteolysis and may also be involved in modulating smooth muscle contraction in uterus and gastrointestinal tract.[10] The side effects commonly include nausea, vomiting, diarrhea, headache and bronchospasm due to smooth muscle contraction while less common side effects are flushing, diaphoresis and restlessness due to increased basal temperatures. It should not be given in patients with major cardiovascular, pulmonary, renal or hepatic dysfunction.[11]

The mode of action of catheter balloon is postulated to be either by direct mechanical effect or by release of prostaglandins secondary to separation of fetal membranes. Combination of double balloon catheter and continuous instillation of extra-ovular PGF2-alpha has resulted in very short mean induction to abortion interval and minimal side effects. This method is well tolerated by most of the women who can remain mobile while device is in place. In comparison with the five different methods, the use of extra amniotic balloon was found to provide more effective treatment than intra-cervical PGE-2.[12]

Obstetrical services are generally poor in our country. Bahawal Victoria Hospital, Bahawalpur is an extremely over loaded facility and is located in relatively poor area of the country. We had conducted this study to see which regimen is more effective so that this study would provide evidence for clinical use of more rapid, safe and cost effective method for induction of therapeutic termination of second trimester pregnancy.

OBJECTIVES

The objective of the study is to compare efficacy of extra-amniotic foley's catheter balloon alone versus combined use of foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha in therapeutic termination of second trimester pregnancy."

PATIENTS & METHODS

Study Design

Randomized controlled trial.

Setting

Department of Obstetrics & Gynecology, Bahawal Victoria Hospital, Bahawalpur.

Duration of Study

Duration of study was two years. July 2014 to June 2016

Sample Size

Sample size of one group (n) = 128
Total number of patients included in the study= 256

Sample Technique

Non-probability, consecutive sampling.

Sample Selection

Pregnant women of age between 16-38 years who have mid-trimester (14-24 weeks of gestation) fetal death or missed abortion, confirmed on ultrasonography were included in the study group. Women having previous uterine surgery or have more than four deliveries before P4 or more were excluded.

Data Collection Procedure

After approval from local ethical committee, 256 cases admitted to the Department of Obstetrics & Gynaecology, Bahawal Victoria Hospital, Bahawalpur, fulfilling the inclusion/exclusion criteria were selected. Informed, written consent was taken after explaining the aims, methods, reasonably anticipated benefits, and potential hazards of the study. After a patient had given informed consent for participation in the study, all selected cases were divided into two groups by lottery method. Each patient was offered to pick up a slip from total mixed up slips (half-slips were having letter 'A' and other half were having letter 'B') and she was placed in that respective group.

Foley's catheter of 16fr was inserted through the internal cervical OS of uterus in all cases of Group A. While in Group B, all patients were given PGF2-a in addition to Foley's catheter balloon. One milliliter of PGF2-a containing 5mgs was diluted in 20ml disposable syringe by addition of 19ml of normal saline, to make total of 20mls solution. Two milliliters were instilled through the catheter after its insertion, extra-amniotically, and then 1ml was instilled at hourly interval till the expulsion of balloon of Foley's catheter. Soon after expulsion of Foley's catheter balloon, 30units oxytocin in 100cc Ringer lactate solution was started in both groups at a rate of 10 drops/min which was increased up to 60 drops/min till expulsion of fetus and placenta. Patients in both groups were monitored until the expulsion of fetus. If the expulsion occurred within 24 hours, it was termed as successful abortion otherwise it was regarded as unsuccessful. All this data was recorded on a predesigned proforma.

Statistical Analysis

The data was entered and analyzed by using computer software SPSS version-14. Mean and standard deviation was calculated for quantitative variables like age and gestational age in weeks. Frequencies and percentages was calculated for qualitative variables like efficacy of extra-amniotic Foley's catheter balloon alone and efficacy of combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha. Efficacy of both groups was compared by chi square test. P value <0.05 was taken as significant.

Effect modifiers were controlled by stratification of data in terms of age, gestational age and co-morbid conditions like DM and HTN. Chi square test was applied to see the effect of these on primary variables. P value <0.05 was taken as significant.

RESULTS

Age range in this study was from 16 to 38 years with mean age of 24.62 $\pm$ 4.73 years. The mean age of women in group A was 24.51 $\pm$ 4.77 and in group B was 24.29 $\pm$ 4.48 years. Majority of the patients 132 (51.56%) were between 16 to 25 years of age as shown in Table-I. Gestational age was from 14 to 24 weeks with mean age of 21.54 $\pm$ 1.89 weeks. The mean gestational age in group A was 21.65 $\pm$ 2.01 weeks and in group B was 21.28 $\pm$ 1.93 weeks. Majority of the patients 145 (56.64%) were between 20 to 24 weeks of gestation as shown in Table-II. %age of patients according to parity and co-morbid conditions has shown in Table-III respectively.

There was expulsion of fetus within 24 hours in 103 patients in Group A while in Group B, it was seen in 119 patients as shown in Table-IV. So, efficacy was 80.47% in group A (extra-amniotic Foley's catheter balloon alone) and 92.97% in group B (combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha) with p-value of 0.003 as shown in Table-IV.

Stratification of age of patients, parity, gestational age and co-morbid conditions i.e. HTN, DM has shown in Table-V,VI,VII & VIII respectively.

Age (years)	Group A (n=128)		Group B (n=128)		Total (n=256)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
16-25	67	52.34	65	50.78	132	51.56
26-30	38	29.69	39	30.47	77	30.08
31-38	23	17.97	24	18.75	47	18.36
Mean ± SD	24.51 ± 4.77		24.29 ± 4.48		24.62 ± 4.73	

Table-I. Age distribution for both groups (n=256).

Gestational Age (weeks)	Group A (n=128)		Group B (n=128)		Total (n=256)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
14-17 weeks	21	16.41	23	17.97	44	17.19
>17-20 weeks	33	25.78	34	26.56	67	26.17
>20-24 weeks	74	57.81	71	55.47	145	56.64
Mean ± SD	21.65 ± 2.01		21.28 ± 1.93		21.54 ± 1.89	

Table-II. %Age of patients according to gestational age in both groups.

Parity	Group A (n=128)		Group B (n=128)		Total (n=256)	
	Frequency	%age	Frequency	%age	Frequency	%age
0	14	10.94	17	13.28	31	12.11
1	18	14.06	18	14.06	36	14.06
2	47	36.72	49	34.38	96	37.5
3	49	38.28	44	4.55	93	36.33

Table-III. %Age of patients according to parity in both groups.

		Group A (n=128)		Group B (n=128)	
		No. of Patients	%age	No. of Patients	%age
Efficacy	Yes	103	80.47	119	92.97
	No	25	19.53	09	7.03

Table-IV. %Age of patients according to efficacy between both groups.
P value is 0.003 which is statistically significant.

Age of patients (years)	Group A (n=128)		Group B (n=128)		P-value
	Efficacy		Efficacy		
	Yes	No	yes	No	
16-25 years	50 (74.63%)	17 (25.37%)	58 (89.23%)	07 (10.77%)	0.030
26-30 years	31 (81.58%)	07 (18.42%)	37 (94.87%)	02 (5.13%)	0.070
31-38 years	22 (95.65%)	01 (4.35%)	24 (100.0%)	00 (0.0%)	0.302

Table-V. Stratification of age according to efficacy in both groups.

Parity	Group A (n=128)		Group B (n=128)		p-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
0	08 (89.83%)	06 (10.17%)	16 (75.41%)	01 (24.59%)	0.014
1	07 (77.78%)	11 (22.22%)	16 (65.22%)	02 (34.78%)	0.002
2	43 (77.78%)	04 (22.22%)	45 (71.43%)	04 (28.57%)	0.951
3	45 (83.33%)	04 (16.67%)	42 (20.0%)	02 (80.0%)	0.478

Table-VI. Stratification of parity according to efficacy in both groups.

Age of patients (years)	Group A (n=128)		Group B (n=128)		P-value
	Efficacy		Efficacy		
	Yes	No	yes	No	
14-17 weeks	17 (74.63%)	04 (25.37%)	22 (89.23%)	01 (10.77%)	0.125
>17-20 weeks	28 (81.58%)	05 (18.42%)	31 (94.87%)	03 (5.13%)	0.425
>20-24 weeks	58 (95.65%)	16 (4.35%)	66 (100.0%)	05 (0.0%)	0.013

Table-VII. Stratification of gestational age according to efficacy in both groups.

Co-morbid conditions		Group A (n=128)		Group B (n=128)		P-value
		Efficacy		Efficacy		
		Yes	No	yes	no	
Hypertension	Yes	39	14	49	03	0.004
	No	65	11	70	06	0.198
Diabetes Mellitus	Yes	43	09	48	04	0.138
	No	60	16	76	05	0.006

Table-VIII. Stratification of Co-morbid conditions i.e. HTN, DM according to efficacy in both groups.

DISCUSSION

Therapeutic abortion is indicated in the following situations: when continuing the pregnancy could jeopardize the woman's life or affect her health;[13] when the fetus presents severe physical anomalies or risk of mental retard (eugenic abortion).[13]

In developed countries TOP is generally safe, but increasing gestational age is associated with an increased risk of complications. Most TOPs are performed before 13 weeks of gestation and only 5 to 15% later, during the second trimester.[4,6,14] Recent advances in prenatal screening technology increased the need for safe methods for terminating second trimester pregnancy, when the principle of necessity of ensuring the uterine cavity vacuity (to avoid hemorrhagic and infectious consequences) is unanimously accepted. In general, all methods of inducing abortive labor in the second trimester of pregnancy have the following common consequences: failure in producing abortion, incomplete abortion, placental retention, hemorrhage, infection and embolic phenomena.

A variety of techniques for termination of second trimester pregnancy can be used but the optimal method for TOP between gestational weeks 13 to 24 continues to be a matter of debate. Studies in which surgical and medical methods are compared are rare and randomized comparison has proven difficult to carry out.[15,16,17] Krause in 1833 was the first to use Foley's catheter for termination of pregnancy.[18] The proposed mechanism behind this may be direct mechanical dilatation and endogenous release of prostaglandin which causes are cervical ripening and this effect is enhanced when traction is applied. PGs also play a major role in human reproduction.[19] PG receptors are present in myometrial tissue[19] and during pregnancy PGs stimulate human uterine contractility and cause cervical ripening and dilatation.[20] The most important PGs that are involved in pregnancy, labor, delivery and puerperium are those of the E and F series.[19] This randomized controlled study has compared the efficacy of extra-amniotic Foley's catheter balloon alone versus combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha in therapeutic termination of second trimester pregnancy.

In our study, we have found that there was expulsion of fetus within 24 hours in 80.47% in extra-amniotic Foley's catheter balloon alone group and 92.97% in combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha group.

In his study Halimi S. et al[21] has found the intra cervical Foleys catheter balloon along with extra amniotic instillation of PGF2 alpha more effective, safe and cost effective method for therapeutic termination of second trimester pregnancy with minimal side effects and good patients compliance compared to intra-cervical Foleys catheter balloon alone. In another study conducted by Halimi M[22] the mean induction to Foleys catheter expulsion interval with combined use of Foleys catheter balloon and extra amniotic PGF2 alpha compare to Foleys catheter balloon alone was less and expulsion within 24 hours was seen in 86.66% and 6.06% patients respectively.

Nasreen A et al1[12] in his study has shown the expulsion of fetus within 24 hours in 32% in extra-amniotic Foley's catheter balloon alone group and 96% in combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha group. In the study conducted by Pushpa et al[23] the mean induction to abortion interval with Foleys catheter balloon

was >24 hours that means its efficacy is low in 2nd trimester pregnancy termination. Similar results were also observed by Imran F et al[24] and found the efficacy of 92%.

Fariha A et al[25] has compared the Misoprostol with extra-amniotically administered prostaglandin F2 alpha and found the mean interval of 20 hours for fetus expulsion. On the other hand, in a study by Amjad T et al the mean duration for fetus expulsion was found to be less than 24 hours in both groups i.e. Foley's catheter balloon alone versus combined Foleys catheter balloon and extra amniotic PGF2 alpha. He has shown the efficacy of 72.27% and 76.66% for both groups respectively which is not statistically significant.

Many previous studies have compared the use of Foley's catheter and prostaglandins for termination of pregnancy in the 2nd trimester and have justified the use of later. This would indicate that developed nations prefer the use of prostaglandins used alone and have generally abandoned the use of Foley's catheter. Although the use of PGF2 alpha significantly reduces the time required for termination of pregnancy in majority of patients but it is more expensive, having complications and practical difficulties for obstetricians in routine practice as compared to Foley's catheter. The combined use of Foley's catheter balloon and instillation of extra amniotic PGF2-alpha at regular interval has resulted in very short mean induction to expulsion interval and with minimal side effects. So, on the whole it is concluded that combined use of Foley's catheter balloon and extra-amniotic instillation of prostaglandin F2-alpha is more efficacious than Foley's catheter balloon alone in 2nd trimester termination of pregnancy.

CONCLUSION

Combined use of Foley's catheter balloon and extra amniotic instillation of prostaglandin F2 alpha is better and more efficacious than extra amniotic Foley's catheter balloon alone in therapeutic termination of second trimester pregnancy.

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