ORIGINAL ARTICLE

Phloroglucinol for Acceleration of Labour: Double Blind, Randomized Controlled Trial

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ABSTRACT

Objective: To determine the effect of Phloroglucinol Trimethylether vs Placebo on the duration of 1st stage of labour in term pregnancies.

Study Design: Quasi experimental study.

Place and Duration of Study: Obs/Gynae wards IIMC, Railway hospital, Rawalpindi from June 2011 to May 2012.

Materials and Methods: A double blind randomized placebo controlled trial was conducted on 131 patients in active phase of uncomplicated labour. The patients were randomized into two groups by simple random technique. After evaluation, patients were divided into group A and B. Neither the patients nor the doctor knew about the injection of phloroglucinol or distilled water. Sixty five patients in group a received Phloroglucinol Trimethylether 40 mg (4 ml) intravenous and 66 patients in group B received distilled water as placebo at 4 cm cervical dilatation. Dose was repeated after 60 minutes. Maximum 3 doses were given. Progress of labour was plotted on partogram. Any adverse effects of the drug on mother and fetus were noted. Student't-test was applied for statistical analysis.

Results: Out of 131 labouring patients, 61 patients from group A and 61 patients from group B were included in analysis. During 1st stage of labour 61 cases(100%) received 1 injection, whereas 11 cases (18.0%) were given 2 injections and 3 cases (4.91%) received 3 injections during the 1st stage of labour in group A and in group B 61 patients (100%) received 1 injection , 52 patients (85.2%) were given 2 injection and 37 cases (60.6%) were received 3 injection. The average duration of observed active phase of 1st stage of labour was shortened by almost two hours in patients receiving Phloroglucinol. The mean duration of 2nd stage of labour in group A was 25.16 mins and 34.52 mins in group B.

Conclusions: Phloroglucinol definitely has a therapeutic role to play in obstetrics with its strong antispasmodic effect. In the presence of good and regular uterine contractions, it shortens the duration of labour, is non toxic to both mother and fetus and it also decreases the severity of labour pain.

Keywords: *Phloroglucinol, First stage of labour, Duration of labour, Placebo*

Introduction

The problems and hazards of prolonged labour both for the mother and fetus have been recognized for many years. The mother is exposed to a higher risk of 0infection, ketosis, and obstructed labour, while the foetus faces the dangers of infection, asphyxia and excessive cranial moulding. Professor O'Driscoll at the National Maternity Hospital, Dublin (1973), introduced the concept of "active management of labour" and this has influenced the obstetricians to change their outlook regarding first stage of labour.[1] The Causes of prolong 1st stage of labour is multifactorial and cervical dilatation is the end result of these factors.[2] Active management of labour is associated with the low incidence of prolonged labour and low Cesarean Section rate.[3]

Various drugs have been tried over the last few decades, which accelerate labour either by increasing the uterine activity or by accelerating cervical dilatation. Oxytocin and prostaglandins are used to intensify uterine contractions. Sedatives and belladonna alkaloids have been tried to hasten cervical dilatation, but many have adverse effects on the mother or the feotus.[4] Drotaverine and Vaethamate bromide have

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been used to accelerate cervical dilatation but many have anticholinergic side effects like dryness of mouth, tachycardia and vomiting. An ideal antispasmodic for acceleration of cervical dilatation should have a prompt and long lasting action, no adverse effects on uterine contractility and be free from the risk of uterine inertia. It should also minimal side effects in the mother and the foetus.[5] Spasmolytics and spasmoanalgesics mixtures are administered to facilitate dilatation of the cervix during delivery and to shorten the 1st stage of labour. Which results in reduced need of analgesia, decreasing patient's anxiety and less amount of time spent in painful process of parturition.[6] Phloroglucinol trimethyle ether is primarily used in gastrointestinal tract colics.[7] It was used for augmentation of labour in some centres in 1970. Recently there is again a surge for the use of Phloroglucinol Trimethyl Ether to accelerate the first stage of labour in many centers. It is extensively used in obstetrics. It can relieve the spasm and edema of cervix and can lower the tension of cervix muscles. So, can be used to improve dilatation of cervix and promote the progression of labour.[8] It modulates the release of prostaglandin and other inflammatory mediators as nitricoxide.[9] It reduces the glycerol induced abdominal pain by reducing smooth muscle contraction without affecting tone.[10]

The rationale of the study is to shorten the duration of labour, thus avoiding the complications of prolonged labour and instrumental deliveries and to lower the Cesarean Section rate.

Materials and Methods

A Randomized controlled trial was conducted in labour ward of obstetric unit.All patients fulfilling inclusion criteria admitted through OPD and ER of Obs/Gynae unit IIMC, Railway Teaching Hospital Rawalpindi were recruited and divided into 2 equal groups. Permission from hospital ethical committee was taken and patients were appraised of merits and demerits of study. Proper informed consent was taken from each woman. Inclusion Criteria was laboring patients including term primigravida and multigravida, having singleton fetus with cephalic presentation, in active phase (4cm) of uncomplicated labour (active phase was defined as 3cm > cervical dilatation with regular uterine contractions).Exclusion Criteria were any contraindication to vaginal delivery e.g. CPD, placenta previa ,Multigravida , Multiple gestation ,Pre-term Meconium stained liquor ,CTG abnormalities and any obstetrical, surgical or severe medical complications such as heart disease or eclampsia. The patients were randomized into two groups by simple random technique. Sixty one patients in the study group received phloroglucinol 40mg (4ml) I/V at 4cm dilatation and 61 patients in the control group received placebo (distilled water) 4ml I/V .Dose was repeated after 60min. Neither patient nor observer knew the content of the injection. Maximum 3 doses were given. Labour progress was plotted on partograph. All data pertaining to labour events, maternal and neonatal outcome, adverse effect of drug or placebo (nausea, vomiting, giddiness, palpatation , hypo/hypertension, tachycardia, dry mouth , blurring of vision, fetal heart rate) were recorded.Amout of blood loss after second stage of labour was estimated subjectively by the attending doctor and objectively by weighing the soaked pads. Blood loss of > than 500ml was considered abnormal.Follow up of the patients was done till 24 hours after delivery. Four hypothesis were tested in the study. First was that pholoroglocinol can safely reduce the duration of labour, secondly they donot have any maternal and neonatal adverse effects, third do not cause primary

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postpartum hemorrhage and finally it can significantly reduce the pain of labour. Primary outcomes measures was duration of labour. Secondary outcomes was foetal outcome, maternal side effects and effect of drug on blood loss after second stage of labour. Data was entered on the proforma and was analyzed by SPSS version 18.Mean and SD were calculated for quantitative variables i.e. age, gestational age, duration of active 1st stage, 2nd stage, 3rd stage and total duration of labour. Frequencies and percentages were calculated for number of doses used. Independent sample t-test was used to compare duration of 1st stage of labour in drug and placebo group. P-value < 0.05 was taken as significant.

Results

Table I shows baseline demographic and clinical characteristics of the patients. The primary analysis was intention to treat and involved all patients who were randomly assigned.Out of 131 labouring patients , 4 pateints in group A (out of 65 patients) and 5 patients in group B(out of 66 patients) were removed from consideration because they were delivered by Cesarean Section. 5 patients developed fetal distress and 4 patients had failed progress in 2nd stage. Therefore 61 patients from group A and 60 patients from group B were included in analysis. Mean age of patients in group A was 24.4± 3.51 years and in group B was 23.1±3.26 years. Mean gestational age in both groups was 38.8 ± 0.76 weeks. During 1st stage of labour 61 cases(100%) received 1 injection, whereas 11 cases (18.0%) were given 2 injections and 3 cases(4.91%) received 3 injections during the 1st stage of labour in group A and in group B 61 patients (100%) received 1 injection ,52 patients (85.2%) were given 2 injection and 37 cases (60.6%) were received 3 injection .

The average duration of observed active phase of 1st stage of labour was shortened by almost two hours in patients receiving

Table I: Baseline Characteristics of Patients of both Groups. (n = 122)

Characteristics	Group A N=61 Mean (SD)	Group B N=61 Mean(SD)	*P*-value
Age (years)	26.62(6.09)	25.83(5.38)	0.620
Height (cm)	155.18(3.37)	155.64(3.06)	0.314
Weight(Kg)	66.72(4.52)	69.09(3.73)	0.642
Period of gestation(weeks)	38.61(1.26)	38.70(1.35)	0.778

Phloroglucinol. The mean duration of the observed active phase of 1st stage of labour in drug group was 183.04 mins(35.64) and 316 mins(52.29) in placebo group.The mean duration of 2nd stage of labour in drug group was 25.16 mins(6.21) and 34.52mins(5.57) in placebo group.The mean duration of 3rd stage of labour in drug group was 8.72mins(3.47) and 11.1mins(2.02) in placebo group.

The mean total duration of labour in drug group was 216.88 mins(38.94) and 358.52 mins(65.88) in placebo group.The mode of delivery was not altered in 2 groups (Table II).

Table II: Summary of Results of Primary Outcomes

STAGES OF LABOUR	GROUP A		GROUP B		P VALUE
	MEAN	S.D	MEAN	S.D	
IST STAGE	183.0	35.6	316.0	52.2	.0.00
2ND STAGE	25.1	6.2	34.5	5.5	0.00
3RD STAGE	8.7	3.4	11.1	2.0	0.00
TOTAL DURATION	216.8	38.9	358.5	65.8	0.00

The mode of delivery was not altered in two groups. Frequencies of normal vaginal delivery was 80% and 85% in group A and group B respectively. In group A 2 patients (4%) and 3 in group B (6%) had outlet forceps delivery due to fetal distress whereas 2 patients (4%) and 3 patients (6%) in group B underwent cesarean section for foetal distress and non progress of labour. Table III showed Secondary outcome measures.

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Neonatal outcome as assessed by APGAR Score at 1 minute 9.70 in group A Vs 9.14 in group B and 5 minute 9.90 in group A Vs 9.80 in group B were similar in both groups. There were no complications like cervical tear and vaginal laceration in either group. No side effects like nausea, vomiting, hypotension and dry mouth were noted in any of the groups. Due to analgesic action of drug the patients in group A were calmer and intensity of labour pain was lesser as compared to group B. They did not need analgesia while patients in group B did so.

Table III. Summary of Secondary Outcome Measures

Measures	Group A Mean (SD)	Group B Mean (SD)	P-Value
Fetal outcome (APGAR score)			
At 1 minute	9.70(0.44)	9.14(0.77)	0.000
At 2 minute	9.90(0.20)	9.80(0.39)	0.000
Blood loss after second stage(ml)	405.5(72.9)	426.0(62.5)	0.005
Maternal side effects	0.00	0.00	

Discussion

In modern obstetrics a drug that offers convenience and assures shortening of first stage of labour without compromising the mother or fetus is a welcome drug. In primary gravidas,the cervix normally dilates at the rate of 1cm/hour. Phloroglucinol accelerates the labour by relieving the spasm and edema of cervix,facilitate dilatation,shorten process of labour,harmonize the shrinkage of uterus and has no effect on the rhythm and the strength of uterine contraction.[8] Since 1960s foreign research indicated that phloroglucinol could obviously improve the dilatation of the cervix during the process of labour especially after the cervix dilated 4cm,the effect is better.[2] A review of literature showed that the drug was extensively used during 1970s and early

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