

## **Phloroglucinol for Acceleration of Labour: Double blind, randomized controlled trial**

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### **Abstract**

**Objectives:** To determine the effects of Phloroglucinol in acceleration of labour and its adverse effects on mother and foetus.

**Methods:** A double blind randomized, placebo controlled trial was conducted on 100 patients in active phase of uncomplicated labour selected by convenient sampling. Patients were given Phloroglucinol or Placebo (distilled water) intravenously. Progress of labour was plotted on Partogram. Any adverse effects of the drug on mother and fetus were noted. Student's t-test was applied for statistical analysis.

**Results:** In patients receiving Phloroglucinol there was a mean 34% reduction in duration of 1st stage of labour and a mean 23% reduction in 2nd stage as compared to Placebo group respectively. Blood loss >500ml was observed in 2% patients. Otherwise there were no adverse effects on mother or foetus.

**Conclusion:** Phloroglucinol shortens the duration of labour, is non toxic to both mother and fetus and does not cause primary post partum haemorrhage (JPMA 55:270;2005).

### **Introduction**

The problems and hazards of prolonged labour, both for the mother and foetus have been recognized for many years. The mother is exposed to high risk of infection, ketosis and obstructed labour while the foetus faces the danger of infection, asphyxia and excessive cranial moulding. O'Driscoll at the National Maternity Hospital, Dublin, introduced the concept of active management of labour and this has influenced obstetricians to change their outlook regarding the management of first stage of labour.<sup>1</sup> Active management of labour is associated with a low incidence of prolonged labour and low cesarean section rate.<sup>2</sup> Protraction of the first stage of labour, one of the components of prolonged labour, does not necessarily result in less than optimal uterine contractility. Its cause is multifactorial and cervix dilatation is the end result of these factors. Although methods to increase uterine contractility such as amniotomy and use of oxytocics have been shown to accelerate cervical dilation, yet these methods are not without complications.<sup>3</sup> Sedatives and belladonna Alkaloids have been tried to hasten cervical dilatation but many have adverse effects on mother and fetus.<sup>1</sup> Spasmolytics and spasmolytics mixtures are administered to facilitate dilatation of the cervix during delivery and to shorten first stage of labour.<sup>4</sup> An ideal anti-spasmodic for accelerations of cervical dilations should have a prompt and long lasting action, no adverse effects on uterine contractility and be free from risk of uterine inertia. It should also have minimal side effects in the mother and foetus.<sup>5</sup>

Phloroglucinol is one of spasmolytics, primarily used for gastrointestinal tract colic.<sup>6</sup> The drug was extensively used during 1970s and early 1980s for augmentation of labour. There has been a resurgence of interest in the subject.

To our knowledge, there has been no double blind controlled study to evaluate the routine use of this drug to accelerate labour. We evaluated its efficacy for the augmentation of labour in a randomized controlled trial keeping above mentioned points in view.

### **Methods**

#### **Participants and Eligibility**

A randomized controlled trial was conducted in labour ward of Gynae B unit Khyber Teaching Hospital Peshawar from 1st January 2004 to 30th June 2004, to evaluate the effect of Phloroglucinol on the process of labour.

Sample size was 100 and sampling technique was convenient sampling. Inclusion criteria was labouring patients including both primigravida and multigravida, in active phase of uncomplicated labour (active phase was defined as 3 cm or > cervical dilatation with regular uterine contractions), having singleton foetus, with cephalic or breech presentations and period of gestation 34 weeks or more. Women with any obstetrical, surgical and severe medical complications such as heart disease and eclampsia, with period of gestation <34 weeks, and twin pregnancy were excluded. An informed consent obtained from all patients.

A complete history was noted and examination of patient performed. Routine investigations (FBC, urinalysis, random blood sugar, BT, CT, CTG) were performed. Fifty patients in the study group received phloroglucinol 40mg (4ml) i/v and 50 patients in the control group received placebo (distilled water) 4ml i/v at 0 hours. Dose was repeated after 60 minutes. Neither patient nor observer knew the content of the injection. Half hourly monitoring of

vital signs, uterine contractions, foetal heart rate was done. Labour progress was plotted on partogram. All data pertaining to labour events, maternal and neonatal outcome, adverse effects of drug or placebo (nausea, vomiting, giddiness, palpitations, tachycardia, hypotension/ hypertension, dry mouth, blurring of vision, foetal heart rate) were recorded. Amount of blood loss after the second stage was estimated subjectively by the attending doctor and objectively by weighing the soaked pads. Blood loss of >500ml was considered abnormal. Follow up of the patients was done till 24 hours after delivery.

Three hypotheses were tested in the study. The first was that Spasmolytics like Phloroglucinol can safely reduce the duration of labour, secondly they do not have any maternal and foetal adverse effects and finally do not cause primary postpartum hemorrhage.

The primary out come measure was duration of labour. The secondary was rate of cervical dilatation, foetal outcome, any maternal side effect and effect of drug on blood loss after second stage of labour. Data was collected by the attending doctor and entered on the proforma.

Power analysis to estimate the sample size was not possible because there was no consensus on how much reduction in labour duration is of medical importance. (one of the parameters of the equation in power analysis). Therefore a sample size of 100 was taken after considering the number of patients attending the labour ward.

Patients were randomized in double blind fashion in two groups. Hundred identical paper slips (with name of drug written on 50 and placebo written on other 50) were kept in a jar. For each patient the doctor on duty picked up the slip from the jar. The slip was then numbered corresponding to serial number of the patient and kept in another jar. Neither patient nor the doctor knew the contents of the injection. During labour, patients were asked which treatment they had received (phloroglucinol or distilled water) at 3 points in time. The patients were then asked to indicate on what basis they believed the drug to be phloroglucinol or placebo.

The data was analyzed on an intention to treat. Mean (SD) and percentages were calculated. Student t-test was used to compare mean differences between two groups. The results of these two groups were analyzed for statistical significance using student t-test on SPSS version 11 and P-value <0.05 was considered significant.

## Results

Flow diagram shows flow of participants through each stage in this trial. Patients were recruited and follow up was done from 1st January 2004 to 30th June 2004.

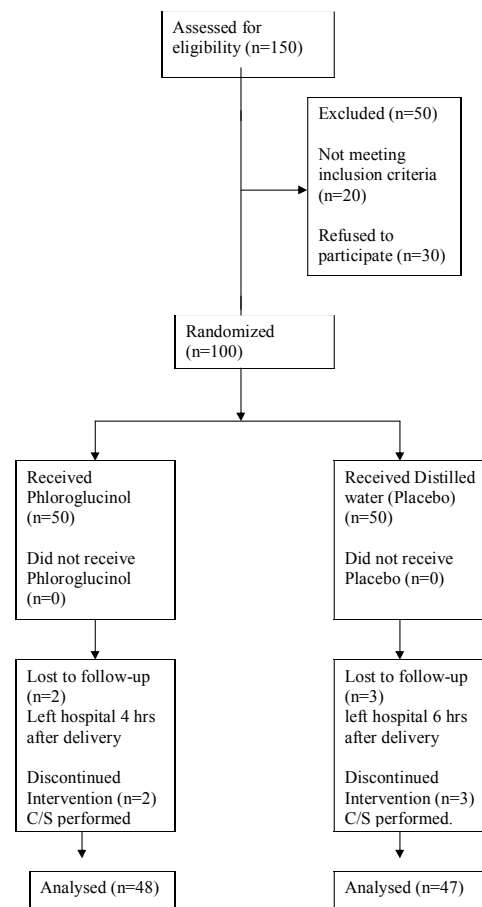


Figure. Flow diagram shows flow of participants through each stage in this trial.

Table 1 shows baseline demographic and clinical characteristics of the patients. The primary analysis was intention to treat and involved all patients who were randomly assigned. Two patients in drug group and 3 patients in placebo group were removed from consideration because they developed foetal distress and were delivered by caesarean section. Therefore 48 patients from drug group and 47 from placebo group were included in analysis.

**Table 1. Baseline characteristics of patients.**

Characteristics	Drug group (n=50) Mean (S.D.)	Placebo group (n=50) Mean (S.D.)	P -value
Age, years.	26.42 (6.09)	25.84 (5.38)	0.621
Height, cm	155.12 (3.37)	155.68 (3.06)	0.315
Weight, kg	66.82 (4.52)	69.04 (3.73)	0.643
Period of gestation (weeks)	38.64 (1.26)	38.72 (1.35)	0.779

Table 2 shows summary of results for primary outcome measures.

The average duration of observed active phase of first stage of labour was shortened by almost 2 hrs in patients receiving phloroglucinol. The mean durations of the observed active phase of first stage of labour and second stage of labour in group A were 66.15% and 77.06% of the corresponding values in the control group. The mean duration of 3rd stage of labour was not statistically significant. The mean total duration of labour in group A was 68.69% of group B.

**Table 2. Summary of results for Primary outcome measures.**

Stage of Labour	Study group (min) Mean (S.D.)	Control group (min) Mean (S.D.)	P-value
Active First stage (Observed)	227.74 (13.60)	344.26 (9.49)	0.001
Second Stage	35.02 (11.93)	45.44 (13.34)	0.001
Third stage	8.92 (2.52)	8.32 (2.49)	0.219
Total duration of labour	273.40 (25.27)	397.98 (16.25)	0.000

Table 3 shows summary for secondary outcome measures.

Rate of cervical dilatation was 0.87 cm/hr faster in group A as compared to group B (p-value 0.000). The mode of delivery was not altered in two groups. Frequencies of normal vaginal delivery was 80% and 85% in the study and control groups respectively. In group A, 2 patients (4%) and 3 in control group (6%) had outlet forceps delivery due to foetal distress whereas 2 patients (4%) in study group and 3 patients (6%) in control group underwent cesarean section for foetal distress and non-progress of labour. There were 3 patients (6%) in study group and 2 patients (4%) in control groups, who had assisted breech deliveries. Neonatal outcome as assessed by Apgar Score at 1 minute (9.74 in study group vs. 9.14 in control group) and at 5 min (9.95 in study group vs. 9.80 in control group) were similar in both groups. No side effects like nausea, vomiting, hypotension, dry mouth, were noted in any of the groups. There were no complications like cervical tear and vaginal lacerations in either group. Only 2% of patients in study group had primary post partum hemorrhage due to uterine atony as compared to 2.1% in control group. The difference was not statistically significant ( $P>0.05$ ).

Another interesting finding was analgesic action of the drug. Patients in drug group were calmer and intensity of labour pains was lesser as compared to control group. They did not need analgesia while patients in control group did so, but analgesic effects were not studied in detail.

**Table 3. Summary of results for Secondary outcome measures.**

Measures	Drug Group	Control Group	P-value
	Mean (S.D.)	Mean (S.D.)	
Rate of Cervical Dilatation (cm/h)	2.14 (0.36)	1.27 (0.36)	0.000
Fetal outcome (apgar Score)			
At 1 Minute	9.74 (0.44)	9.14 (0.77)	0.000
At 5 Minutes	9.95 (0.20)	9.80 (0.39)	0.033
Blood loss after second stage (ml)	406.59 (73.90)	428.0 (64.51)	0.006
Maternal side effects	0.00	0.00	-

## Discussion

In the presented study, the duration of active 1st stage of labour was 116.52 minutes i.e. 33.62% shorter and second stage was 10.42 minutes i.e. 22.93% shorter in study group. The differences were statistically significant and the results are comparable with the studies conducted by Blasko<sup>7</sup> and Sharma<sup>8</sup>, who reported 22% and 53% respectively decrease in the duration of 1st stage. Similar results have been reported by Himangi.<sup>1</sup> The study conducted by Hudecet<sup>4</sup> is in discordance with our study but in that spasmolytic was used in latent phase of labour instead of the active phase. No toxic effects were noted in either mother or foetus and results are comparable with the study conducted by Ahmad<sup>5</sup>, while use of other spasmolytics are associated with side effects as reported by Sharma.<sup>8</sup> Only 2% patients had primary postpartum hemorrhage in our study. Similar results have been reported in the study conducted by Ahmad.<sup>5</sup> However, Singh<sup>3</sup> reported 18% incidence of PPH due to uterine atony with the use of spasmolytics but they used Drotaverine hydrochloride not phloroglucinol. This incidence is statistically significant and limits the use of Drotoverine in labour. In our study 7% of patients had pregnancy induced hypertension, 2% had diabetes mellitus and 4% had previous cesarean section. Although the number of patients with these complications were not large enough but still it is suggested that phloroglucinol can be used in patients with above mentioned complications with no toxic effects and a good outcome. Further randomized controlled trials are needed to establish its efficacy in such cases as well. +In our study, all patients with <37 weeks gestation, delivered healthy babies showing that phloroglucinol can be used in patients with preterm labour without any risk of respiratory depression of foetus.

The drug appeared to have analgesic action which was an observational finding. Since majority of women were already in labour at the time of selection, calculation of exact duration of first stage of labour was not possible. The second dose of drug was given one hour after the 1st dose. Some patients may not need this and just one injection could be enough. In our study we did not segregate primigravida and multigravida while calculating the duration of labour. The drug may have different effects on both.

In conclusion, Phloroglucinol shortens the duration of labour, is non toxic to both mother and foetus and does not cause uterine atony. It also has an analgesic action. Spasmolytics as phloroglucinol have a definite role in obstetrics.

This study was approved by ethical committee of College of Physicians and Surgeons Pakistan and also by institutional local ethical committee. It was self financed.

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