

Effectiveness of Phloroglucinol to accelerate labor in Primigravidas at term: Double blind, randomized controlled trial

SHABNAM TAHIR, MAIMOONA LIAQAT, SAIMA JABEEN, SHAHZIA RASUL

ABSTRACT

Aim: To study the efficacy of phloroglucinol for shortening of labor in primiparous women.

Setting: Department of Obstetrics and Gynecology, Shalamar Teaching Hospital Lahore.

Study design: Double blind randomized controlled trial.

Method: One hundred women in active phase of spontaneous and uncomplicated labour were selected by convenient sampling from Dec, 2009 to May, 2010 and divided into study group (A) and control group (B). Both the study group (n=50) and control group (n=50) received phloroglucinol 4ml (40mg) and placebo (distill water) 4ml intravenously respectively. Progress of labour was plotted on partogram. The primary outcome measure was duration of labor. Secondary outcome measures were blood loss at delivery, rate of cesarean section, and neonatal APGAR scores.

Result: The mean duration of the first of stage labor in the control group was 311.12 minutes, compared with 203.06 minutes in the study group ($P=0.004$). Similarly mean duration of combined first and second stage of labour was also significantly shorter in study group as compare to control group 230.09 minutes & 350.20minuts respectively ($P=0.005$). There was no significant difference in the duration of third stages of labor ($P=0.194$), amount of blood loss at delivery and neonatal Apgar scores between two groups. There was a slightly higher rate of caesarean section in the control group as compared to study group but it was statistically insignificant.

Conclusion: Phloroglucinol shortens the duration of labour effectively. It does not increase the risk of primary post partum hemorrhage and is not associated with any apparent adverse maternal or neonatal outcomes.

Keywords: Labour, phloroglucinol, neonate, mother. first stage, duration

INTRODUCTION

The management of labor is both an art and a science. For decades health providers have worked to manage labor actively and safely, with the goal of shortening the duration of painful labor, reducing the caesarean section rate and complications in the fetus and mother. The safety and efficacy of active management of labor has been demonstrated by several prospective clinical randomized trials^{1,2,3}.

Labour is a natural physiological process characterized by progressively increasing uterine contractions, cervical dilatation and effacement along with descent of fetus through birth canal. Prolongation of labour may cause not only psychological trauma to the mother but also increases incidence of fetal and maternal complications like asphyxia infection and obstructed labor⁴. Active management of labour is being practiced in the clinical practice by obstetricians all over the world. Attempts to accelerate labour and there by shortening its duration with out jeopardizing fetal and maternal out come is welcomed to both mother and obstetrician.

Programmed labor protocol is active management of labour, analgesia and monitoring of events of labour using a partogram.⁵ Uterine activity and rate of cervical dilatation are two basic factors which determine the duration of labour. Various drugs have been tried over last few decades which accelerate labour either by increasing uterine activity or rate of cervical dilatation. Oxytocin, prostaglandin and amniotomy have been shown to accelerate cervical dilatation by increasing uterine contractility but these methods are not without complication. Sedatives and belladonna Alkaloids have been tried to hasten the cervical dilatation but many have adverse effects on mother and fetus. In recent years spasmolytics have been frequently used to facilitate cervical dilatation and to speed up the process of labour. The anticholinergic spasmolytics has some undesirable side effects⁶. Drotaverine being an anticholinergic when used for cervical dilatation was associated with nausea vomiting and dry mouth. Hence non anticholinergic spasmolytics are of preferred choice in pregnancy... Therefore the need of hour is an ideal spasmolytic that would help in the dilatation and effacement of cervix to shorten the duration labour with out interfering with the

Department of Obstetrics & Gynaecology, Shalamar Medical College/Hospital, Lahore
Correspondence to Dr. Shabnam Tahir Email: tahirsaleem30@hotmail.com Cell: 03334427061, 03004345924

uterine contractility and not causing any adverse effects on mother and fetus

Phloroglucinol is one of spasmolytic, primarily used for gastrointestinal tract colic. The drug has been extensively used during 1970s and early 1980s for augmentation of labor. Phloroglucinol has been successfully used to enhance cervical dilatation during labour without being any apparent side effects on mother and fetus⁷. There has been very few double blind controlled studies to evaluate the routine use of this drug. Many studies have been carried out to evaluate the effects of the phloroglucinol on cervical dilatation; although majority of these studies demonstrated the efficacy of phloroglucinol in acceleration of labor but some studies have used oxytocin in active phase of labor to augment it, which would certainly affect the duration of labor and increase bias in the results and some studies have included both primiparous and multiparous patients which also affect the results, because the duration of labor is shorter in multiparous women, even without any method of augmentation. We evaluated its efficacy by a randomized controlled trial by keeping above mentioned points in view. Therefore, in our study, we enrolled only primigravida women in spontaneous labor with no other means of augmentation.

The specific objectives of this study were to assess whether Phloroglucinol is effective in hastening cervical effacement and dilatation, thus shortening the duration of labor in primiparous women without labor augmentation. We also intended to determine whether the use of phloroglucinol in the first stage of labor has any associated increases in complications, such as an increase in blood loss or the rate of cesarean deliveries, or a decrease in neonatal Apgar scores.

MATERIAL AND METHOD

A double blind controlled randomized trial was conducted in Gynae & obstetric department of Shalamar teaching hospital to evaluate the effect of phloroglucinol on the process of labour. Phloroglucinol was compared with control in shortening duration of active phase of labour, its effect on second and third stage of labour and its adverse effects in mother and fetus. Sample size was 100 and sampling technique was convenient sampling. Power analysis to estimate the sample size was not possible because there was no consensus that how much reduction in labour is of medical importance. So a number of 100 was taken after considering number of patients attending the labor ward. Enrollment for this study was commenced in Dec, 2009 and was completed in May, 2010. Women

included in the study were all 18 to 35 years of age, primiparous, had singleton fetus with vertex presentation at term (gestational age between 37–41 weeks) and had no chronic or pregnancy-induced medical illnesses like hypertension and diabetes. None of the women had any contraindications to vaginal delivery, and all were in established, spontaneous labor with either intact membranes or spontaneous rupture of membranes of less than 12 hours. Exclusion criteria included previous uterine scarring, malpresentation, antepartum hemorrhage, twin pregnancy, prolonged premature rupture of the membrane (more than 12 hours), epidural analgesia and those requiring augmentation of labor with syntocinon. Established labor was defined as the presence of regular uterine contractions (3 per 10 minutes) associated with progressive cervical effacement and dilatation.

An informed consent was obtained from all patients participating in the study. Once the patient was admitted in active labor, a history and physical examination was conducted by the attending physician. All base line investigation including blood group, complete blood count, random blood sugar, urine complete examination and CTG were performed. Women in the study group (n=50) received 40mg (5ml) of phloroglucinol intravenously and women in the control group (n=50) received 5ml of Placebo (distill water) intravenously during active phase of labor, at 0 hours and repeated after 60 minutes. Neither patient nor the observer knew the content of the injection. A partograph was maintained throughout labor. Duration of the first stage was calculated from the time of cervical dilatation of 3–4 cm in active labor to full dilatation of cervix by vaginal examination conducted every 2 hours. Oxytocin augmentation was initiated if the initial progress of labor (as assessed through partograph) was unsatisfactory due to ineffective uterine contractions. These patients were excluded from the study. Fetal and maternal monitoring was done half hourly including vital sign record, uterine contractions and fetal heart rate, maternal and neonatal outcome, adverse effects of drug and placebo were recorded. Routine amniotomy was performed for all women in established labor who were found to have cervical dilatation of ≥ 4 cm, and who had not had spontaneous rupture of membranes. Intervention by cesarean delivery or instrumentation was performed by the usual obstetric indications. Amount of blood loss was measured after delivery subjectively by the attending doctor and objectively by weighing soaked pads. Blood loss more than 500ml was considered to be abnormal. The patient was kept under observation for 24 hours after delivery.

Two hypothesis were tested in the study ,first was that spasmolytic like phloroglucinol can effectively reduce the duration of labour and second was that it does not have any maternal or fetal harmful effects . The data was entered in SPSS and analyzed. Means and percentage were calculated, The result of two groups were analyzed to compared for statistical significance using student t test and P value <0.05 was considered significant.

RESULTS

One hundred patients were randomized in two groups .Phloroglucinol(Group A) and Placebo(Group B). The duration of first stage of labour in group A was 203.06±9.21 minutes and in group B was 311.12±10.89 minutes. The difference was statistically significant (P-value - 0.004).Duration of second stage of labour in group A was 27.02± 4.18 minutes and in group B it was 39.08± 5.29min.(P-value -0.001).The duration of both first and second stage of labour in group A was 230.09±3.39 min

while in group B it was 350.20±16.18 minutes, which is again statistically significant. Duration of third stage of labor was 7.66 ±1.21 minutes in patients of group A while for group B it was 6.74±0.92 minutes which is not statistically significant (p- value 0.194). There was no significant differences between the neonatal APGAR score recorded at 1 and 5 minutes between two groups. No side effects like nausea, vomiting . dry mouth and tachycardia were noted in both groups. In both groups no case of postpartum hemorrhage was seen. In group A, 86% patients were delivered vaginally while in group B, 76% patients successfully achieved vaginal delivery. There was a slightly higher rate of C-section 12(24%) in the control group versus 7(14%) in study group; however, the difference was not statistically significant. (P= >0.05). There were 12 caesareans in the control group, five cases due to failure to progress and seven cases due to fetal distress, while in the study group there were seven cases, four due to failure to progress and three due to fetal distress.

Table 1: Baseline characteristic of patients

Characteristics	Drug group (n=50)Mean(SD)	Placebo group(n=50)Mean(SD)	P-value
Age(yrs)	24.06 ±1.21	26.12 ±0.89	0.655
Weight(kg)	68.04± (3.39)	67.86 ± (4.54)	0.644
Height(cm)	156.68 ± (3.05)	156.12± (3.37)	0.325
Period of gestation(weeks)	38.6 ±1.25)	38.68± (1.26)	0.720

Note: For patient characteristics, data are expressed as means (SD – standard deviation).

Table 2 :Summary of results for primary outcome measure (Mean duration of labor)

Stages of labor	Study group Mean (SD)	Control group Mean (SD)	P-value
First stage of labor (minutes)	203.06 ± 921	311.12 ±10.89	0.004
Second stage of lab (minutes)	27.02± 4.18	39.08 ± 5.29	0.001
First + second stage of labour (minutes)	230.09 ± 3.39	350.20± 16.18	0.005
Third Stage of labor (minutes)	7.66 ± 1.21	6.7 ± 0.92	0.194

Note: For primary out come measure, data is expressed as means (SD – standard deviation).

Table 3:Summary of results for secondary outcome measures.

Variables	Group A Mean (SD)	Group B Mean (SD)	P-value
Birth weight (kg)	3.30 ± 0.15	3.12 ± 0.50	>0.05(NS*)
APGAR score(9- 10 verses <9)	45/5	43/7	>0.05(NS*)
Blood loss after delivery(ml)	410±73.00	415.35 ±65.50	>0.05(NS*)

Note: For secondary outcome measures ,data is expressed as means (SD – standard deviation ,NS * - not significant).

DISCUSSION

In modern obstetric a drug that offers convenience and assure shortening of first stage of labour without compromising mother and fetus is always welcomed .Phloroglucinol facilitates the cervical dilatation and effacement without compromising uterine contractions. In our study duration of first stage of labour was 203.06+-9.91 minutes in study group and 311.12+-10.8 9 minutes in control group (P-0.004). Tabassum S, Afridi B⁴, also concluded in their study that use of phloroglucinol reduces duration of labour effectively. In their study in patients receiving phloroglucinol there was 34% reduction of first stage

of labour and a mean 23% reduction in second stage of labor (P-0.001). In another study conducted by S Batool, Phloroglucinol group was compared with drotaverine group for acceleration of labor and it was reported that there is 46.85 minutes (24.49%) reduction in first stage of labor in phloroglucinol group than Drotaverine group⁸

In our study, the difference in the first stage of labor between two groups was 108.06 minute and second stage of labour was also comparatively short in study group than control group (27.02 min versus 39.08 min, P-0.001) .However the women were subjected to examination at regular 2 hour interval but a primigravida can be fully dilated before she

feels the pressure of giving birth, it is impossible to determine the exact time of cervical full dilatation, thus error in measuring the length of first stage of labor may have been ± 1 hr to ± 2 hr, rendering the clinical significance of the result marginal. To assess this possibility, we repeated the analysis by using the duration of combined first and second stage of labor which was 230.09 min and 350.20 minutes in study and control group respectively and result remained nearly the same demonstrating statistically significant difference in the study and control group ($P=0.005$). Thus any error in the measurement of first stage of labor was not contributory to the outcome of study. There was no difference in the duration of third stage of labor, 7.66 min versus 6.74 min in study and control group respectively ($P=0.194$). The results of our study are important because of several reasons. Short duration of active phase of labor not only reduces the duration of painful labor but also the incidence of chorioamnionitis and neonatal sepsis. A reduced need of Opioids analgesic which are usually associated with respiratory depression is a substantial benefit of reduced duration of active phase of labour. Phloroglucinol is a spasmolytic, primarily used for gastrointestinal colic. It has strong relaxing effect on the smooth muscles in spasm. This relaxing effect is very much pronounced in the intestine and urethra and particularly zero on smooth muscles of blood vessels. As for uterus it relaxes lower part of uterus and cervix without interfering with uterine contractility so it does not interfere with labour and does not cause postpartum hemorrhage. No atropine like side effects have been noted with its use as with other antispasmodics and it is non toxic both for the mother and fetus⁷.

Hudecek R, Nagy J in his study concluded that application of spasmolytics did not significantly affect the process of delivery but in this study six different kinds of spasmolytics were used in latent phase of labour⁹.

In our study blood loss after delivery was 410.50 ml in the study group while in control group it was 415.35 ml ($P>0.05$). No case of postpartum hemorrhage was noted in both groups. Many other studies support our results. Drotaverine, another spasmolytic has also been proved to be a good agent for cervical dilatation in different studies but it was noted to be associated with primary postpartum haemorrhage^{8,10}. These results limit the use of Drotaverine Hydrochloride in labour. Although the number of patients with these complications were less but it is suggested that in such patients phloroglucinol can be used safely as it does not cause uterine atony. There was no significant difference in mode of delivery, 86% pts in phloroglucinol group were delivered vaginally while 14% underwent caesarean

section as compared to 76% and 24% respectively in control group ($P>0.05$).

Moreover there was no significant difference in fetal birth weight, and neonatal APGAR score between two groups. No toxic effects were noted in the mother and fetus like nausea, vomiting, dry mouth tachycardia with the use of phloroglucinol and results are comparable with the study conducted by Ahmed⁷.

In our study 40% pts delivered with one injection of phloroglucinol 56% patients with two injections of phloroglucinol and 4% patients three injections while none of them required fourth injection. These results are comparable with the study conducted by S Batool⁸. So Phloroglucinol definitely has a role to shorten the duration of labour⁴.

CONCLUSION

Phloroglucinol has beneficial effects in facilitating cervical dilatation and shortening the duration of active phase of labor significantly without any undesirable effects on fetus. It has no effects on third stage of labour and does not interfere with uterine contractility. There is no increase in rate of caesarean section rate and neonatal outcome is favourable. There are no major side effects or symptoms of intolerance. Use of phloroglucinol is advocated to accelerate the rate of cervical dilatation and hence to shorten active phase of labour. Phloroglucinol has a definitive role in obstetric.

REFERENCES

- 1- Lopez-Zeno JA, Peaceman AM, Adashek JA, Socol ML. A controlled trial of a program for the active management of labor. *N Engl J Med.* 1992;326:450-454.
- 2- Frigoletto FD, Jr, Lieberman E, Lang JM, et al. A clinical trial of active management of labour. *N Engl J Med.* 1995;333:745-750.
- 3- Sadler LC, Davison T, McCowan LM. A randomised controlled trial and meta-analysis of active management of labour. *BJOG.* 2000;107(7):909-915.
- 4- Tabassum S, Afridi B, Aman Z; Phloroglucinol for acceleration of labour: Double blind randomized controlled trial; *J Pak Med Assoc*, Vol. 55, No. 7, July 2005, 270-273.
- 5- Meena J, Singhal P, Chaudhary D. The programmed labour. *J Obstet Gynecol* 2006; 56: 53-55.
- 6- Kulkarni SK, Antispasmodic- A New Perspective. *JAMA India* 2001; 4 (8):119-121.
- 7- Ahmed S, Rauf B, Shafiq A. Use of spasfon in labour. *J Himont med* 2002; 1: 14-8
- 8- B salma, Zaib-un nisa. Efficacy and safety of drotaverine and phloroglucinol in first stage of labor, *Pak J Surg* 2011; 27(1):39-43
- 9- Hudecek R, Nagy J, Unzeeitig V. The effect of spasmolytic on dilatation of uterine cervix. *Ceska Gynaekol* 1997; 62: 11-14
- 10- Singh K.C, P Jain, Goel N, Sexena A. Drotaverine hydrochloride for augmentation of labour. *Int J Gynaecol obstetric* 2004;84:17-22.

