ORIGINAL ARTICLE

Efficacy and safety of drotaverine and phloroglucinol in first stage of labour

Salma Batool Naqvi, Zaib-Un-Nisa Haroon

Abstract

Objective: To compare the efficacy and safety of drotaverine and Phloroglucinol in the duration of first stage of labour. Main outcome measure were duration of first stage of labour, rate of cervical dilatation, maternal and fetal side effects and mode of delivery. Student t- test applied for statistical analysis.

Study design: Randomized controlled trial.

Setting: Department of Obstetrics and Gynaecology, Liaquat National Hospital and Medical College, Karachi, Pakistan.

Subject: One hundred women in active phase of uncomplicated labour. 50 patients in even numbers received phloroglucinol (group A) and 50 patients in odd numbers received drotaverine (group B).

Results: Both phloroglucinol and drotaverine appears to be effective in the acceleration of labour but duration of first stage of labour was 46.85 minutes (24.49%) shorter and cervical dilatation 0.38 centimeters/ hour (15.32%) faster in phloroglucinol group as compare to drotaverine group which was statistically significant ($p< 0.05$), no fetomaternal side effects seen in phloroglucinol group but minor side effects seen in drotaverine group. No Caesarean section was required and less number of injections required in phloroglucinol group. It also has analgesic effect.

Conclusion: Both drugs are effective in acceleration of labour, however phloroglucinol is more effective in shortening the total duration and first stage of labour and safe with no fetomaternal side effect, having analgesic effect, less number of injections required and, no Caesarean section required.

Keywords: Phloroglucinol, Drotaverine, Efficacy, Labour.

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Introduction:

Labour is a multifactorial process which involves myometrial contraction, cervical ripening and dilatation and the expulsion of fetus and placenta in an orderly manner. The first stage of labour in primigravida lasts about 12-16 hours and in a parous woman 6-8 hours.[1] Painless and short labour is desired by every mother and is a constant aim for obstetricians.[2] The active management of labour is associated with a low incidence of prolonged labour and low Caesarian section rate.[3] Protraction of first stage of labour is one of the components of prolonged labour, does not necessarily result in less than optimal contractility. Its cause is multifactorial and cervical 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.[4] Spasmolytic drugs help to relieve the cervical spasm and facilitate cervical dilatation during first stage of labour.[1] An ideal antispasmodic for acceleration of cervical dilatation should have a prompt and long lasting action, no adverse effects on uterine contractility, be free from risk of uterine inertia. It should also have minimal side effects in the mother and fetus.[5] Drotaverine is an isoquino-

line derivative which binds to smooth muscles and change their potential and permeability. It is claimed to be safe with no side effect and no drug interaction. It inhibits phosphodiesterase enzyme(PDE) which break cyclic adenine mono phosphate (cAMP) and guanine mono phosphate(cGMP)which play an important role in regulation of smooth muscles.[6] Phloroglucinol has a strong relaxing effect on the smooth muscle in spasm. This relaxing effect is very pronounced in intestine and urethra and particularly zero on the smooth muscles of blood vessels. As for the uterus, it softens the lower portion and cervix without inhibiting uterine contractions in the body; hence it does not interfere with labour and does not cause bleeding after delivery. No atropine like effect has been noticed with its use as with other anti spasmodics and it is nontoxic to the fetus[5].

Phloroglucinol and drotaverine are commonly used pharmacological agents in labour room in many hospitals, to decrease the duration of first stage of labour in order to prevent the prolonged labour. Because the morale of most women start to deteriorate after six hours in labour and after twelve hours the rate of deterioration significantly accelerates, there is a greater incidence of operative vaginal deliveries, Caesarean section and also fetal hypoxia. So our rationale is to find which drug is more effective in shortening the duration of labour by accelerating the cervical dilatation and safe, having less or no feto-maternal side effects. In this study, we have also assessed the incidence of operative (vaginal/ Caesarean) deliveries.

Methodology:

Randomized controlled trial was conducted in Gynaecology and Obstetrics Unit at Liaquat National Hospital, Karachi from 10th August 2007 to 10th August 2008 to compare the efficacy and safety of phlorolglucinol and drotaverine in duration of labour. Sample size was 100 and sampling technique was purposive. 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 fetus, with cephalic presentation and period of gestation 37 weeks or more. Women with any obstetrical, surgical and severe medical complication such as heart disease and eclampsia, with period of gestation < 37 weeks, and twin pregnancy, malpresentation, cephalo-pelvic disproportion were excluded. An informed consent obtained from all patients.

A complete history was noted and examination of patient performed. Routine investigations (Complete blood count, urine analysis, random blood sugar, clotting profile, CTG) were performed. Fifty patients in the group A , received phloroglucinol 40mg i/v and 50 patients in the group B received drotaverine 40mg i/v at zero hour. Dose was repeated after 60 minutes. Hourly monitoring of vital signs, uterine contraction, and fetal heart rate was done. Labour progress was plotted on partogram. All data pertaining to labour events, maternal and neonatal outcome, adverse effects of drugs (nausea, vomiting, palpitations, tachycardia, hypotension/ hypertension, dry mouth, blurring of vision, fetal heart rate{Tachycardia, Bradycardia}) were recorded.

Two hypotheses were tested in this study. The first was that spasmolytics like Phloroglucinol and Drotaverine can safely reduce the duration of labour by improving the rate of dilation of cervix, secondly they do not have any maternal and fetal adverse effects.

Data was collected by attending doctor and entered on the proforma.

Data analysis procedure was SPSS version 10 + SD for age of the patient and duration of 1st stage of labour frequencies and percentages was calculated for side effects. Student “t” test was applied to compare duration of 1st stage of labour. Chi-Square test was applied to compare side effects. P-value < 0.05 was taken significant.

Results:

One hundred patients randomized to the two groups; phloroglucinol (group A) and drotaverine (group B). 17(34%) of patients were primi-

gravidas and 33(66%) of patients were multigravidas in group A while 21(42%) of patients were primigravidas and 29(58%) of patients were multigravidas in group B.

Mean period of gestation was 38.6 ± 1.16 weeks and 38.6 ± 1.05 weeks and mean age in years was 27.3 ± 3.71 and 27.3 ± 3.82 in group A and B respectively and were not statistically significant. 44 (88%) patients in group A and 43 (86%) patients in group B had spontaneous labour while 6 (12%) patients in group A and 7 (14%) patients in group B had induced labour due to various indication and method of induction was misoprostol. Artificial rupture of membrane (ARM) was done in 70% and 68% of patients in group A and B respectively. There was no significant difference in the effacement of the cervix, station of presenting part or position of the cervix. The numbers of injections required were least in the phloroglucinol group. A total of 18 (36%) women delivered with one injection, 30 (60%) delivered with two injections, 2 (4%) with three injections and no one required fourth injection while in drotaverine group 8 (16%) women delivered with one injection, 21 (42%) delivered with two injections, 13 (26%) delivered with three injections and 6 (12%) required fourth injection. A total number of 84 and 113 injections required in group A and B respectively. Mode of delivery was not altered in two groups but four patients in group B were delivered by cesarean section, two were due to meconium stained liquor so excluded from study and two due to non descent of head after full dilatation of cervix were excluded from the study. So 50 patient in group A and 48 patients in group B were included for analysis.

The duration of first stage of labour in group A was 144.40 ± 30.78 minutes and group B was 191.25 ± 76.89 minutes, difference was statistically significant ($p < 0.05$) so duration of first stage of labour was 46.85 minutes (24.49%) faster in group A (as shown in table.1) . Rate of cervical dilatation in group A was 2.86 cm per hour and 2.48cm per hour in group B although difference was not statistically significant but dilatation of cervix 0.38(15.32%) cm per hour faster in group A as compare to group B.

Frequency of normal vaginal delivery was 49(98%) and 44 (88%) in group A and B respectively. 1 (2%) in group A and 2 (4%) in group B had vaccum vaginal delivery due to fetal distress (as shown in figure I). Duration of second stage of labour was 22.40 ± 10.50 minutes and 23.91 ± 11.05 minutes and third stage of labour was 6.51± 2.71 and 6.52 ± 2.55 in group A and B respectively and difference was not statistically significant.

Neonatal outcome as assessed by APGAR score in one minutes was good (>7) in phloroglucinol group in all cases but in drotaverine group 3 (6%) babies had satisfactory APGAR score (between 5-7) but after five minutes it was good and no there was need of intensive care unit in any case.

No side effects like nausea , vomiting , hypotension , dry mouth, tachycardia were noted in group A but in group B headache was seen in 2 (4%) , nausea 2 (4%) and dry mouth 1 (2%) of the cases. There were no complication like cervical tear or vaginal laceration and primary post partum hemorrhage seen in both groups.

Table 1: *Stages of labour and cervical dilatation*

	Phloroglucinol Mean (S.D)	**Drotaverine Mean (S.D)**	**P value**
First stage of labour (min.)	144.40 (30.78)	191.25 (76.89)	<0.05
Second stage of labour	22.40 (10.50)	23.91 (11.05)	-
Third stage of labour (min.)	6.50 (2.71)	6.52 (2.55)	-
Total duration of labour(min.)	172.30 (43.98)	221.68 (90.44)	
Rate of cervical dilatation(cm/h)	2.86 (0.74)	2.48 (1.14)	0.52

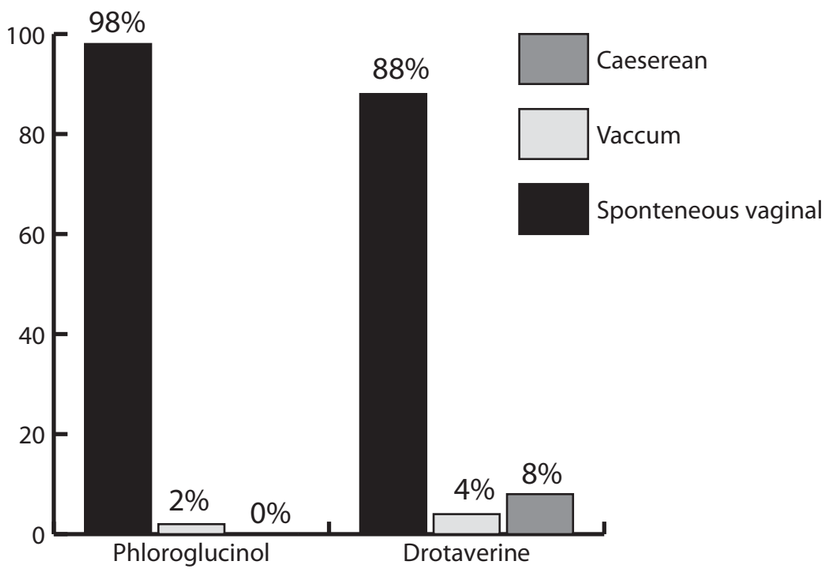

Figure 1: *Mode of delivery*

Another interesting finding was analgesic action of the drug. Patient in group A were calmer and intensity of labour pain was slightly lesser as compared to group B but analgesic effect were not studied in detail, as this was not the objective of the study.

Discussion:

This is a Randomized controlled trial that has compared the efficacy and safety of two drugs (Phloroglucinol and Drotaverine) in shortening the duration of active labour.

Labour is a multifactorial process which involves myometrial contraction, cervical ripening and dilatation and expulsion of fetus and placenta in an orderly manner.[1] in the process of labour, polarity of uterus is maintained by active contraction of upper uterine segment. The driving forces of uterine contraction act upon the cervix to overcome tissue resistance, overacting of circular smooth muscle fibers of the cervix results in cervical spasm which may increase in presence of inflammation, injury or fibrosis of cervix due to fear tension pain syndrome.[6] There are various mechanical and pharmacological methods by which cervical dilatation can be facilitated. Sweeping and stretching of the cervix causes local release of prostaglandins resulting in a reduction in the need for formal induction of labour. Amniotomy, especially done early, augments labour and shortens the duration of labour slightly.[4,8] Amniotomy can be combined with oxytocin for better results. Cervical application of relaxin,[9] estradiol, and hylase has been used with some success. Oxytocin is proven to induce and augment labour but has no pain relieving effect and is generally given intravenously. Prostaglandins have been used in various formulation for induction of labour specially prostaglandin E2 gel for cervical ripening. Unfortunately oxytocin can cause neonatal jaundice.[2]

Spasmolytics and spasmoanalgesics mixtures are administered to facilitate dilatation of cervix during delivery to shorten the first stage of labour. An ideal antispasmolytic have a prompt and long lasting action, no adverse effect on uterine contraction and be free from risk of uterine inertia. It should also have minimal side effect on the mother and fetus.[8]

Phloroglucinol is a spasmolytic, primarily used for gastro intestinal 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 the smooth muscles of blood vessels.

As for the uterus, it softens the lower portion and cervix without inhibiting contraction in the body, hence it does not interfere with labour and does not cause bleeding after delivery, no atropine like effects have been noticed with its use as with other antispasmodics and it is nontoxic to fetus.[5]

Drotaverine hydrochloride or isoquinolone 1, 2, 3, 4-tetrahydro 6, 7 diethoxy -1-(C-3, 4-diethoxy phenyl methylene) hydrochloride is a highly potent spasmolytic agent acting on smooth muscles but it is devoid of anticholinergic effects and it acts through inhibitory effect on phosphodisterase enzymes(PDE), mainly PDE IV. Near term, human myometrium contains a higher proportion of rolipram sensitive type IV PDE isform. Drotaverine inhibits them in turn increases the intracellular concentration of cAMP and cGMP and cause smooth muscles relaxation. It does not cross the placenta and hence no effect on fetus.[6]

In the present study, duration of first stage of labour was 46.85 minutes (24.49%) shorter and difference was statistically significant (<0.05) and cervical dilatation 0.38 cm per hour (15.32%) faster in phloroglucinol group as compare to drotaverine and findings are consistent with the study conducted by Tabassum[8] who concluded that total duration of first stage of labour and rate of cervical dilatation in phloroglucinol group was 227.74±13.60 and 2.14±0.36 cm per hour respectively, in our study it was 144.40 ± 30.78 and 2.86 cm per hour respectively.

Study conducted by Sharma[2] who concluded that duration of first stage of labour and rate

of cervical dilatation in drotaverine group was 194±57.04 minutes and 2.04±0.68 cm per hour and in our study it was 191.25±76.89 minutes and 2.48 cm per hour respectively, so results are comparable with other studies.

No toxic effects were noted in either mother or fetus in phloroglucinol group and results are comparable with the study conducted by ahmed.[5] While use of drotaverine associated with side effects as reported by Sharma[2] no primary postpartum hemorrhage seen in our study as it was 2% seen by Tabassum[6] and Ahmed[5] in phloroglucinol and 18 % reported by Singh[4] due to uterine atony with use of drotaverine hydrochloride.

62.6% of patient delivered after receiving one injection of phloroglucinol as study conducted by Ahmed[5] while in our study 36% of patient delivered with one injection, 60% with two, 4% with three and no patient required fourth injection. 10% of patients delivered with one injection of drotaverine as study conducted by Sharma[2] but in our study 16% of patients delivered with one injection 42% with two, 26 % with three and 12% required fourth injection.

No cesarean section required in phloroglucinol group had 100% normal vaginal deliveries out of which 2% of patients had vaccum delivery while in drotaverine group 92% had normal vaginal deliveries ,out of which 4% of patients had vaccum delivery and 8% had cesarean section.

Conclusion:

Both phloroglucinol and drotaverine appears to be effective in the acceleration of labour but phloroglucinol is superior which further shortens the duration of labour with no fetal and maternal side effect, no increased in cesarean section rate, less number of injection required and also has an analgesic effect. Phloroglucinol has a definitive role in obstetrics.

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