

■ *Original Article*

## Comparative study of efficacy of drotaverine hydrochloride and valethamate bromide with control in first stage of labour

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### Abstract

**Background:** Labour is the most perilous journey a woman has to undertake. Painless and short labour is desired by every woman and is a constant aim for obstetrician. **Objective:** To analyze and compare the efficacy and safety of drotaverine and valethamate with control group on improving cervical dilatation and promoting progress of labour. **Method:** Three hundred demographically similar women, both primigravida and multigravida with a term pregnancy in established labour were randomly divided into three groups. One hundred women (group 1) were given injection valethamate intramuscularly, 100 women (group 2) were given drotaverine and the rest 100 (group 3) were not given any drug. Comparative analysis was carried out as regards to duration of first stage of labour, mode of delivery, maternal side effects and fetal outcome. **Results:** The mean duration of active phase of labour in group 1, 2 and 3 was 254.29±96.621 min, 178.31±73.412 min and 346.31±123.351 min respectively. The duration of injection to end of first stage of labour in valethamate and Drotaverine group was 228.12±84.626min and 168.89±69.576min respectively (p value<0.0001). The duration of injection to delivery in Valethamate was 249.13± 88.321 min and in Drotaverine was 192.56±75.479min (p value<0.0001). There were no serious maternal and fetal adverse effects in any group but minor side effects were more common in valethamate group. **Conclusion:** The reduction of the duration of the first stage of labour was apparently more in drotaverine group as compared to valethamate and control group. Drotaverine was found to be safe with minimal or no adverse effect on the mother and the fetus.

**Keywords:** stages of labour, cervical dilatation, drotaverine, valethamate

### Introduction

Labour is defined as painful uterine contraction that bring about demonstrable effacement and dilatation of the cervix.<sup>1</sup> It is not a pathological process rather it is complex physiological and psychological process with acute pain.<sup>2</sup> Labour is completed within 12-14hrs in about 80% of nulliparous women, whereas it is usually shorter in multipara. It is considered to be prolonged if delivery of the fetus is not completed within 24hrs.<sup>3</sup>

The aim of active management is to reduce the total duration of labour without causing any adverse effects to the mother and fetus.<sup>4</sup> Uterine activity and the rate of cervical dilatation are the two basic factors that determine the duration of labour. Many times it is observed that despite of good uterine contraction, cervix fails to dilate or dilates very slowly and is known as functional cervical dystocia. Methods that aim at minimizing the incidence of functional cervical dystocia and cutting short the first stage of labour are welcomed by both the obstetrician and women. Various drugs like antispasmodics, tranquilizers, prostaglandins and psychotherapeutics measures have been tried over the last few decades which

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accelerate labour either by increasing uterine activity or by accelerating cervical dilatation.<sup>5-10</sup> But majority of these were found to have ill effect on both the mother and fetus.

Valethamate bromide is one of the drug of esocin group which have neurotropic and musculotropic actions that results in relaxation of cervical musculature leading to quick dilatation of the cervix and shortens labour.<sup>11-12</sup>

Recently a new drug, Drotaverine hydrochloride, an isoquinoline used primarily to relieve gastrointestinal and renal colics has been tried and found to be effective in reducing the duration of dilatation stage of labour with excellent results.<sup>13-18</sup>

Drotaverine hydrochloride and Valethamate bromide exert their main effect on the cervix, facilitating its dilatation and can only be used for augmentation of labour in women with established labour preferably with 4 cm dilatation of cervix and good uterine contractions. We chose these two drugs to ascertain their role in augmentation of labour as to whether they can be recommended in routine use.

Shortening the duration of painful first stage of labour without having any effect on mother and fetus is very crucial. However, there were no adequate controlled studies in this subject. This study was conducted to find out the efficacy and safety of Drotaverine and Valethamate with control in our set up.

## Methods

This study is a single blind randomized controlled trial conducted in the Department of Obstetrics and Gynaecology, BPKIHS from March 2007 to December 2007. The study was approved by BPKIHS ethical committee. In this study 300 demographically similar women, both primigravida and multigravida with term pregnancy in early active stage of labour having 2-3 contractions per 10 minutes lasting for 30 seconds and both induced and spontaneous labour in vertex presentation were included. Women with previous uterine scar, malpresentation, multiple pregnancies, antepartum haemorrhage, cephalopelvic disproportion, preeclampsia and other hypertensive disorder, patient with glaucoma and heart disease were excluded from the study. Complete physical examination, obstetric examination, routine investigations (Hemoglobin, urine analysis and blood grouping) was performed in

all cases. Patients were shifted to labour room after they entered into early active phase of labour. Informed consent was taken from women satisfying the inclusion criteria. They were randomly assigned to group 1, 2 and 3 by computer generated randomization and the time was noted. Group 1 consisted of 100 women who were administered an injection of Valethamate bromide (8 mg) intramuscularly every half an hour for three doses. Group 2 consisted of 100 women who were administered one injection of Drotaverine hydrochloride (40 mg) intramuscularly and repeated 2 hourly for maximum of three injections. Group 3 (n=100) acted as a control and were not given any drug. Any change in pulse, blood pressure or any side effects like fever, flushing, dryness of mouth, nausea, vomiting, headache, giddiness, urinary retention seen following administration of drug was assessed and recorded. Maternal monitoring was done by recording the pulse rate every half hourly and the blood pressure every two hourly. Fetal monitoring was done by auscultating the fetal heart rate half hourly. Progress of labour was recorded by observing uterine contractions (intensity, frequency and duration in 10 minutes) and abdominal descent of fetal head. A vaginal examination was performed at every four hours and this was plotted on partograph. Amniotomy was performed once cervical finding was > 4cm or if Bishop's score was favourable. Post amniotomy FHS was noted. Non Stress Test was done if liquor was meconium stained to rule out fetal distress. Augmentation with oxytocin was done if inadequate contractions were documented even after one hour of amniotomy and it was titrated according to labour ward protocol.

Duration of active phase, second and third stage of labour was recorded. Appropriate intervention was done if any abnormality was seen. Amount of blood loss after the second stage was estimated subjectively by the attending obstetrician and objectively by weighing the soaked pads. Blood loss of more than 500ml was considered abnormal. Vaginal delivery was carried out in the usual manner. Cesarean or instrumental delivery was performed as and when indicated. Any significant findings and complications of instrumental vaginal delivery and cesarean section were documented. Pediatrician was called for resuscitation if vacuum or forceps were applied or if there was meconium stained liquor or

after delivery respiratory distress, delayed cry and low Apgar was noted.

### Results

In all the three groups both primigravida and multigravida were included. Mean age in Valethamate, Drotaverine and control was 23.53, 23.09 and 23.38 years respectively. Parity and age had no statistical significance.

**Table 1: Parity distribution**

Gravida	Valethamate	Drotaverine	Control	P-Value
Primigravida	60	56	65	>0.05
Multigravida	40	44	35	>0.05

**Table 2 : Cervical dilatation at the start of study**

Out of 300 patients, 141(47%) had cervical dilatation of 3cm and 159(53%) had cervical dilatation of 4cm. Their distribution in three groups is shown in Table 2.

**Table 3 : Duration of active phase of labour**

Drug	Mean duration (mins)	Standard deviation	P value
Valethamate	254.29	±96.621	<0.0001
Drotaverine	178.31	±73.412	<0.0001
Control	346.31	±123.351	<0.0001

The mean duration in Drotaverine is comparable to Valethamate and control with p value <0.0001.

**Table 4: Comparison of duration between three groups**

Group	Mean difference	P-value
1 vs 2	75.97	<0.0001
3 vs 1	92.03	<0.0001
3 vs 2	168.00	<0.0001

Table 4 shows the comparison of mean difference in duration of active phase of labour among the three groups. It is seen that this difference is comparable and is statistically significant.

**Table 5: Comparison of injection to end of 1<sup>st</sup>stage of labour in two drug groups**

Drug	Mean duration (mins)	Standard deviation	P-value
Valethamate	228.12	±84.626	<0.0001
Drotaverine	168.89	±69.576	<0.0001

The mean duration of injection to end of first stage in two drug groups are comparable and statistically significant with p value <0.0001.

**Table 6: Comparison of injection to delivery interval in two drug groups**

Drug	Mean duration (min)	SD	P value
Valethamate	249.13	±88.321	<0.0001
Drotaverine	192.56	±75.479	<0.0001

As shown in Table 6, the mean duration from injection to delivery in Valethamate is 249.13 min and Drotaverine is 192.56 min with p value <0.0001.

Out of 300 patients, 97% had spontaneous vaginal delivery. Two patients in Valethamate had forceps delivery and two had emergency LSCS. Four patients in control had vacuum delivery and one had emergency LSCS. None of the patient in Drotaverine group had either instrumental delivery or cesarean section. Total 8 babies were admitted for neonatal sepsis, meconium aspiration syndrome and birth asphyxia, but were discharged in good condition. Out of 8 babies, 4 were in Valethamate, 2 in Drotaverine and 2 in control group.

Side effects like dryness of mouth, vomiting, tachycardia, retention of urine was seen more with Valethamate group.

### Discussion

Though the labour is a natural physiological phenomenon, the management of labour remains an important issue both in the developing and the developed world. In the developing world prolonged and often neglected labour is associated with high rates of maternal infection, obstructed labour, uterine rupture and postpartum haemorrhage which may all end in maternal mortality. Improper estimation of time duration of normal labour may also lead to morbidity, mortality or disability of the newborn.

We had enrolled 300 women and they were randomized into three groups. All the parameters in all the patients were comparable at the start of study. Out of 300 patients, 141 had cervical dilatation of 3cm at the time of start of study and remaining 159 had 4cm. When compared to see whether drug given at dilatation of 4cm was more effective in shortening the duration of first stage of labour, it was found that there was no difference whether drug was given at 3 or 4cm dilatation. (table 2)

In our study, the mean duration of active phase of labour in three groups was  $254.29 \pm 96.621$ ,  $178.31 \pm 73.412$  and  $346.31 \pm 123.351$  min respectively. The results were comparable with similar study done by Anju Huria et al.<sup>19</sup>

In study by Anju Huria et al, both Valethamate and Drotaverine caused highly significant reduction in duration of first stage as compared to control in nulliparous as well as in multiparous ( $p < 0.001$ ). Valethamate was significantly more effective than Drotaverine in nulliparous ( $p < 0.0014$ ) but not so in multiparous.<sup>19</sup> In our study both Valethamate and Drotaverine caused significant reduction in the duration of early active phase of labour irrespective of parity. Drotaverine was significantly more effective than Valethamate ( $p < 0.0001$ ).

When injection to end of first stage were compared between two drug groups, it was found that the mean duration in Valethamate was  $228.12 \pm 84.626$  min and in Drotaverine was  $168.89 \pm 69.576$  min. Injection to delivery interval was  $249.13 \pm 88.321$  min and  $192.56 \pm 75.479$  min in Valethamate and Drotaverine group respectively. In study of J.B sharma mean injection to delivery interval was  $220.07 \pm 86.12$  min and  $194 \pm 57.04$  min respectively.<sup>20</sup> There was significant difference when two study groups were compared.

**Table 7: Injection to delivery interval (min)**

Injection to delivery interval	Valethamate	Drotaverine	p-value
Present study	$249.13 \pm 88.321$	$192.56 \pm 75.479$	$< 0.0001$
J.B sharma et al	$220.07 \pm 86.12$	$194 \pm 57.04$	$< 0.001$

In this study it was seen that there was no difference in the duration of active phase of labour in two groups even if the drug was given at higher Bishop score. In our study, it was found that total 30(10%) patients had tachycardia, out of them 21 were in Valethamate,

4 in Drotaverine and 5 in control group. 7(2.3%) patients had fever, out of them 5 were in Valethamate and 2 in control group. 9(3%) patients complained of flushing, 17(5.7%) complained of giddiness and 15(5%) complained of nausea. Only one patient had urinary retention and was catheterized and she was in Valethamate group.

Total 14(4.7%) patients had atonic PPH. Out of them 5 were in Valethamate, 5 in Drotaverine and 4 in control. In study by J.B sharma, there was 18% incidence of PPH in Drotaverine group.<sup>20</sup>

Out of 300 patients, 97% had spontaneous vaginal delivery, 1.3% had vacuum delivery, 1% had LSCS and 0.7% had forceps delivery. Fetal outcome was comparable in three groups.

### Conclusion

Thus, we can definitely conclude that promising beneficial effects of Drotaverine hydrochloride are available in obstetric practice and in our study. It has definitely proven to shorten the duration of labour and provide early relief from distress for the labouring women.

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