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Research Article

# DROTAVERIN VERSUS EPIDOSIN IN CERVICAL DILATION DURING LABOR

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**ABSTRACT**

**Objective:** The objective of the study is to compare the efficacy and safety of drotaverine hydrochloride and epidosin on cervical dilatation.

**Methods:** A total of 80 patients (aged 20–30 years) including both primigravidae and multigravida labor were divided randomly into two groups with 40 patients in each. The drotaverin (D) and epidosin (V) groups were given intravenously, 40 mg drotaverine hydrochloride to the former with every 2 h for a maximum of 3 doses and 8 mg epidosin to the latter with maximum of 6 doses half an hour apart.

**Results:** The mean duration of active phase of labor (hour) was significantly lower in the drotaverin group compared to epidosin group. Furthermore, the cervical dilatation rate was significantly faster in the drotaverin group. There was a significantly higher probability of faster delivery among women who were given drotaverin. The oxytocin augmentation rate, incidence of prolonged labor, labor pain scores, mode of delivery, and maternal and neonatal outcomes were not significantly different among the groups.

**Conclusion:** This study concluded that drotaverin is a new aid in the management of a convenient, shorter, physiological, and uncomplicated delivery.

**Keywords:** Cervical dilation, Drotaverine hydrochloride, Valethamate.

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## INTRODUCTION

A painless and short labor is a shared goal for both mothers and obstetricians. Labor progress is measured by cervical dilation and the descent of the presenting part (likely the baby's head or other presenting part) [1].

Cervical dilation is one of the important factors which determines the duration of labor and is the resultant of all the driving forces of uterine contraction acting against passive tissue resistance. Failure of the cervix to dilate in labor can cause prolonged labor. There are various mechanical and pharmacological methods by which cervical dilation can be facilitated. Sweeping and stretching of the cervix cause local release of prostaglandins resulting in a reduction in the need for formal induction of labor [2]. Amniotomy, especially done early, augments labor and shortens the duration of labor slightly. Amniotomy can be combined with oxytocin for better results [3]. Cervical application of relaxin, estradiol, and hyalase has been used with some success. Buscopan and scopolamine have been used for pain relief and shortening of labor [4]. Oxytocin is proven to induce and augment labor but has no pain relieving effect and is generally given intravenously [5]. Prostaglandins have been used in various formulations for induction of labor, especially prostaglandin $E_2$ gel for cervical ripening. Unfortunately, both prostaglandins and oxytocin can cause neonatal jaundice. Various drugs such as tranquilizers, especially diazepam and antispasmodics, have been used for shortening labor. Epidosin having neurotropic and musculotropic actions results in relaxation of cervical musculature leading to quick dilation of the cervix and shortened labor. It acts by competitively inhibiting the muscarinic receptors of smooth muscle cells followed by inhibition of phospholipase C and decreases intracellular calcium [6,7]. The effects of DH and VB have superiority over other smooth muscle relaxants routinely used in clinical practice, easy available even in rural setup, cheap and have no proven adverse effects on mothers, fetuses, and the new born. The objective of this study was to compare and evaluate the efficacies of DH and VB for effective cervical dilatation in labor.

## METHODS

It is double-blind, randomized controlled study conducted on 80 uncomplicated labor cases who were selected for the study from labor cases admitted in tertiary care center in Department of Gynecology. Group-D: Each case received 2 mL of injection drotin containing 40 mg DH intravenously, dose repeated after 2 h if necessary up to a maximum of 3 doses. Group-V: These cases received 2 mL of injection epidosin containing 8 mg of VB intravenously every half an hour up to a maximum of 6 doses.

Among both the group, all cases were having established labor, i.e., cervical dilatation approximately 3 cm and three uterine contraction per 10 m between 38 and 41 weeks of gestation with vertex presentation. Any patient having any type of antenatal or intranatal abnormality was excluded from the study. After every dose, i.e., after 1/2 h, pelvic examination was done to assess the cervical dilatation in cms. If full dilatation was achieved or going to be achieved after second dose, third dose was not given and side effects if any were noted on partogram.

### Inclusion criteria

Age group between 20 and 30 years, no obstetric complications, cervical dilatation of 3–4 cm, more than 80% effaced cervix, intact membranes, regular established uterine contractions at the rate of 3/10 min each lasting for 30–40 s either spontaneously or with oxytocin.

### Exclusion criteria

Pregnancy-induced hypertension, post-term pregnancy, induced labor, multiple pregnancy, malpresentations, drug hypersensitivity.

This study was conducted among in term pregnancy admitted in active phase of labor in the study facilities during the study period. The

eligible participants were consenting women at term (gestational age 37+0–41+6 weeks) in active phase of labor carrying singleton fetus in cephalic presentation and cervical dilatation of 4–5 cm. The exclusion criteria for this study were the presence of either one or more of the following: Abnormal fetal presentation, non-reassuring fetal status, multiple gestation, antepartum hemorrhage, coexisting uterine fibroid, previous uterine or cervical surgery, medical disorders in pregnancy, or refusal to give consent.

On admission, the gestational age was calculated according to the Naegele rule and confirmed by reviewing early pregnancy ultrasound scans. Active labor was diagnosed by the presence of regular uterine contractions (each lasting for 30 s or more) at a rate of at least 2 every 10 min, with or without rupture of membranes and cervical dilatation of 4–5 cm.

These patients were monitored for vital data, rate of cervical dilatation, injection dilatation interval, mode of delivery, duration of second and third stages of labor, neonatal outcome, side effects to drug, and patient's satisfaction regarding pain reduction.

**Statistical analysis**

The results were tabulated and analyzed. The Statistical Package for the Social Sciences (SPSS) for Windows Version 10.0 (SPSS Inc., USA) was used for the statistical analysis. The Chi-square/and the Fisher's exact tests of significance were used wherever they were applicable and $p \leq 0.05$ were considered significant.

## RESULTS

We studied 80 patients in labor with 40 patients each in drotaverine (D) and epidosin (E) groups including both primigravidae and multigravidae. The age distribution in both groups is comparable, i.e., between 20 and 30 years.

There were no difference between the study groups as regard to age (years), body mass index, gestational age at delivery (weeks), and cervical dilatation at randomization (cm) (Table 1).

Although they were not statistically significant, the incidence of oxytocin augmentation of labor and prolonged labor was lower in the drotaverin group when compared in groups (Table 2).

There was no difference in the labor pain scores at randomization, 30 min, 60 min, and 120 min after randomization (Table 3).

The mode of delivery and estimated blood loss did not differ between the 2 groups. There was no significant difference between the 2 groups in maternal adverse events (Table 4).

Neonatal adverse events such as Apgar scores <7 at 1 and 5 min and rate of admission to the neonatal intensive care unit did not differ significantly between the study groups (Table 5).

## DISCUSSION

In our study, we evaluated and compared the effect of DH and VB on cervical dilatation, duration of second and third stages of labor and third-stage complications. After intravenous (IV) administration, the drotaverin is rapidly absorbed and half-life is 12 min, reaches maximum concentration in 45 min. The primary elimination half-life is 2.4 h. It does not cross placental barrier and metabolized by liver. It is excreted through urine and feces as unchanged drug. IV Epidosin starts its action within 5-10 min, its plasma half life is 4 hrs. Its plasma half-life is 4 h. It crosses the placental barrier and is also secreted in breast milk but has no proven deleterious effects on fetus and baby. It is completely metabolized by liver and excreted in urine as both unchanged drug and metabolites [6,7].

**Table 1: Baseline characteristics of the study participants**

| Variable | Drotaverin (n=40) Mean±SD | Epidosin (n=40) Mean±SD | p-value |
|---|---|---|---|
| Maternal age (years) | 23.1±32 | 22.3±3.3 | >0.05 |
| BMI (kg/m$^2$) | 23.6±3.6 | 22.1±3.7 | >0.05 |
| Gestational age (weeks) | 39.4±1.2 | 39.1±1.1 | >0.05 |
| Cervical dilatation (cm) | 4.23±1.3 | 4.24±1.5 | >0.05 |

BMI: Body mass index

The baseline variables of the participants in the 2 study groups were similar. Some of these baseline variables can directly or indirectly affect the progress and duration of labor. Therefore, the similarities of baseline variables in both study groups showed that they were unlikely to affect the findings of this study.

This study shows that the rate of cervical dilatation was faster in the drotaverin group when compared to the epidosin group. This finding was similar with the results from previous studies done in which a faster cervical dilation rate was obtained when compared with the epidosin [8-12]. From this study also, it can be deduced that a single dose of drotaverin was able to achieve the desired effect when compared with other studies, in which multiple doses of the drug were administered 2 h apart if labor was not progressing. Ibrahim *et al*. used a standard intrapartum protocol as in the index study but administered multiple doses of the drug intravenously up to 2 repeat doses [2]. This shows that the desired effect of drotaverin in labor can be achieved with IV administration of a single dose of the drug because its half-life is 7–12 h.

The duration of active phase of labor was significantly shorter in the drotaverin group when compared to the epidosin group. However, there was no difference in the duration of second and third stages of labor in the 2 groups. When all the stages of labor were taken into account, the total duration of labor was significantly shorter among participants that received drotaverin when compared to those administered with the epidosin. Although not statistically significant, the risk of prolonged labor was lower in the drotaverin group when compared with those in the epidosin group of the study. This is supported by the studies done by Sharma *et al*. [13] Anju *et al.* [14] and Madhu *et al*. [12] Some obstetricians have reserved opinions that the cervical spasmolytic action of drotaverin could weaken the uterine contractions thus delaying the progress of labor. However, no scientific studies are available in defense of such opinions. However, our study and previous studies proved that drotaverine hydrochloride had no such effect.

In this study, the rate of oxytocin augmentation did not differ in both study groups. This is probably because drotaverin does not enhance myometrial contractility but rather inhibits type IV phosphodiesterase which is predominantly high in the myometrium during the third trimester and near term. This process leads to smooth muscle relaxation and cervical dilatation. The oxytocin augmentation rate for this study is similar to that observed by Ibrahim *et al.* [2].

The cesarean section rate was comparable for both groups of the study. Participants who had caesarean section were 11 and 8 in the drotaverin and epidosin groups, respectively. The cesarean deliveries observed in both groups were mainly due to cephalopelvic disproportion unlike in the study by Ibrahim *et al*. [2] in which fetal distress was the most common indication. In this study, the duration of active phase of labor was the primary outcome. Therefore, participants who delivered by caesarean were excluded from data analysis.

Maternal side effects are mild and rare. It usually occurs when the drug is given rapidly during IV administration [2]. Since these findings were

**Table 2: Duration of active phase of labor in D and V groups**

| Primary outcome measure | Drotaverin (n=40) Mean±SD | Epidosin (n=40) Mean±SD | p-value |
|---|---|---|---|
| Mean duration of active phase of labor (hour)±SD | 4.21±1.98 | 6.61±2.79 | <0.001* |
| Secondary outcome measures | | | |
| Mean cervical dilatation rate (cm/hour)±SD | 1.68±1.02 | 1.06±0.53 | <0.001* |
| Mean duration of second stage of labor (hour)±SD | 0.76±0.37 | 0.78±0.39 | >0.05 |
| Mean duration of third stage of labor (hour)±SD | 0.16±0.07 | 0.16±0.08 | >0.05 |
| Mean total duration of labor (hour)±SD | 6.23±2.21 | 8.23±3.54 | <0.001 |
| Oxytocin augmentation of labor, n (%) | 48 (43.6) | 53 (47.7) | >0.05 |
| Prolonged labor (injection to full cervical dilatation >12 h), n (%) | 1 (2.5) | 2 (5) | >0.05 |

Mean duration of active phase of labour and total duration of labour is significantly more in epidosin and Mean cerivical dilatation rate and mean is significantly less

**Table 3: Labor pain score in D and V groups**

| Median labor pain score (VAS) (IQR) | Drotaverin (n=40) Mean±SD | Epidosin (n=40) Mean±SD | p-value |
|---|---|---|---|
| At randomization | 8 (5–10) | 7 (5–9) | >0.05 |
| At 30 min | 7 (4–8) | 8 (5–10) | >0.05 |
| At 60 min | 8 (6–9) | 8 (6–10) | >0.05 |
| At 120 min | 8 (6–10) | 8 (6–10) | >0.05 |

VAS: Visual Analog Scale, IQR: Interquartile range

**Table 4: Mode of delivery and side effects in D and V groups**

| Mode of delivery | Drotaverin (n=40) Mean±SD | Epidosin (n=40) Mean±SD | p-value |
|---|---|---|---|
| Vaginal delivery (including instrumental) | 36 | 35 | >0.05 |
| Cesarean section | 4 | 5 | >0.05 |
| Mean estimated blood loss (mL)±SD | 320.1±85.4 | 324.3±82.4 | >0.05 |
| Side effects | | | |
| Headache, n (%) | 1 (2.5) | 0 (0) | >0.05 |
| Nausea, n (%) | 2 (5) | 2 (5) | >0.05 |

**Table 5: Neonatal outcome in D and V groups**

| Neonatal outcome | Drotaverin (n=40) Mean±SD | Epidosin (n=40) Mean±SD | p-value |
|---|---|---|---|
| Mean birth weight (kg)±SD | 2.62±1.2 | 2.64±1.2 | >0.05 |
| Apgar scores <7 at 1st min, n (%) | 4 (3.6) | 2 (1.8) | >0.05 |
| Apgar scores <7 at 5th min, n (%) | 1 (0.9) | 0 (0) | >0.05 |
| NICU admission, n (%) | 6 (5.5) | 5 (4.5) | >0.05 |

NICU: Neonatal intensive care unit

not statistically significant, it can be deduced that the side effect profile of drotaverin is safe. Ibrahim *et al*. reported palpitations, hypotension, and tachycardia, in addition to nausea and headache in their study [2]. Palpitations, hypotension, and tachycardia were not observed in our study participants. In the study conducted by Soni *et al*. [15] and Madhu *et al*. [12], they proved that both the drugs were effective in cervical dilatation but drotaverine hydrochloride is superior to Epidosin with less side effects. Drotaverin does not cross the placenta and as such has no significant fetal adverse effects.

Comparison of Apgar scores at 1 min and 5 min and neonatal intensive unit admissions were similar for both groups of the study. Ibrahim *et al*. reported similar findings in their studies [2]. Our findings are consistent with the findings of Anju *et al*. [14], Mishra *et al*. [16], and Soni *et al*. [15]. More studies are needed to assess the maternal and perinatal side effects of drotaverin.

## CONCLUSION

Our study found an increasing role of drotaverine hydrochloride in reducing the total duration of labor, hastening cervical dilatation, ensuring smooth progress of labor with good maternal and fetal outcome. It is concluded that overall efficacy of drotaverin was superior than the epidosin. The drugs drotaverin and epidosin are in the practice of clinical obstetrics. Both the drugs effectively relieve the maternal pain by reducing the cervical contractile response and shorten the duration of labor. Drotin is a safer and convenient approach toward acceleration of labor. Maternal complications were also fewer in patients treated with drotin as compared to epidosin. Thus, it can be concluded that drotaverin is a new aid in the management of a convenient, shorter, physio logical, and uncomplicated delivery.

## AUTHOR CONTRIBUTION

No other authors.

## CONFLICT OF INTEREST

Nil.

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