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Original Research Article

Drotaverine to improve progression of labour among parturient women- a case control study

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ABSTRACT

Background: Prolonged labour contributes to increased perinatal and maternal morbidity. Pharmacological interventions can hasten cervical dilation and help obstetrician to accomplish the delivery in the shortest possible time without compromising maternal and fetal safety. Aims and objectives were to evaluate the acceleration effect of drotaverine on the dilatation of the cervix in both primigravidae and multigravida and compare it with control group.
Methods: A total of 70 patients were studied (35 in drotaverine group and 35 in control group). The inclusion criteria were pregnancy with at least 37 weeks completed, cervical dilatation 3-4 cm, regular uterine contractions and cephalic presentation. The study group received 40 mg drotaverine hydrochloride i.m. in active phase of labour, control group received standard delivery care. Parameters such as duration of first and second stage of labour, mode of delivery, neonatal outcome and side effects to drug was recorded.
Results: 6 subjects from the study group and 4 from the control group developed complications in first stage of labour and were taken up for operative delivery and hence they were excluded from calculation of various labour parameters. The mean rate of cervical dilatation with drotaverine was 2.26 cm/hour, while it was 1.67 cm/hour without any intervention (p value <0.05). Mean duration of active phase of first stage of labor was 3.09 hours in drotaverine group against 4.98 hours in study group (p value <0.05). There were no significant untoward effects noted in either of the groups.
Conclusions: Drotaverine was found to be an effective and safe drug in shortening the duration of the first stage of labor without any significant detrimental effects on the mother and newborn. Drotaverine did not interfere with uterine contractility and there was no increased incidence of operative deliveries.

Keywords: Cervical dilation, Drotaverine hydrochloride, Labour augmentation

INTRODUCTION

Labor is a complex process and is characterized by the onset of effective uterine contractions leading to the progressive effacement and dilatation of cervix resulting in the delivery of the fetus, placenta and the membranes.[1]

Prolonged labour is associated with both fetal and maternal morbidity and hence it would be safer for the obstetrician as well as parturient woman to deliver within modest time frame without any compromise.[2] In the modern era of day care obstetrics, a smooth timely delivery and early return to the routine activity is desired by everyone. More and more clinical trials have been devoted to the acceleration of labor to prevent the complications of prolonged labor like maternal exhaustion, dehydration, infection, postpartum hemorrhage and ketoacidosis; fetal complications like distress, birth asphyxia, birth trauma and even still births.

During pregnancy the contractility of the myometrium is usually diminished to accommodate and protect the growing products of conception, whereas the cervix forms a tight sphincter to ensure the integrity of pregnancy.[3]

However during process of parturition, the cervix should dilate in time to allow the process of expulsion of the fetus. In spite of good uterine contractions, the cervical dilation may be hampered because of inhibitory impulses in the form of spasm leading to prolonged labour. In such cases antispasmodics for example, drotaverine hydrochloride, help in the dilatation of cervix. Drotaverine, an isoquinoline derivative, is a phosphodiesterase (PDE) inhibitor and is selective for type IV isoenzyme. It acts specifically on spastic sites and corrects the cAMP and calcium balance relieving smooth muscle spasm.[4]

Various studies have been conducted in India and elsewhere suggesting the role of antispasmodics in acceleration of labour by promoting cervical softening and dilatation. The present study aims at comparison of cervical dilatation and duration of labor using Drotaverine with Control group in 1st and 2nd stage of labor and to assess the perinatal outcome and maternal side effects of drug.

Aim and objectives

To evaluate the acceleration effect of drotaverine on the dilatation of the cervix in both primigravidae and multigravida and compare it with control group. To determine deleterious side effects of drotaverine affecting either mother or foetus.

METHODS

It was a comparative, hospital based study carried out at Kasturba Medical College, Manipal for a period of 6 months from January 2022 to June 2022. A total of 70 patients were studied (35 in drotaverine group and 35 in control group), after taking approval from institutional ethical committee clearance. Informed consent was taken from all participant parturient women.

Inclusion criteria

The inclusion criteria were pregnancy with at least 37 weeks completed, cervical dilatation 3-4 cm, regular uterine contractions with frequency of 2-3 contractions every 10 minutes and cephalic presentation.

Exclusion criteria

Exclusion criteria were patients with preterm labour, uterine inertia, cephalo-pelvic disproportion, polyhydramnios, multiple pregnancy, associated medical, surgical or obstetrical complications. Study group received 40 mg drotaverine hydrochloride i.m. in active phase of labour (each ampoule contained 40 mg of drotaverine hydrochloride in 2 ml aqueous solution). Vaginal examination was done to note the cervical dilation and effacement, station of head, membrane status and adequacy of pelvis. All patients were regularly monitored at one-hour intervals in terms of blood pressure (mmHg), pulse rate (beat/minute), uterine contraction and fetal heart rate (beat/minute), and side effects of valethamate bromide (tachycardia, dry mouth, flushing, fever, headache, and nausea, vomiting). Parameters such as duration of first and second stage of labour, mode of delivery, neonatal outcome and side effects to drug was recorded. The cases which had caesarean section were excluded from the analysis involving labour duration, rate of cervical dilatation etc.

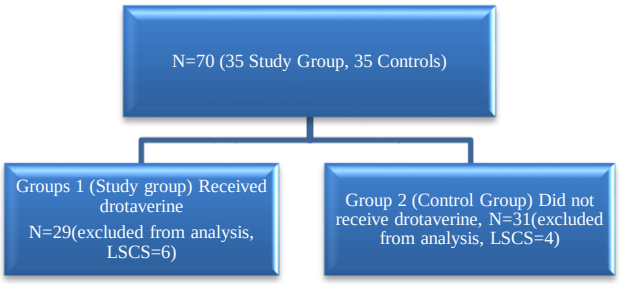

Figure 1: Consort statement.

The data collected was entered in to excel software and mean, standard deviation was calculated by analyzing on SPSS software. Appropriate statistical tool and technique was used to identify the significant of the variables depending upon the nature of data. ANOVA and Chi-square tests were used to find the statistical correlation. P value less than 0.05 was considered significant.

RESULTS

During the study, 70 women were assessed for eligibility to participate in the study. 35 women were assigned to drotaverine group and 35 women were considered under control group. However, those who underwent caesarean delivery in both groups were not considered for analysis of cervical dilation and duration of labour. The mean gestational age at the time of delivery in study group was 39.2 weeks and 39.4 weeks in control group and the difference was not statistically significant ($p<0.05$). The birth weight of the neonates in study group was 2.92 kg and study group was 2.98 kg, indicating that birth weight did not influence the outcome variables.

Table 1: Age among study and control group (N=70).

Age/groups	Drotaverine (n=35)	Control (n=35)
<20 years	4 (11.43%)	3 (8.57%)
21 to 30 years	19 (54.29%)	21 (60.00%)
>30 years	12 (34.29%)	11 (31.43%)

*P value: NS

Table 1 shows distribution of age among the study and control groups. It can be seen that cases and controls were well matched and age wise there were no significant differences between two groups ($p<0.05$).

Table 2: Parity status among study and control group (N=70).

Parity/groups	Drotaverine (n=35)	Control (n=35)
Primigravida	21 (60%)	20 (57.1%)
Multigravida	14 (40%)	15 (42.9%)

*P value: NS

Table 2 shows distribution of parity status among the study and control groups. It can be seen that cases and controls were well matched and parity wise there were no selection bias (p<0.05)

Table 3: Mode of delivery among study and control group (N=70).

Type of delivery	Drotaverine (n=35)	Control (n=35)
LSCS	6 (17.1%)	4 (11.4%)
Vaginal delivery without instrumentation	26 (74.3%)	30 (85.7%)
Forceps delivery	2 (5.7%)	1 (2.9%)
Vacuum delivery	1 (2.9%)	0 (0.0%)

*Chi square p value: NS

Table 3 shows mode of delivery in two groups. There were no significant differences with respect to mode of delivery in either of the groups.

Table 4: Adverse effects among study and control group (N=70).

Adverse effects	Drotaverine (n=35)	Control (n=35)
Nausea and vomiting	2	1
Headache	0	0
Dryness of mouth	1	0
Tachycardia	0	1
Hypotension	0	0
Cervical tears	2	1
Lacerations	0	0
PPH	0	1

*Chi square p value: NS

Table 4 shows adverse maternal side effects in two groups. There were no significant differences with respect to various untoward outcomes in either of the groups.

6 subjects from study group and 4 from control group developed complications (study group; fetal distress- 3, non-progress of labour 3, control group; fetal distress- 1, non-progress of labour 3) in first stage of labour and were taken up for operative delivery and hence they were excluded from calculation of various labour parameters.

Table 5 shows duration of labour (according to phases of labour) in two groups. It can be seen that active of labour was significantly shortened in drotaverine group, compared to control group (p<0.05). However, there were no differences in the second and third stage of labour in both the groups.

Table 5: Duration of labour among study and control group (N=60).

Labour duration/groups	Drotaverine (n=29)	Control (n=31)	P value
Active phase, hours	3.09±0.95	4.98±0.69	<0.05 (S)
second stage, minutes	23.46±3.9	29.7±4.6	>0.05 (NS)
Third stage, minutes	17.9±5.3	16.7±4.9	>0.05 (NS)

Table 6: rate of cervical dilatation in study and control group (N=60).

Rate of cervical dilatation/groups	Drotaverine (n=29)	Control (n=31)	P value
Mean cervical dilatation (cm/hour)	2.26±0.88	1.67±0.38	<0.05 (S)
Primigravida	2.1±0.78	1.62±0.68	<0.05 (S)
Multigravida	2.3±0.87	1.56±0.76	<0.05 (S)

Table 6 shows rate of cervical dilatation in study and control groups till the patients achieved full cervical dilatation. It can be inferred that drotaverine administration resulted in quicker cervical dilatation resulting in faster delivery.

Table 7: APGAR scores of the neonates in study and control group (N=70).

APGAR scores/groups	Drotaverine (n=29)	Control (n=31)
4-6	0 (0.0%	0 (0.0%)
7-8	12 (41.4%)	14 (45.2%)
9-10	17 (58.6%)	17 (54.8%)

*Chi square p value: NS

Table 7 shows APGAR scores of neonates in study and control group and it can be seen that drotaverine administration did not lead to any adverse neonatal outcome.

DISCUSSION

The subject of cervical dilatation and progress of labor has puzzled obstetricians for a long time, with prolonged labor having implications for both the mother and the fetus. Acceleration of labor is considered to be an important factor in reducing maternal morbidity as well as the neonatal complications. Despite good uterine contractions, inhibitory impulses in the form of spasm often impair

cervical dilatation and prolong the duration of labour. Cervical ripening, expressed as a remodelling of the cervical connective tissue, has been proven to be necessary for an uncomplicated vaginal delivery.[5] Any method which aids in reducing the tone of cervical musculature will certainly favour early dilatation of cervix and hasten labour. Several drugs like antispasmodics, tranquillizers, prostaglandins and psychotherapeutic methods have been tried in the past to facilitate cervical dilatation and hence augment labour, but majority of these were found to have ill effect on the mother and the fetus. Drotaverine hydrochloride is one antispasmodic agent which is safe and effective in shortening duration of labor, without much effect on mother and fetus.

Drotaverine hydrochloride or isoquinoline 1,2,3,4-tetrahydro 6,7 diethoxy-1-(c-3,4- diethoxy phenyl methylene) hydrochloride is a highly potent spasmolytic agent, acting on the smooth muscle but is devoid of anticholinergic effects as it acts through inhibitory effect on phosphodiesterase enzyme, mainly PDEIV. Near term, human myometrium contains a higher proportion of rolipram sensitive type IVPDE isoforms. Drotaverine inhibits them and in turn increases the intracellular concentration of cAMP and cGMP and causes smooth muscle relaxation. It does not cross the placenta, hence no side effects on the foetus.[6]

The potential role of drotaverine hydrochloride and hyoscine butyl bromide in enhancing the progress of the first stage of labour and thereby shortening the duration of labour has been investigated in many trials.

Singh et al conducted a double-blind placebo-controlled randomized study among 100 uncomplicated primigravidas in spontaneous labour to evaluate the efficacy of intramuscular drotaverine hydrochloride in augmentation of labour.[7] They found intramuscular drotaverine hydrochloride to be safe and effective in augmentation of labour.

Roy A and coworkers, in their study observed that the mean duration of the active phase of labor in primigravida and multigravida were 148.9 minutes and 99.5 minutes in the drotaverine group whereas in the control group were 331.6 minutes and 227.9 minutes respectively. They concluded that drotaverine was highly effective.[8]

Sharma et al, in their study reported that drotaverine accelerated labor more rapidly and was associated with lesser side effects.[9] The rate of cervical dilatation was highest in the drotaverine hydrochloride group (2.04 cm/hour) compared with the control group (1.01 cm/hour).

In a study done by Sinhasane et al, who reported that the rate of cervical dilatation in primigravida females was more (1.83 cm) in the drotavarine group as compared to control group in which it was 1.12 cm. Similarly, in multigravidas, it is 2.82 cm with drotavarine 1.34 cm in controls.[10]

Gupta et al studied 535 cases of delivery with drotaverine. They concluded that drotaverine is effective in reducing the duration of labour by hastening cervical dilatation. It is more effective when membrane has been ruptured. It is also found that drotaverine does not increase in the incidence of operative delivery.[11]

Muralidhar Pai et al reported that after 40 mg of Drotaverine was administered intramuscularly on 141 labouring patients; mean duration of active phase was reduced by 17.3% in primi patients given drotaverine, whereas in multigravidae there was 15.6% reduction as compared with controls which were not given any drug.[12] Equal number of women delivered spontaneously in both the groups. They concluded that drotaverine is more effective when the membranes have ruptured either spontaneously or by amniotomy.

Ibrahim et al in a randomized, double-blind, placebo-controlled trial conducted among 422 young nulliparous women to re-evaluate the role of 48 drotaverine in progression of labour concluded that it can be used effectively and safely to shorten the duration of the first stage of labour among nulliparous women with active spontaneous labour.[13]

CONCLUSION

This study proves the promising and beneficial effect of drotaverine hydrochloride in management of labour without any ill effects on the mother or the neonate. From the above study we conclude that injection drotaverine significantly reduces the duration of active phase of labor with improvement in rate of cervical dilatation. Thus, it can be safely used as potent agent for augmentation of labor. We strongly advocate its use to reduce the agony which mother faces due to prolonged labour.

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REFERENCES

1. Sir Sabaratnam Arulkumaran, Gita Arjun, Leonie Penna. Psychopharmacology of labour, The Management of Labour. 3rd ed. 2012;1:1.
2. Madhu C, Mahavarkar S, Bhave S. A randomized Controlled study comparing drotaverine hydrochloride and valethamate bromide in the

augmentation of Labour. Arch Gynecol Obstet. 2010;282:11-15.
3. Leppert PC. Anatomy and physiology of cervical ripening. Clin Obstet Gynaecol. 1995;38(2):267-78.
4. Gupta K. Emerging role of drotaverine in emergency medicine: A review. J Am Med Assoc Ind Phys Update. 1999;2:57-64.
5. Granstrom L, Ekman G, Malmstrom A. Insufficient remodelling of the uterine connective tissue in women with protracted labour. Br J Obstet Gynaecol. 1991;98(12):1212-6.
6. Mishra SL, Toshniwal A, Banerjee R. Effect of drotaverine on cervical dilatation: a comparative Study with epidosin (valethamate bromide). J Obstet Gynaecol India. 2002;52(3):76-9.
7. Singh KC, Jain P, Goel N, Saxena A. Drotaverine hydrochloride for augmentation of labour. Int J Gynecol Obstet. 2004;84(1):17-22.
8. Roy A, Patra KK, Mukhopadhyay S, Guha S. Study of drotaverine on first stage of labour and pregnancy outcome. J Indian Med Assoc. 2007;105(8):450-2.
9. Sharma JB, Pundir P, Kumar A, Murthy NS. Drotaverine hydrochloride versus valathamate bromide in acceleration of labour. Int J Gynaecol Obstet. 2001;74(3):255-60.
10. Sinhasane H, Nishty GM. A comparative study on the efficacy of drotaverine and valethamate on cervical dilatation during labour. Int J Reprod Contracept Obstet Gynecol. 2017;6(2).
11. Gupta K, Mukharjee K, Chowdhary B. Effect of drotaverine on the first stage of labour. Obstet Gynaecol Today. 2003;8(3).
12. Pai MV, Sreekumar S, Gupta K, Chatterjee N. Effect of drotaverine on active phase of labour. Obs Gynae Today. 2003;VIIII(3).
13. Ibrahim MI, Alzeeniny HA, Ellaithy MI, Salama AH, Abdellatif MA. Drotaverine to improve progression of labor among nulliparous women. Int J Gynaecol Obstet. 2014;124(2):112-7.

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