Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Disease

journal homepage: www.elsevier.com/locate/apjtd

Document heading doi:

The comparative study of Drotaverine hydrochloride and Valethamate bromide in first stage of labour

Sudhir Babu Palii [1*], Vijaya Lakshmi Akkupalli[2], Suneetha Maddi[1]

[1]Department of Obstetrics and Gynaecology, Santhiram Medical College & General Hospital, Nandyal, Kurnool Dist, Andhra Pradesh, India

[2]Department of Physiology, Santhiram Medical College & General Hospital, Nandyal, Kurnool Dist, Andhra Pradesh, India

PEER REVIEW

Peer reviewer
P

Comments
T
(Details on Page 933)

ABSTRACT

Objective: To evaluate and compare the effects of drotaverine and valethamate on cervical dilatation **Methods:** Total of 100 patients (aged 20 to 30 years) including both primigravidae and multigravidae in first stage of labour, were divided randomly into two groups with 50 patients in each. The drotaverine(D) and valethamate (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 Valethamate bromide to the latter with maximum of 6 doses half an hour apart. **Results :** In primigravidae and multigravidae the average duration of active phase is shortened by 3 hours with 1.92 cm/hour cervical dilatation in drotaverine group and 1 hour 45 minutes with 1.44 cm/hour in valethamate group ($P<0.05$). There was no significant difference in the duration of second and third stages in both groups. No obstetrical complications or major side effects observed in both groups. **Conclusion:** Drotaverine accelerates labour better than of valethamate. The reduction of pain during labour is better with drotaverine when compared with valethamate.

KEYWORDS
Cervical dilatation, Drotaverine, Valethamate

1. Introduction

Both the obstetrician and the laboring woman would like to accomplish the delivery in the shortest possible time without compromising the maternal and fetal safety. Hence, along with early amniotomy and early administration of oxytocin, to accelerate labor many advise the use of antispasmodic agents like drotaverine, hyoscine butylbromide, dicyclomine valethamide bromide etc. to hasten the first stage of labor [1] . Among these drugs we selected two drugs drotaverine hydrochloride (DH) and valethamate bromide (VB) to compare their efficacy in accelerating the rate of cervical dilatation.

DH is an isoquinoline derivative and its chemical name is 3, 4, 6, 7 tetraethoxy-1 benzyl 1, 2, 3, 4 tetrahydro isoquinoline hydrochloride[2]. It is an unique smooth muscle relaxant and acts by inhibiting phosphodiesterase-IV enzyme that results in increased cAMP[3]. VB is an anticholinergic smooth muscle relaxant. It is an ester with chemical name ethanaminium N, N - diethyl N-methyl 2(3 methyl-1-oxo-2 phenyl pentyl) bromide. It acts by competitively inhibiting the muscarinic receptors of smooth muscle cells followed by inhibition of phospholipase C and decreases intracellular calcium[4,5].

*Corresponding author: Dr. Sudhir Babu Palii, MBBS,MD (OBG), Departments of Obstetrics and Gynaecology, Santhiram Medical College and General hospital, NH-18,Nandyal- 518 501, Kurnool Dist, Andhra Pradesh, INDIA
Tel: +91-9666019888
Email: magadhira@gmail.com

Article history:
Received
Received in revised form
Accepted
Available online
Online First

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, foetuses 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 first stage of labour.

2. Material and methods

2.1 Study design

The study was conducted in Santhiram General Hospital, Nandyal over a period of 1½ years from November 2009 to April 2011. This is a prospective comparative study involving two groups of patients. One hundred patients with 38–41 weeks of gestational age were selected. They were divided into two groups randomly with 50 patients in each group: Group–D : Each case received 2ml of injection drotin containing 40 mg DH intravenously, dose repeated after 2 h if necessary upto 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 upto a maximum of 6 doses.

2.2 Inclusion criteria and exclusion criteria of the study

Inclusion criteria

- Consent.
- Age group between 20–30 years.
- No obstetric complications.
- Cervical dilatation of 3–4 cms
- More than 80% effaced cervix.
- Intact membranes.
- Regular established uterine contractions at the rate of 3/10 minutes each lasting for 30–40 seconds either spontaneously or with oxytocin.

Exclusion criteria

- Pregnancy induced hypertension.
- Post term pregnancy.
- Induced labour.
- Multiple pregnancy.
- Malpresentations.
- Drug hypersensitivity.

2.3. Evaluation criteria

After considering inclusion criteria and after taking informed consent, patient was examined in detail at 80% effacement and 3–4 cm cervical dilatation with adequate uterine contractions. The drug was given intravenously. These patients were monitored for vital data, rate of cervical dilatation, injection dilatation interval, mode of delivery, duration of second and third stages of labour, neonatal outcome, side effects to drug and patient's satisfaction regarding pain reduction

2.4.Statistical analysis

The results were tabulated and analysed. 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 –values less than or equal to 0.05 were considered significant.

3. Results

We studied 100 patients in first stage of labour with 50 patients each in drotaverine (D) and valethamate (V) groups including both primigravidae and multigravidae. The age distribution in both groups is comparable i.e. between 20 to 30 years.

3.1. Effect of DH and VB on different stages of labour

As observed in table 1, in primigravidae for D group , 14% of patients had active stage duration of <2 hours , 63% of them had 2–4 hours and 23% of patients had 4–6 hours. In secondgravidae of D group , 21% of patients had duration of active phase of <2 hours, 73% of them had duration of 2–4 hours, and in 6% of secondgravidae the duration of active phase was 4–6 hours. While in 55% of thirdgravidae the duration of active phase was <2 hours and 45% of them had duration of active phase of 2–4 hours .

In primigravidae of V group, 4% of patients had the duration of active phase of <2 hours,

26% of them had the duration of 2–4 hours, and in 67% of primigravidae the duration was 4–6 hours. In remaining 3% of primigravidae the duration of active phase was 6–8 hours. In Secondgravida of V–group, 17% of preganant women showed the duration of active phase to be <2 hours, 42% of them had the duration of active phase of 2–4 hours and in 41% of pregnant women h the duration was 4–6 hours. Where as in thirdgravida of V group, 27% of them had the duration of <2 hours and 73% patients showed the duration of active phase to be 2–4 hours (Table 1).

D–group: with respect to second stage of labor , 17%, 78%

Table 1

Duration of active phase of labour in D – group and V– group

Gravida	< 2 Hours		2 – 4 Hours		4 – 6 Hours		6 – 8 Hours	
	D group	V group	D group	V group	D group	V group	D group	V group
Primigravida (n=24)	3	1	15	6	5	15	0	1
Secondgravida (n=15)	3	3	11	7	1	7	0	0
Thirdgravida (n=11)	6	3	5	8	0	0	0	0

Table 2

Duration of second and third stage of labour in D– group and V–group

SECOND STAGE							THIRD STAGE				
Gravida	< ½ Hour		½ – 1 Hour		1 – 2 Hours		Gravida	0–10 Min.		10–20 Min.	
	D group	V group	D group	V group	D group	V group		D group	V group	D group	V group
Primigravida	4	2	18	17	1	2	Primigravida	21	19	2	2
Secondgravida	11	11	4	6	0	0	Secondgravida	15	16	0	1
Thirdgravida	8	7	3	4	0	0	Thirdgravida	11	11	0	0

and 5% of primigravidae exhibited the duration of < ½ hour, ½ – 1 hour and 1 – 2 hours respectively. Whereas 73% and 27% of secondgravidae had the duration of < ½ hour and ½ – 1 hour respectively. Accordingly in 73% and 27% of thirdgravidae the duration of second stage were < ½ hour and ½ – 1 hour. Regarding third stage of labour, 91% and 9% of primigravidae the duration were 0–10 minutes and 10–20 minutes respectively. But 94% and 6% of secondgravidae the duration of third stage were 0–10 minutes and 10–20 minutes correspondingly. However, 100% of thirdgravidae had the duration of third stage of 0–10 minutes (Table 2).

V– group: regarding second stage of labor, 9%, 81% and 10% of primigravidae had the duration of second stage of < ½ hour, ½ – 1 hour and 1 – 2 hours respectively . where as 65% and 35% of secondgravidae , the duration of second stage showed were < ½ hour and ½ – 1 hour respectively . Additionally, in 64% and 36% of thirdgravidae the duration of second stage in V–Group is < ½ hour and ½ – 1 hour (Table 2). With reference to third stage of labor, in 90% and 10 % of primigravidae the duration of third stage were 0–10 minutes and 10–20 minutes respectively. While in 94% and 6% of secondgravidae the duration of third stage were 0–10 minutes and 10–20 minutes correspondingly. Further in 100% of thirdgravidae the duration of third stage was 0–10 minutes (Table 2).

3.2 Apgar scores of neonates in D–group and V group

With reference to APGAR score for D group , 92% and 8% of primigravidae had a score of 8–10 and 6–8 respectively. While 100% of secondgravidae and thirdgravidae patients had a score of 8–10 (Table 3) . The APGAR score in 86% and 14% of primigravidae in V group had 8–10 and 6–8 respectively. While 100% of secondgravidae and thirdgravidae of V–group had a score of 8–10 (Table 3)

Table 3

Apgar scores of neonates between D and V groups

Gravida	APGAR SCORE					
	8 – 10		6 – 8		< 6	
	D group	V group	D group	V group	D group	V group
Primigravida	22	19	2	3	0	0
Secondgravida	15	17	0	0	0	0
Thirdgravida	11	11	0	0	0	0

3.3 Comparison of different stages of labour between D and V groups

In primigravidae the average duration of active phase is 3 hours 6 minutes and cervical dilatation rate is 1.92 cm/hour in D group whereas it is 4 hours 14 minutes and 1.44 cm/hour in V group. With reference to secondgravidae the average duration of active phase is 2 hours 28 minutes and cervical dilatation rate is 2.46 cm/hour in D group whereas it is 3 hours 12 minutes and 1.86 cm/ hour in V group. In thirdgravidae the average duration of active phase is 2 hours 10 minutes and cervical dilatation rate is 2.76 cm/hour in D group whereas it is 2 hours 21 minutes and 2.52 cm/hour in V group. (Table 4, Figure 1).

Table 4

Comparison of active stage of labour between D and V groups

Gravida	<2 hours		2–4 hours		4–6 hours		6–8 hours	
	D group	V group	D group	V group	D group	V group	D group	V group
Primigravida	14	4	63	27	21	68	0	4
Secondgravida	21	17	73	41	6	41	0	0
Thirdgravida	54	27	45	72	0	0	0	0

Values expressed in percentage

Two cases of primigravidae one from each group resulted in caesarean section due to foetal distress. But this complication was not due to drug administration.

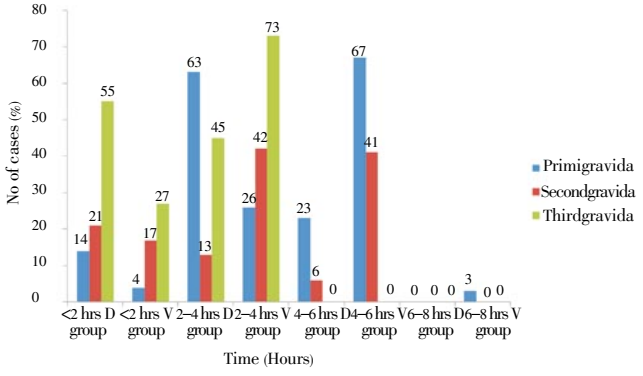

Figure 1. Active stage comparsion between D and V groups

The total number of cases in primigravidae, secondgravidae and thirdgravidae in drotaverine group with injection dilatation interval less than 4 hours was significantly more than valethamate bromide group (P–value < 0.05 which is statistically significant.)

In drotaverine group the average duration of second stage is 39.5 minutes in primigravidae, 24.26 minutes

in secondgravida and 24.5 minutes in thirdgravida. In valethamate group average duration of second stage is 44 minutes in primigravidae and 28.8 minutes in secondgravidae, and 24 minutes in thirdgravidae. There is no statistical difference in both groups. Even there was no statistical difference in the duration of third stage in both groups (Table 5 and Table 6).

Table 5

Comparison of second stage of labour between D and V groups

Gravida	½ hour		½ – 1 hour		1–2 hours	
	D group	V group	D group	V group	D group	V group
Primigravida	17	9	78	81	5	10
Secondgravida	73	65	27	35	0	0
Thirdgravida	73	64	27	36	0	0

Values expressed in percentage

Table 6

Comparison of third stage of labour between D and V groups

Gravida	½ hour		½ – 1 hour	
	D group	V group	D group	V group
Primigravida	91	90	9	10
Secondgravida	94	94	6	6
Thirdgravida	100	100	0	0

Values expressed in percentage

No obstetrical complications like cervical tears, post partum haemorrhage (PPH) were noted in any group.

4. Discussion

The concept of active management of labour gained strength in clinical practice with the availability of cervical smooth muscle dilators. Drotaverine and valethamate are more frequently used by many institutes of obstetrics and foetal medicine.

In our study we evaluated and compared the effect of DH and VB on cervical dilatation, duration of second and third stages of labour and third stage complications. After intravenous(IV) administration the drotaverine is rapidly absorbed and has half life is 12 minutes, reaches maximum concentration in 45 minutes. The primary elimination half life is 2.4 hours. It doesn't cross placental barrier and metabolised by liver. It is excreted through urine and faeces as unchanged drug[6,7]. After intravenous(IV) of valethamate action starts with in 5–10 minutes. Its Plasma half–life is 4 hours. It crosses the placental barrier and is also secreted in breast milk, but has no proven deleterious effects on foetus and baby. It is completely metabolised by liver and excreted in urine as both unchanged drug and metabolites[4,5]

The first stage of labour is longest and more painful especially in primigravidae. The smooth muscle content of cervix is 6 – 25% that offers contractile response to the advancing foetal head. This provides the physiological basis to use smooth muscle relaxants. The administration of smooth muscle relaxants at an appropriate time and dilatation phase can reduce the duration of labour successfully while providing pain reduction.

Ever since Farkas *et al* (1967)[8]concluded that drotaverine effectively relieves the cervical smooth muscle spasm, many obstetricians used drotaverine for accelerating labour and proved it as an effective cervical dilator. Our study also proved the same.

In the study done by Sharma *et al* (2001)[9]with drotaverine and valethamate in acceleration of labour, he concluded that both are effective but drotaverine accelerated labour more rapidly with less side effects. The injection dilatation interval was significantly reduced with drotaverine 193.96 minutes (3 hours 13 minutes) in contrast to valethamate bromide group 220.68 minutes (3 hours 40 minutes)

In the study conducted by S.L Mishra et–al (2002)[10]it was proved that drotaverine is highly effective cervical dilating agent compared to valethamate and control groups.

The average duration of 3 cm to full cervical dilatation was 3 hours 25 minutes (205 minutes) in primigravidae and 1 hour 45min (105 minutes) in multigravidae with drotin and 4 hours 35 minutes (275 minutes) in primigravidae and 3 hours 30min (210 minutes) in multigravidae with epidosin. They concluded that both the drugs were effective but epidosin was better in multigravidae.

In the study conducted by Monika Soni *et al* (2008)[11]and C Madhu *et al* (2009)[12]they proved that both the drugs were effective in cervical dilatation but drotaverine hydrochloride is superior to valethamate bromide with less side effects.

In the present study the mean duration of active phase was 186.3 minutes (3 hours 6 minutes) with drotaverine and 254.2 minutes (4 hours 14 minutes) with valethamate in primigravidae and 140.76 minutes (2 hours 20 minutes) with drotaverine and 172.82 minutes (2 hours 52 minutes) with valethamate in multigravidae. The rate of cervical dilatation is 1.92 cm/hour and 2.58 cm/hour with drotaverine in primigravidae and multigravidae respectively whereas it is 1.44 cm/hour and 2.19 cm/hour with valethamate in primigravidae and multigravidae respectively. Both drotaverine and valethamate are effective in cervical dilatation but drotaverine is superior to valethamate. The data from the studies of J.B Sharma *et al*[9], S.L Mishra *et al*[10]and C.Madhu *et al*[12]also support this findings.

In the present study there is no significant difference in the duration of second and third stages with both the drugs and no increase in obstetrical complications. This is supported by the studies done by Sharma *et al*[9], Anju *et al*[13]and C. Madhu *et al*[12]. Some obstetricians have reserved opinions that the cervical spasmolytic action of drotaverine could weaken the uterine contractions thus delaying the progress of labour. However no scientific studies are available in defence of such opinions. But our study and previous studies proved that drotaverine hydrochloride had no such effect.

In our study 6% of cases in valethamate group experienced vomiting, tachycardia and dryness of mouth. In drotaverine

group patients had no such complaints. Our findings are consistent with the findings of Anju *et al*[13], S.L. Misra *et al*[10]and Monika *et al*[11].

The APGAR scores were also not effected in both groups. Multigravidae expressed definite satisfaction with pain experience compared to their previous labour pains. This is more with drotaverine than valethamate. This comparison is not obtained in primigravidae as they have no such experiences of labour pains previously.

The sum effect of reduction in total duration of labour reduced the maternal morbidity and did not adversely affect the foetal outcome. The process of labour as such becomes less anxious and less painful experience fulfilling the aim of the obstetrician and desire of the patient.

Both the drugs are easily available even in rural set up, less expensive, easy to administer, no need of anaesthetist and easy to monitor with less side effects.

Our study found an increasing role of drotaverine hydrochloride in reducing the total duration of labour, hastening cervical dilatation, ensuring smooth progress of labour with good maternal and foetal outcome. It is concluded that overall efficacy of drotaverine was superior than the valethamate bromide.

The drugs drotaverine and valethamate 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 labour. Drotaverine is found to be better than valethamate in shortening the duration of labour and gives better pain relief. But both the drugs had no major side effects. .

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

We sincerely thank all pregnant women who gave consent and participated in this study.

Comments

Background

M

Research frontiers

S

Related reports

O

Innovations & breakthroughs

D

Applications

I

Peer review

T

References

[1] Tehalia M K, Sajjan G R, Korbu J, Venkatesh S, Biradar R. A comparative study of Hyoscine butylbromide versus Drotaverine hydrochloride in first stage of labor. *J Obstet Gynecol India* 2008; **58**(3):230–234.

[2] Balaji O . Pharmacokinetics and Bioavailability of drotaverine in Humans. Europ J. Drug Metab. *Pharmacokinet*. 1996; **21**: 217–221.

[3] Leroy MI., Legnier G., Merezak. Isolation and Characterisation of Rolipram Sensitive CAMP– Specific Phosphodiesterase (Type intravenous(IV) PDE) in Human Term Myometrium. *Cell Signal* 1994;**6**: 405–412.

[4] Ajay K T, Abhishek R, Manmohan S, Harsh S, Ranjan B, Rajendra K S. significant combination of preferential cox–2 inhibitor and non–anticholinergic spasmolytic used in labor augmentation. *Pharmacologyonline* 2011; **2**: 470–476.

[5] Tripathi KD. Essentials of Medical Pharmacology. 6th edition. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2008.

[6] Bolaji OO, Onyeji CO, Ogundaini AO, Olugbade TA, Ogunbona FA. Pharmacokinetics and bioavailability of drotaverine in humans. *Eur J Drug Metab Pharmacokinet*. 1996;**21**(3):217–221

[7] Vargay Z. Summary of the Pharmacokinetic and Metabolism Studies of drotaverine. *Therapia Hungarica* 1989; **15** : 21–29.

[8] Farkas M, Viski S. Relief of Pain In Child Birth by a new Antispasmodic, Ther, Hung 1967 ; **15**: 4–8.

[9] Sharma JB, Pundir P, Kumar A, Murthy NS. Drotaverine hydrochloride vs. valethamate bromide in acceleration of labor. *Int J Obstet Gynecol* 2001;**74**:255–260

[10] Mishra SL, Toshniwal A, Benerjee R. Effect of drotaverine on cervical dilatation : a comparative study with epidosin. *Obstet. Gynacol Ind*. 2002; **52**(3):76–79

[11] Monica Soni. Intravenous drotaverine hydrochloride vs. valethamate bromide in acceleration of labour. *Obstet Gynaecol Today* 2008; **6**:239–241

[12] Madhu C, Mahavarkar S, Bhave S. A randomised controlled study comparing drotaverine hydrochloride and valethamate bromide in the augmentation of labour. *Arch Gynecol Obstet* 2010;**282**:11–15.

[13] Anju HK, Indu B, Krishna D, Krishna S. A Comparative study of the efficacy of valethamate bromide with drotaverine in Normal Labour. *Obstet Gynaecol Ind*. 2003; **53**: 568–570.