COMPARATIVE EFFICACY OF DROTAVERINE HYDROCHLORIDE VALETHAMATE BROMIDE EFFECTS ON CERVICAL DILATATION IN ACTIVE PHASE OF LABOUR IN PRIMIGRAVIDA

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AIMS AND OBJECTIVES:

Aim: To compare the effects of drotaverine hydrochloride and epidosin on cervical dilation in active phase of labour in primigravida.

Objectives:

1. To study the effectiveness of Drotaverine in active labour.
2. To study the effectiveness of Epidosin in active labour.
3. To compare their effects on patients.

INTRODUCTION: One of the most significant periods in a woman's life is labour. The length of labour during labour has a significant impact on both maternal and perinatal morbidity. In order to expel the uterine foetus from the intrauterine to the extrauterine environment, labour is a contraction process that aims to produce increasing cervical effacement and dilatation.

MATERIALS AND METHODS: A descriptive study with a sample size of 300 patients was conducted in our labour room between October 2020 to may 2022.

OBSERVATION AND RESULTS:

The patients were divided into 3 groups as follows,

Group 1=Control Group

Group 2= Received 1 ampoule of Drotaverine Hydrochloride 40 mg intravenously at 2 hourly intervals up to a maximum of 3 doses,starting at 3-4 cms cervical dilatation.

Group 3= Received, 1 ampoule of Valethamate bromide 8mg intravenously at hourly intervals up to a maximum of 3 doses, starting at 3-4 cms cervical dilatation.

RESULTS:

- In our study, it was observed that the majority of the patients belonged to the age group of 23-26 years, followed by 27-30 years. Very few patients were less than 22 years of age.
- Drotaverine was seen to decrease the duration of active stage of labour by 27% as compared to Valethamate that decreased it by 24%.

- The cervical dilatation in group II was increased by 2.3 cm/hr while in group III it was increased by 1.3 cm/hr. There was a significant increase in rate of cervical dilatation in both the groups.
- The mean duration of second phase of labour was 144.23 ± 3.57 minutes in Group I, 102.42 ± 1.75 minutes in Group II and 116.56± 2.34 minutes in Group III
- The mean injection delivery interval was found to be 101.58±78.06 mins in Drotaverine Group and 134.24±94.12 mins in Valethamate Group.[1]
- Maternal complications like Dryness of mouth,Tachycardia,Vomiting were noted in a few cases.
- Drotaverine hydrochloride is a superior cervical dilatation agent than Valethamate bromide in significantly reducing the duration of labor with fewer side effects on the mother or the fetus (17).
- Drotaverine hydrochloride and valethamate bromide are better labor accelerators. But drotaverine accelerates labor better than valethemate. The reduction of pain during labor is better with drotaverine than valethamate.

CONCLUSION:

The duration of active phase was significantly reduced in Drotaverine group compared to control.
The duration of active phase was lesser than the control in the Episodin group too. On comparing the three groups, Drotaverin group was more effective than Valethamate group in accelerating the active phase of labour and the result was statistically significant.Hence, Drotaverine hydrochloride is more effective in accelerating active phase of labour than Valethamate bromide. It is also a more potent cervical dilator. Both the drugs reduce the duration of labour significantly without any maternal or fetal complications.
Hence, Drotaverin and Valethamate are potent cervical dilators that can be used in active labour to accelerate labour and reduce maternal distress. Due to it's efficacy, Drotaverin can also be tried in prolonged labour

INTRODUCTION:

One of the most significant periods in a woman's life is labour. The length of labour during labour has a significant impact on both maternal and perinatal morbidity[1]. In order to expel the uterine foetus from the intrauterine to the extrauterine environment, labour is a contraction process that aims to produce increasing cervical effacement and dilatation[2].

The cervix is affected by the forces that cause uterine contraction and acts as an innocent blockage as a result of passive tissue resistance. Cervical dilatation has been shown to be one of the key elements affecting how long labour lasts. Even when uterine contractions are strong, it occasionally happens that the cervix fails to dilate, dilates extremely slowly, or dilates only partially. Cervical dystocia is present here[1]. Obstetricians have always had trouble with protracted labour. It consistently causes mother tiredness, increased fetomaternal morbidity, and an increase in the frequency of surgical deliveries. Both obstetricians and women are in favour of techniques that try to reduce the incidence of functional cervical dystocia and shorten the first stage of labor[3].
A more recent spasmolytic medication called drotaverine is said to shorten labour by speeding cervical dilatation without having any negative side effects. It works by inhibiting the phosphodiesterase enzyme IV. Due to its neurotropic or atropine-like action and musculotropic or papaverine-like action, epidosin (valethamate bromide) is also an antispasmodic that aids in cervical dilatation. In order to compare the effectiveness of injecting Drotaverine and injecting Valethamate on

the length of the active phase of labour, the rate of cervical dilatation, and its effects on the mother and foetus, this study was conducted[3].

In this study, the effectiveness of Drotaverine hydrochloride and Valethamate bromide on cervical dilatation during the active phase of labour is compared.

MATERIALS AND METHODS:

Type of Study : Descriptive Study

Place of Study : Conducted at the labour room of Dr. D. Y. Patil Medical College, Hospital & Research Centre Pimpri, Pune- 411018, a Teritary Care Hospital.

Period of Study **:** October 2020 to May 2022

Sample Size **:** Different studies give various SD and Mean in duration the labour therefore form the study reference article[13,14].
Assuming an effect size of 0.4 (small to medium effect) with an $\propto$ error of 0.05 and power of 0.8 the sample size calculated to the 100 in each group. The software used for the same was G' power 3.1.9.2

Ethics and Consent: Institute ethics committee clearance will be obtained before start of the study. Written and informed consent will be obtained from all patients.

METHOD OF STUDY:

Data will be collected using pretested and validated questionnaire meeting the objectives of the study. Informed consent will be obtained from the participant after being informed about the survey, its objectives and procedures and assured that the information collected would be treated as confidential and used only for research purpose.

Inclusion Criteria:

1. Singleton term program
2. Term pregnancy in active labour, initial cervical dilatation 3-4 cm and effacement of >50%
3. Cephalic presentation
4. No cephalopelvic disproportion
5. No high risk factors
6. Regular established uterine contractions at the rate of ≥12 contractions per hour, each contraction lasting for at least for 30-40 sec.
7. Intact fetal membranes
8. Primigravida
9. Willingness to participate in study.

Exclusion Criteria:

1. Medical disorders complicating pregnancy
2. Obstetric complications within high risk category
3. Malpresentation
4. Women with previous caesarean section history

OBSERVATION AND RESULTS

The sample size n= 300, with 100 patients in each group.

Group 1=Control Group

Group 2= Received 1 ampoule of Drotaverine Hydrochloride 40 mg intravenously at 2 hourly intervals up to a maximum of 3 doses,starting at 3-4 cms cervical dilatation.

Group 3= Received, 1 ampoule of Valethamate bromide 8mg intravenously at hourly intervals up to a maximum of 3 doses, starting at 3-4 cms cervical dilatation.

Table 1. Age distribution of the sample

Age(yrs)	Group			Total(%)	X^2	p value
	1	2	3			
15-20	7	2	4	4.3	6.99	0.14
21-25	42	49	57	49.3		
26-30	51	49	39	46.3		

Table 2. Mean duration of active phase of labour

Group	N	Mean Duration (min)	Std. Deviation	Difference in means	Percentage	F	p value
1	100	215.10	54.460			54.462	**<0.02****
2	100	156.57	48.874	58.53	27.2		
3	100	163.89	15.729	51.21	23.8		
Total	300	178.52	50.349				

Table 3. Rate of cervical dilatation in active phase of labour

N	Cervical dilatation (cm/hr)	Std. Deviation	Difference in means	F	p value
100	2.163	.5438		659.554	**<0.02****
100	4.382	.4478	2.3000		
100	3.465	.2634	1.3000		
300	3.337	1.0094			

Table 4. Mean duration of second phase of labour

Group	N	Mean Duration (min)	Std. Deviation	Difference in means	Percentage	F	p value
1	100	25.21	3.577			51.332	**<0.02****
2	100	22.34	1.748	2.9	11.500		
3	100	21.56	2.397	3.6	14.300		
Total	300	23.04	3.102				

Table 5. Interval between first injection and active phase of labour

Group	N	Mean Duration (min)	Std. Deviation	Difference in means	Percentage	F	p value
1	100	246.33	18.029			142.153	**<0.02****
2	100	184.22	24.193	62.000	25.000		
3	100	191.17	39.163	55.000	22.400		
Total	300	207.24	39.798				

Table 6. Characteristics of amniotic fluid

Amniotic fluid	Group			Total	X2	p value
	1	2	3			
Clear	91	94	92	277	0.659	.719
Meconium stained	9	6	8	23		

Table 7. Fetal outcome in the three groups-APGAR score

Group	1 minute		5 minutes	
	<7/10	>7/10	<7/10	>7/10
1	3	97	0	100
2	2	98	0	100
3	2	98	0	100

Table 8. Comparison of number of injections given

No. of injections given	Group			Total
	1	2	3	
1	0	95	38	133
2	0	5	62	67
Nil	100	0	0	100

DISCUSSION:

- Various prospective randomized controlled clinical studies have compared Drotaverine hydrochloride with placebo, and / or Valethamate bromide.
- In the present study, Drotaverine hydrochloride and Valethamate bromide were given intravenously at 3-5 cms cervical dilatation in 2 groups of demographically similar women with term pregnancy in active labor.
- They were compared with a control group.
- A total of 300 patients were randomly allotted to the three groups, with 100 patients in each group.

Age distribution of the sample:

- In our study, the majority of the patients belonged to the age group of 23-26 years, followed by 27-30 years. Very few patients were less than 22 years of age.

- The mean age in all the three groups was around 25 years and there was no significant difference between the age distribution of the three groups. Therefore, the three groups were comparable in terms of distribution of age.
- Similar mean age group was obtained in other similar studies.[1,4,9]

Mean duration of active phase of labour:

- Drotaverine was seen to decrease the duration of active stage of labour by 27% as compared to Valethamate that decreased it by 24%.
- Both the drugs caused significant reduction in duration of active phase of labour.
- Randomised controlled clinical studies presented at the XVII FIGO World Congress held that the decrease in mean duration of Active phase with Drotaverine was 109 minutes compared with placebo, and 37.6 minutes compared with Valethamate. In the present study, the decrease is 96.81 minutes in Drotaverine group compared to control, and 24.58 minutes compared with Valethamate(6).
- Deepshikha et al., 2020[1] found that Drotaverine and Valethamate decrease the duration of active stage of labour significantly, with Drotaverine being more effective.
- Neerja Agarwal et al., 2017[4] and Palii S.B et al., 2012[9] reported similar findings with a decrease in 3 hours in Drotaverine group and 1.45 hrs in Valethamate group.

Rate of cervical dilatation in active phase of labour:

- The rate of cervical dilatation was 2.16 ± 0.54 cm/hr in Group I, 4.38 ± 0.44cm/hr in Group II, and 3.46+-0.26 cm/hr in Group III respectively which is comparable to the study by Devinder et al (2001) (4.99 ± 2.21 cm/hr with Drotaverine and 3.74 ± 1.72 cm/hr with Valethamate).
- The cervical dilatation in group II was increased by 2.3 cm/hr while in group III it was increased by 1.3 cm/hr. There was a significant increase in rate of cervical dilatation in both the groups.

Average duration of second stage of labour:

- The mean duration of second phase of labour was 144.23 ± 3.57 minutes in Group I, 102.42 ± 1.75 minutes in Group II and 116.56± 2.34 minutes in Group III.
- The average duration of II stage of labor was affected by administration of drugs compared to control group, and the difference was not statistically significant.
- Drotaverine decreased the duration of second stage of labour more when compared to Valethamate, but they did not reduce the duration significantly.

Injection delivery interval:

- The mean first injection delivery internal with Drotaverine was 184.22 ±24.19 minutes and 191.17 ± 39.16 minutes with Valethamate which is comparable to the study by Devinder et al (129.82 ± 63.75 minutes with Drotaverine and 151.53 ± 60.47 minutes with Valethamate).
- It was seen that both Drotaverine and Valethamate significantly reduced the interval between first injection and active phase of labour.
- In similar studies, the mean injection delivery interval was found to be 101.58±78.06 mins in Drotaverine Group and 134.24±94.12 mins in Valethamate Group.

Characteristics of amniotic fluid:

- Meconium-stained liquor was noted in 9%, 6% and 8% of cases in Group I, II and III respectively.

- There was no significant difference between the three groups in terms of meconium staining of amniotic fluid.
- Palii S.B et al., 2012[9] and Neerja Agarwal et al., 2017[4] too did not find any major adverse fetal or maternal outcome in their studies.

Fetal outcome:

- Regarding fetal outcome, all the cases were NST reactive, delivered vaginally, and had Apgar >7/10 at 5 minutes.
- At 1 minute, 3 cases in group l, and two cases in the other two groups had Apgar scores less than 7/10. These findings improved on subsequent recording.
- Hence, Drotaverine and Valethamate did not increase the fetal complications as compared to the control group.

Effect of weight of the baby on cervical dilatation:

- In our study, it was seen that 58 patients in group l, 50 in group ll. and 48 in group lll had weight of the baby between 2.5-3 kgs; 25, 27 and 26 patients respectively in each group had weight of baby 2-2.5 kg and very few had weight above 3.5 kgs.
- The weight of baby effected cervical dilatation.
- The three groups had comparable distribution of weight of the baby.

Maternal outcome:

- Maternal complications like Dryness of mouth,Tachycardia,Vomiting were noted in a few cases.
- No patient in the control group developed untoward maternal effects.
- Hence, Valethamate was seen to increase untoward maternal effects little more than Drotaverine but the two drugs did not have significant untoward effects on maternal outcome.
- In their study, Neerja Agarwal et al., 2017[4] too found that minor side effects were more commonly seen in Valethamate group as compared to Drotaverine and control groups.
- K Devinder et al[11] noted that side effects were fewer in the Drotaverine group as compared to the other groups.

Conclusion:

Hence, Drotaverine significantly shortens the duration of the first stage of labor and does not interfere with uterine contractility. Moreover, it is found to be safe with no adverse effects on mother and foetus. For this reason, it is a better choice than Valethamate Bromide for shortening at the first stage of labor (16).

- Drotaverine hydrochloride is a superior cervical dilatation agent than Valethamate bromide in significantly reducing the duration of labor with fewer side effects on the mother or the fetus (17).
- Drotaverine hydrochloride and valethamate bromide are better labor accelerators. But drotaverine accelerates labor better than valethemate. The reduction of pain during labor is better with drotaverine than valethamate (18).
- Effect of Drotaverine on shortening duration of labor is significantly better than Valethamate with fewer side effects. Thus, Drotaverine is a safe, potent and effective drug to shorten the first stage of labor (19).
- Drotaverine is associated with higher cervical dilatation, shorter 1st stage duration and very less adverse effect in therapeutic doses as compared to valethamate bromide (20).

Both Drotaverin and Valethamate accelerate the labor and do not have any major untoward effects on the maternal and fetal outcome.

As Valethamate has more incidence of minor complications, strategies to prevent and treat these complications can be applied whenever required in order to benefit from the potential actions on cervical dilatation.

Therefore, Drotaverin is a potent and safe cervical dilator.

Valethamate is less potent option that should be used with caution considering it's side effect profile.

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