



## To Study the Efficacy and Side Effects of Drotaverine and Epidosin (Valethamate) in Acceleration of Labor and to Study their Effects on the Fetal Outcome

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### Abstract

**Background:** Labor is the most perilous journey a woman has to undertake. Painless and short labor is desired by every woman and is a constant aim for obstetrician.

**Objectives:** To study the efficacy and side effects of Drotaverine and Epidosin (Valethamate) in acceleration of labor and to study their effects on the fetal outcome.

**Purpose:** This study was undertaken to compare effectiveness of Drotaverine and Epidosin in acceleration of labor.

**Method:** The present study is a prospective comparative study conducted at Raipur Institute of Medical Sciences, Raipur, from October 2014 to September 2016 over a period of 2 years. 150 antenatal women with 38-41 weeks of gestational age were included in study and were divided into three groups randomly. Group V consisted of 50 women who received Valethamate, group D consisted of 50 women who received Drotaverine and Group C also consisted of 50 cases who received normal saline. Various parameters of duration of labor, mode of delivery, maternal and fetal complications and side effects of these drugs were compared in three groups.

**Results:** The present study showed that both the drugs shorten the duration of first stage of labor when compared to control, but Drotaverine reduces the duration more than Valethamate bromide. Both in primi and multi this difference was statistically significant. There was no significant difference in duration of second and third stages of labor in between the three groups. Mode of delivery, neonatal outcome were almost similar in the three groups. Minor side effects were more common in Valethamate group than in Drotaverine and control group.

**Conclusion:** Drotaverine is found to be better than Valethamate in shortening the duration of labor with less side effects. Both the drugs have no major side effects and have good fetomaternal outcome. Thus these drugs are safe, potent and effective drug to be used in active phase of labor.

**Keywords:** Labor, Drotaverine, Valethamate (epidosin).

### Introduction

Childbirth is one of the most important events in the life of a woman. The process by which it normally occurs is called Labor. It is defined as

painful uterine contractions that bring about demonstrable effacement and dilatation of cervix.<sup>1</sup> It is not a pathological process rather it is complex physiological process with acute pain.<sup>2</sup> It is ideal

for any obstetrician to achieve reduction of pain and suffering for the women in Labor.

In 1848, doctors began using ether as a pain reliever during childbirth. This resulted in even more problems as children were born sick and mothers were often overdosed during childbirth. Later in 1914 doctors introduced twilight sleep which involved using morphine and other drugs to render the women basically unconscious during childbirth.

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. It has been observed that the most common cause of the prolonged first stage of labor is cervical spasm which may be due to inflammation, injury, or fibrosis of cervix leading to cervical dystocia.<sup>3</sup>

A short first stage of labor is naturally of dual advantage for both obstetrician and the patient. The pain experienced is beyond description and is basically due to process of cervical dilatation. The duration of the first stage is longest of the three stages of labor and it is due to painful progressive cervical dilatation. It is ideal for any obstetrician to achieve reduction of pain and suffering during labor by accelerating the rate of cervical dilatation.

In addition to mechanical factors such as sweeping of membranes, cervical stretching<sup>4</sup> and amniotomy,<sup>5</sup> (ARM) various pharmacological agents have been found to facilitate cervical dilatation. The role of oxytocin and prostaglandins has been established worldwide in augmentation of Labor<sup>6</sup> and cervical application of Hyaluronidase has also been used with some success.<sup>7</sup> Buscopan and Scopolomine have been used for pain relief and shortening of Labor.<sup>8</sup> Various drugs such as tranquillizers, especially diazepam, have been used for shortening Labor

but the majority of them were found to have ill effect on the mother and the fetus.

A major breakthrough was achieved with the introduction of Esocin group of drugs by Steinman in 1953. Valethamate bromide (epidosin)<sup>9</sup> is one of the drugs of this group. It is a potent, rapidly acting, spasmolytic and musculotropic agent, which relieves the spasm of the smooth muscles of the cervix. In the 1960s, Drotaverine, a benzyl isoquinoline derivative was introduced. It is a selective inhibitor of phosphodiesterase type 4 enzyme<sup>10</sup> which is present in high concentration in myometrium near term, thus acts as a spasmolytic agent, facilitating cervical dilatation during labor. The present study was undertaken to analyse and compare the efficacy of these two drugs in normal labor.

### Aim

- To compare effectiveness of Drotaverine and Epidosin (Valethamate bromide) in acceleration of labor.

### Objectives

1. To study the effects of Drotaverine and Epidosin in normal labor with respect to:
  - a) Duration of Labor .
  - b) Mode of delivery.
  - c) Obstetric complications like perineal /cervical /vaginal tear or postpartum Hemorrhage (PPH).
  - d) Side effects of drugs.
2. To study the effects of Drotaverine and Epidosin on the fetal outcome

### Results

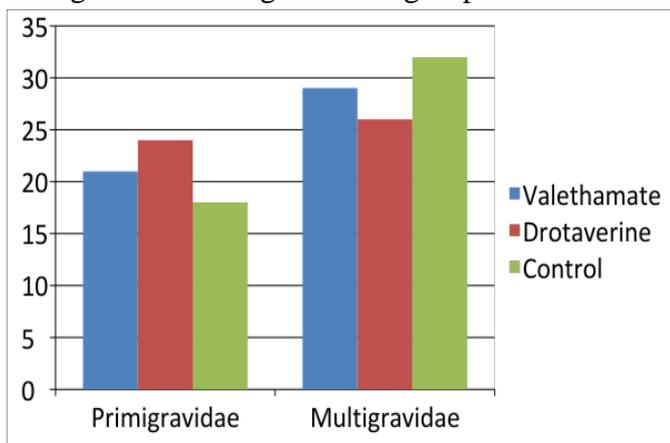
**Table 1:** Distribution of Primi & Multigravidae among the 3 Groups:

GROUP	PRIMI (n=63)	MULTI (n=87)
Valethamate bromide (n=50)	21	29
Drotaverine (n=50)	24	26
Control (n=50)	18	32

In the present study there were 21 Primi cases and 29 Multigravidae in Valethamate group. In Drotaverine group there were 24 Primi and 26 Multigravidae. In control group, there were 18 primi and 32 Multigravidae.

In the present study, in all the three groups there were more multigravidae than primigravidae.

**Figure: 7-** Distribution of primigravidae and multigravidae among the three groups:

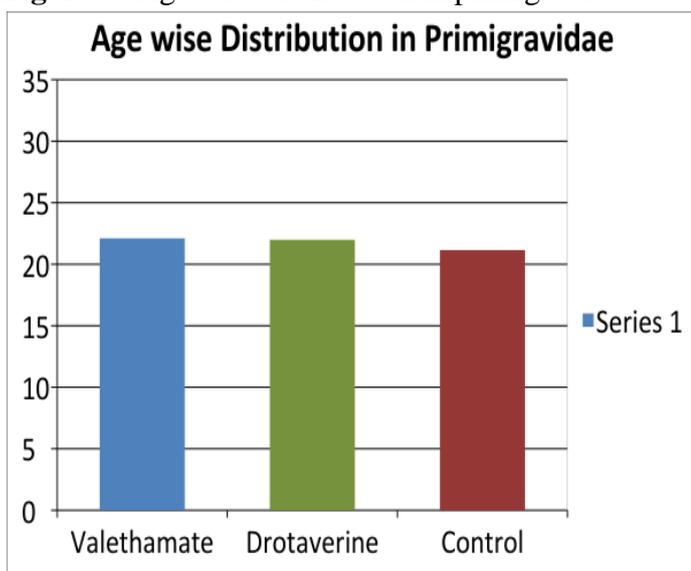


**Table 2:** Age wise distribution of Primigravidae between the three groups:

GROUP	Mean Age	SD	P VALUE	Not significant
Valethamate bromide (n=21)	22.09	2.527	0.364	Not significant
Drotaverine (n=24)	22.00	1.769		
Control (n=18)	21.16	2.332		

In the present study, in Primigravidae mean age of cases in V group was 22.09, in D group was 22.00 and in C group was 21.16. The P value was 0.364. Thus, in this study there was no significant difference ( $p > 0.05$ ) between the mean age of primigravidae patients in three groups.

**Figure 8-** Age wise distribution in primigravidae:

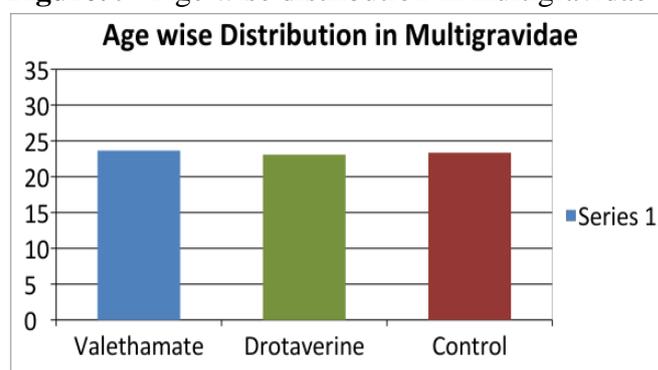


**Table 3:** Age wise distribution of Multigravidae between the three groups

GROUP	MEAN AGE	SD	P VALUE	Not significant
Valethamate bromide (n=29)	23.65	2.482	0.701	Not significant
Drotaverine (n=26)	23.11	2.371		
Control (n=32)	23.34	2.308		

In the present study, in Multigravidae mean age of cases in V group was 23.65, in D group was 23.11 and in C group was 23.34. The P value was 0.701. Thus, in this study there was no statistically significant difference ( $p > 0.5$ ) between the mean age of multigravida patients in three groups.

**Figure: 9-** Age wise distribution in multigravidae



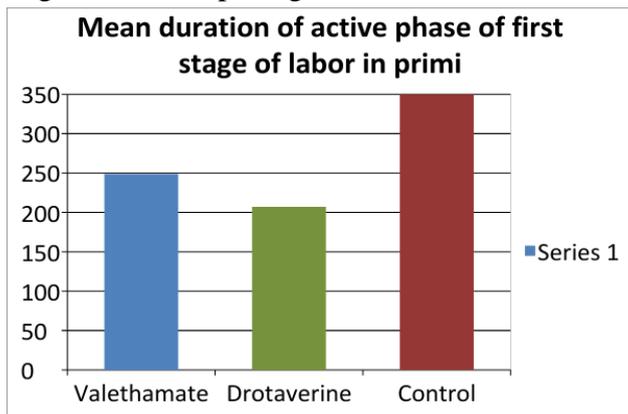
**Table 4:** Comparison of mean duration of Active Phase of first stage of Labor in Primigravidae between the three groups

GROUP	Mean duration (min)	SD	P VALUE	SIGNIFICANT
Valethamate bromide (n=21)	248.57 (4.1hrs)	60.00	0.000	SIGNIFICANT
Drotaverine (n=24)	207.08(3.46hrs)	60.73		
control (n=18)	370.83(6.2 hrs)	63.43		

In the present study the mean duration of active phase of labor in V group was 248.57mins, in D group was 207.08 mins, and in C group was 370.83mins. The P value was 0.000, showing statistical significance.

Thus in primigravidae, Mean duration of active phase of labor was significantly less in drotaverine group when compared to valethamate bromide and control group. Also it was significantly less in valethamate group than in control.

**Figure 10-** Mean duration of active phase of first stage of labor in primigravidae



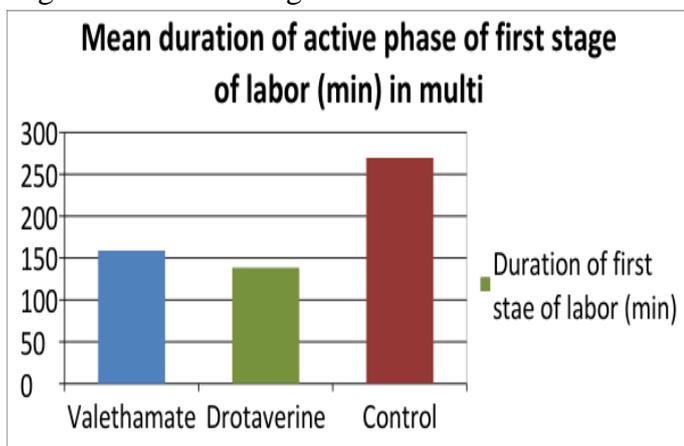
**Table 5:** Comparison of mean duration of active phase of first stage of labor in Multigravidae between the three groups

GROUP	Duration of first stage of labor(min)	SD	P Value	
Valethamate bromide (n=29)	158.96(2.65 hrs)	65.78	0.000	Significant
Drotaverine (n=26)	138.46(2.3 hrs)	43.46		
Control (n=32)	269.84(4.5 hrs)	88.48		

In the present study the mean duration of active phase of labor in V group was 158.96mins, in D group was 138.46mins, and in C group was 269.84mins. The P value was 0.000, showing statistical significance

Thus, in multigravidae, Mean duration of active phase of labor was significantly less in drotaverine group when compared to valethamate bromide and control group. Also it was significantly less in valethamate group than in control.

**Figure: 11-** Mean duration of active phase of first stage of labor in multigravidae



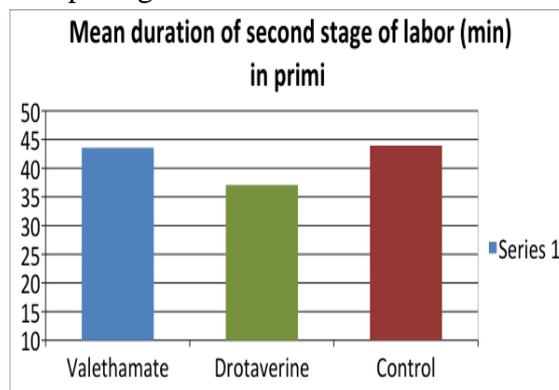
**Table 6:** Comparison of duration of second stage of labor in Primigravidae between the three groups

GROUP	Mean duration of second stage of labor(min)	SD	P Value	
Valethamate (n=21)	43.57	11.53	0.080	Not Significant
Drotaverine (n=24)	37.08	12.93		
Control (n=18)	43.94	8.88		

In the present study the mean duration of Second stage of labor in V group was 43.57mins, in D group was 37.08mins, and in C group was 43.94mins. The P value was 0.080, showing no statistical significance

Thus there was no statistically significant difference in the mean duration of second stage of labor between the 3 groups in Primigravidae.

**Figure: 12** Mean duration of second stage of labor in primigravidae:



**Table 7:** comparison of mean duration of second stage of labor in multi between the three groups

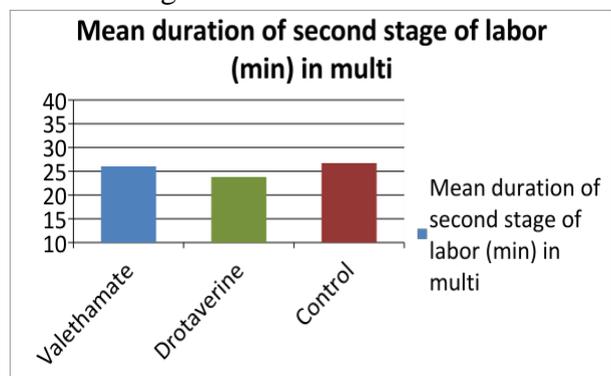
GROUP	Mean duration of second stage of labor (min)	SD	P Value	
Valethamate bromide (n=29)	26.03	9.94	0.570	Not Significant
Drotaverine (n=26)	23.80	9.82		
Control(n=32)	26.71	11.88		

In the present study the mean duration of Second stage of labor in V group was 26.03mins, in D group was 23.80 mins, and in C group was 26.71

mins. The P value was 0.570, showing no statistical significance

Thus there was no statistically significant difference in the duration of second stage of labor in between three groups in multigravidae.

**Figure 13-** Mean duration of second stage of labor in multigravidae



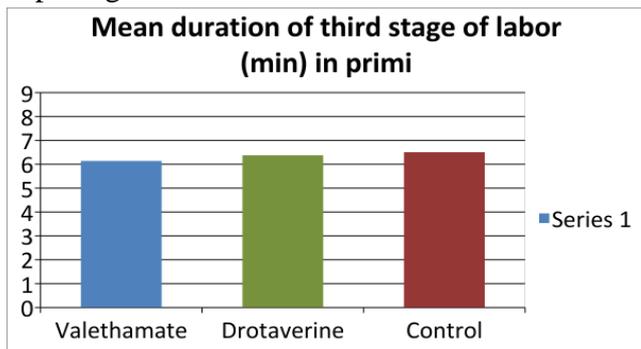
**Table 8** Comparison of mean duration of third stage of labor in Primigravidae between the three groups

GROUP	Mean duration of third stage of labor (min)	SD	P Value	Not Significant
Valethamate bromide (n=21)	6.14	1.71	0.862	Not Significant
Drotaverine (n=24)	6.37	2.53		
Control (n=18)	6.50	1.82		

In the present study the mean duration of Third stage of labor in V group was 6.14mins, in D group was 6.37mins, and in C group was 6.50mins. The P value was 0.862, showing no statistical significance

Thus there was no statistically significant difference in the mean duration of third stage of labor of primigravidas between the three groups.

**Figure 14-** Mean duration of third stage of labor in primigravidae:



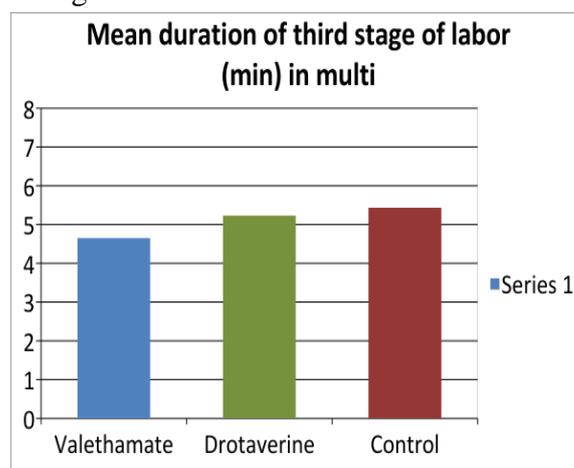
**Table 9:** comparison of mean duration of third stage of labor in Multigravidae between the three groups:

GROUP	Mean duration of third stage of labor (min)	SD	P Value	Not Significant
Valethamate bromide (n=29)	4.65	1.17	0.046	Not Significant
Drotaverine (n=26)	5.23	1.21		
Control(n=32)	5.43	1.88		

In the present study the mean duration of Third stage of labor in V group was 4.65mins, in D group was 5.23mins, and in C group was 5.43mins. The P value was 0.046, showing no statistical significance

Thus there was no statistically significant difference between the mean duration of third stage of labor between the three groups in multigravidae.

**Figure: 15-** Mean duration of third stage of labor in multigravidae:



**Table 10:** Mode of delivery among Primigravidae in the 3 Groups

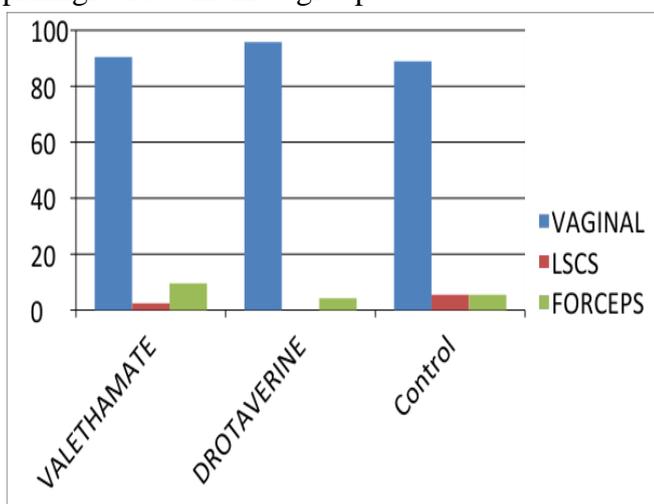
Group	Vaginal	Percentage(%)	LSCS	Percentage(%)	Forceps	Percentage(%)
Valethamate bromide (n=21)	19	90.47	0	0	2	9.52
Drotaverine (n=24)	23	95.83	0	0	1	4.16
Control (n=18)	16	88.88	1	5.55	1	5.55

In the present study in primigravidae, in V group 90.47% cases had SVD. 9.52%(2 cases) required Forceps indication being fetal distress in one case

and prolonged second stage in other case and no cases required LSCS. In D group, in primigravidae 95.83% cases had SVD and 4.16% (1 case) required Forceps indication being fetal distress and no cases underwent LSCS. In C group, inprimigravidae 88.88% cases had SVD and 6.55% (1 case) underwent LSCS indication being fetal distress and 5.55% (1 case) required Forceps indication being prolonged second stage of labor.

Hence, it can be seen that incidence of operative interference was least in Drotaverine group but it is not significant.

**Figure: 16-** Mode of delivery among primigravidae in three groups:



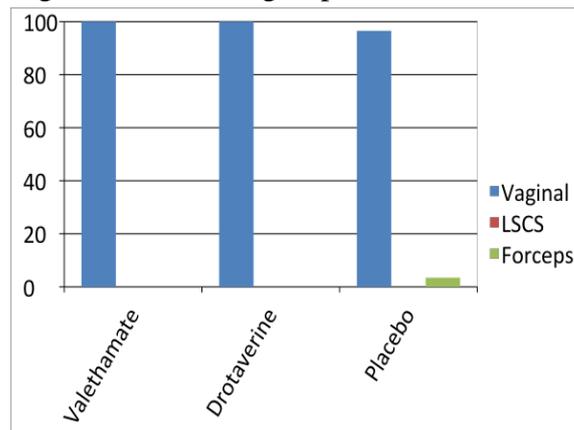
**Table 11:** Mode of delivery among Multigravidae in the 3 groups

Group	Vagi nal	Percent age(%)	LS CS	Percent age(%)	Forcep s	Percenta ge(%)
Valethamate bromide (n=29)	32	100	0	0	0	0
Drotaverine (n=26)	26	100	0	0	0	0
Control(n=32)	28	96.55	0	0	1	3.44

In Multigravidae, all cases (100%) had SVD in both V and D groups. And no cases required either Forceps or LSCS. In control group, 96.55% of cases had SVD and 3.44% (1 case) required forceps indication being fetal distress and no case underwent LSCS.

Hence, it can be seen that the incidence of operative interference was less in cases that were given Drotaverine or Valethamate.

**Figure: 17-** Mode of delivery among multigravidae in three groups:

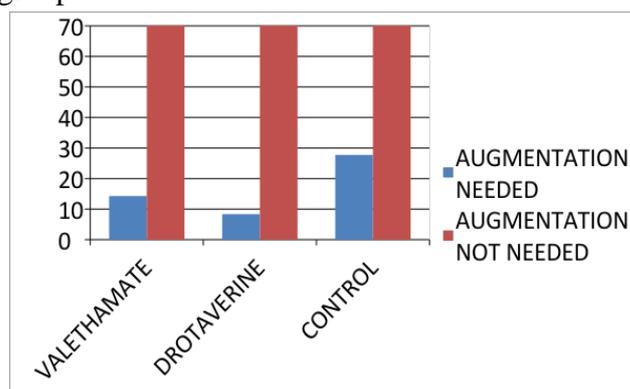


**Table 12:** Comparison of oxytocin augmentation in Primigravidae between the three groups

Group	Augmentatio n needed	Percentag e(%)	Augmentatio n not needed	Percentage( %)
Valethamate bromide (n=21)	3	14.28%	18	85.71%
Drotaverine (n=24)	2	8.33%	22	91.66%
Control (n=18)	5	27.77%	13	72.22%

In primigravidae, oxytocin augmentation was required in 14.28% cases in V group, 8.33% cases in D group and 27.7% in C group. Thus, oxytocin augmentation was required more in the cases of control group.

**Figure: 18-** Comparison of Oxytocin augmentation in primigravidae between the three groups:



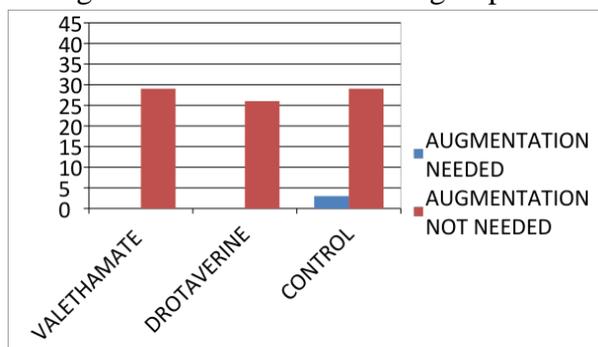
**Table 13:** Comparison of oxytocin augmentation in Multigravidae between the three groups

Group	Augmentatio n needed	Percentag e(%)	Augmenta tion not needed	Percentag e(%)
Valethamate bromide (n=29)	0	0	29	100%
Drotaverine (n=26)	0	0	26	100%
Control (n=32)	3	10.34%	29	89.65%

No cases required oxytocin augmentation in Multigravida in Valethamate and Drotaverine group and 10.34% of the cases in control group required oxytocin augmentation.

Thus, oxytocin augmentation was required more in cases of control group.

**Figure: 19** Comparison of Oxytocin augmentation in multigravidae between the three groups:



**Table 14 :** Maternal side effects of Valethamate Bromide( N =50) :

Side effects	Frequency
Giddiness	5 (10%)
Vomiting	3 (6%)
Tachycardia, dryness of mouth	20 (40%)

In valethamate group, 10% of the cases had giddiness, 6% of the cases had vomiting and 40% of the cases had Tachycardia, Dryness of mouth.

**Table 15:** Maternal side effects of Drotaverine (N=50)

Side effects	Frequency
Giddiness	4 (8%)
Vomiting	1 (2%)
Tachycardia, dryness of mouth.	1 (2%)

In Drotaverine group, 8% of the cases had giddiness, 2% of the cases had vomiting and 2% of the cases had Tachycardia, Dryness of mouth.

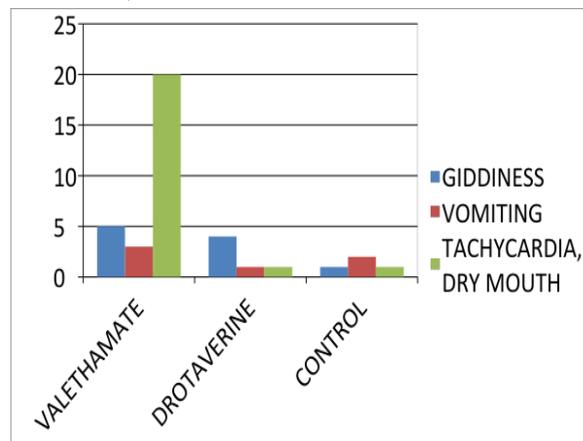
**Table 16:** Maternal side effects of Control group (N=50)

Side effects	Frequency
Giddiness	1 (2%)
Vomiting	2 (4%)
Tachycardia, dryness of mouth.	1 (2%)

In Control group, 2% of the cases had giddiness, 4% of the cases had vomiting and 2% of the cases had Tachycardia, Dryness of mouth.

Thus, it can be seen that maternal side effects were more common in Valethamate group because of its Anti-Cholinergic properties.

**Figure 20-** Side effects of Valethamate, Drotaverine, and Control

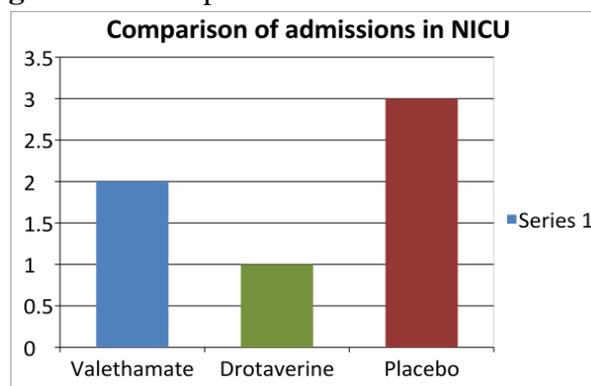


**Table 17:** comparison of admissions in NICU

Group	NICU admission
Valethamate bromide (n=50)	2
Drotaverine (n=50)	1
Placebo.(n=50)	3

In Drotaverine group, one NICU admission was for neonatal jaundice. In Valethamate group, one admission was for neonatal jaundice and other was for birth asphyxia .In control group, one was for congenital heart disease, one for neonatal jaundice and third admission was for birth asphyxia.

**Figure: 21-** Comparison of admissions in NICU



**Discussion**

Labor is a physiological process characterized by progressive increase in frequency and duration of uterine contractions, effacement and dilatation of

cervix with descent of fetus through the birth canal. Prolonged labor contributes to increased perinatal morbidity and mortality as well as increased physiological burden on the mother, eventually leading to complications in the second stage of labor and puerperium. Thus, acceleration of labor is considered to be an important factor in reducing maternal morbidity as well as neonatal complications.

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 labor successfully while providing pain reduction.

In our study we evaluated and compared the effect of drotaverine hydrochloride and valethamate bromide on duration of active phase of first stage of labor, second and third stage of labor, third stage complications, side effects of drugs and neonatal outcome.

Ever since Farkas et al<sup>55</sup> (1967) concluded that drotaverine effectively relieves the cervical smooth muscle spasm, many obstetricians used drotaverine for accelerating labor and proved it as an effective cervical dilator. Our study also proved the same.

In the present study, the three groups were matched statistically in terms of mean age in both primigravidas and multigravidas.

**Table 18** Comparison of Mean Age Distribution in the three groups with other studies

Studies		Valethamate	Drotaverine	Control
Present Study	Primi N=63	22.09	22.00	21.16
	Multi N=87	23.65	23.11	23.34
Change de PR <sup>56</sup> (2016)	Primi N=60	24.6	25.9	23.4
	Multi N=60	26	28.2	25.9
Dahal P et al <sup>43</sup> (2013)		23.53	23.09	23.38
Selvaraj SM et al <sup>48</sup> (2016)		22.2	22.3	22.2
Kaur D et al <sup>57</sup> (2003)		25.18	24.97	-
Batukan AC et al <sup>58</sup> (2006)		25.5	-	26.4

In our study, the average age in Primigravida patients in Valethamate group was 22.09 whereas

in Multigravidae it was 23.65. The average age in Primigravida patients in Drotaverine group was 22.00 whereas in Multigravidae it was 23.11. The average age in Primigravida patients in control group was 21.16 whereas in Multigravidae it was 23.34.

Hence there was no statistically significant difference among the three groups regarding age distribution.

Similarly, In the study done by Change de PR<sup>56</sup> (2016) no significant difference in age of patients was found. In Primigravida the mean age were 24.6, 25.9 and 23.4 in Valethamate, Drotaverine and control groups respectively. In Multi it was 26, 28.2 and 25.9 in Valethamate, Drotaverine and Control groups respectively.

Our Study is comparable with the study done by Dahal P et al<sup>43</sup>(2013). The mean age in years were 23.53, 23.09 and 23.38 in Valethamate, Drotaverine and control groups respectively.

Selvaraj SM et al<sup>48</sup>(2016) also have shown no significant difference among the groups regarding age distribution. The mean age in years were 22.2, 22.3 and 22.2 in Valethamate, Drotaverine and Control groups respectively.

The average maternal age in our study are comparable to the studies done by Kaur D et al<sup>57</sup> (2003), Batukan AC et al<sup>58</sup>(2006) fall within the same range.

Valethamate bromide. 8 mg was administered every half an hourly in epidural (valethamate) group (n=50), IV. Drotaverine was administered in the dose of 40 mg IV in drotaverine group (n=50), every 2 hourly. While in the Control group (n=50), cases received Normal Saline 1 cc every 2 hourly iv. In primigravida the mean duration of first stage of labor was 248.57 (+/- 60.00 SD) mins in valethamate group and in drotaverine group 207.08 (+/- 60.73 SD) minutes and 370.83 (+/- 63.43 SD) min in the control group. The difference is statistically significant in all the three groups. (P<0.05).

In multigravidas it was 158.96 +/- 65.78 SD min in valethamate bromide group, 138.46 +/- 43.46 SD min in drotaverine group while 269.84 +/- 88.48

SD min in the control group. The difference being statistically significant in between all the three groups.

Thus our study shows that drotaverine more effectively shortens the duration of active labor than valethamate bromide as well as control. And valethamate bromide is more effective than control.

Statistical comparison between all the three groups was done using one way annova test.

**Table 19 :** Comparison of Mean Duration of Active Phase (in mins) of first stage of labor in Primigravidae between the three groups with other studies

Studies	Valethamate	Drotaverine	Control
Present Study N=63	248.57	207.08	370.83
Change de PR <sup>56</sup> (2016) N=60	156.7	110.7	229.7
Jogi SR <sup>47</sup> (2015) N=110	321.71	170.22	-
Aziz M <sup>46</sup> (2015) N=75	293	247	348
Palii SB et al <sup>45</sup> (2013)	254.2	186.3	-
JayashreeS et al <sup>44</sup> (2013) N=127	160	123.12	-
Roy A et al <sup>37</sup> (2007)	-	148.9	331.6
Batukan AC et al <sup>58</sup> (2006)	210.3	-	287.1
Kaur D et al <sup>57</sup> (2003)	180.40	143.91	-
Mishra SL et al <sup>34</sup> (2002)	275	205	-
Malaysarkar <sup>59</sup> (2001)	196	174.7	-

**Table 20 :** Comparison of Mean Duration of Active Phase (in mins) of first stage of labor in Multigravidae between the three groups with other studies

Studies	Valethamate	Drotaverine	Control
Present Study N=87	158.96	138.46	269.84
Change de PR <sup>56</sup> (2016) N=60	126.3	96.2	173.2
Jogi SR <sup>47</sup> (2015) N=90	267.54	129.35	-
Aziz M <sup>46</sup> (2015) N=75	222	199	283
Palii SB et al <sup>45</sup> (2013)	172.82	140.76	-
JayashreeS et al <sup>44</sup> (2013) N=72	147.12	113.94	-
Roy A et al <sup>37</sup> (2007)	-	99.5	227.9
Batukan AC et al <sup>58</sup> (2006)	187.1	-	241.9
Kaur D et al <sup>57</sup> (2003)	146.4	99.7	-
Mishra SL et al <sup>34</sup> (2002)	210	105	-
Malaysarkar <sup>59</sup> (2001)	176.1	148.2	-

Similar results were also reported by Change de PR<sup>56</sup>(2016). In Primigravida, the mean duration of active phase of First stage of Labor was 156.7

mins, 110.7 mins, 229.7 mins in Valethamate, Drotaverine, and control group respectively. In Multigravida, the mean duration of active phase of First stage of Labor was 126.3mins, 96.2mins, 173.2mins in Valethamate, Drotaverine, and control group respectively.

The results of another study done by Jogi SR<sup>47</sup>(2015) were similar showing the mean duration of Active phase of First stage of Labor in Primigravida to be 321.71mins, 170.22mins in Valethamate, Drotaverine group. In Multigravida, the mean duration of Active Labor was 267.54 mins, 129.35 mins in Valethamate, Drotaverine group respectively.

Similar findings were reported by a Study done by Aziz M<sup>46</sup> in 2015 which showed the mean duration of Active Phase of First stage of Labor in Primigravida to be 293mins, 247mins, 348mins in Valethamate, Drotaverine, Control groups respectively while in Multigravida the mean duration of Active Phase of Labor was 222mins, 199mins, 283mins in Valethamate, Drotaverine, control groups respectively.

This study is comparable with the study done by Jayasree S et al<sup>44</sup>(2013) which reported the mean duration of Active phase of First stage of Labor in Primigravida as 160mins, 123.12mins in Valethamate and Drotaverine groups respectively and in Multigravida the mean duration was 147.12mins, 113.94mins in Valethamate and Drotaverine groups respectively.

Palii SB et al<sup>45</sup>(2013) also found the mean duration of Active phase of First stage of Labor to be less in women given Drotaverine (186.3mins in Primigravida& 140.76mins in Multigravida) compared to the Valethamate group (254.2mins in Primigravida&172.82mins in Multigravida).

The results of another study done by Roy A et al<sup>37</sup> in 2007 were similar showing the mean duration of Active phase of First stage of Labor in Primigravida to be 148.9mins, 331.6mins in Drotaverine and Control group respectively. In Multigravida, the mean duration of Active Labor was 99.5mins,227.9mins in Drotaverine and Control groups respectively.

Batukan AC et al<sup>58</sup> in 2006 also found the mean duration of Active phase of First stage of Labor to be less in women given Valethamate (210.3mins in Primigravida & 187.1mins in Multigravida) compared to the control group (287.1mins in Primigravida & 241.9mins in Multigravida).

Similar results were also reported by Kaur D et al<sup>57</sup> (2003). In Primigravida, the mean duration of active phase of First stage of Labor was 180.40mins, 143.91mins in Valethamate and Drotaverine group respectively. In Multigravida, the mean duration of active phase of First stage of Labor was 146.4mins, 99.7mins in Valethamate and Drotaverine group respectively.

Mishra SL et al<sup>34</sup>(2002)also found the mean duration of active phase of First stage of Labor to be less in women given Drotaverine (205mins in Primigravida & 105mins in Multigravida) compared to the Valethamate group (275mins in Primigravida & 210mins in Multigravida).

The results of another study done by Malaysarkar<sup>59</sup>(2001)were similar showing the mean duration of active phase of First stage of Labor in Primigravida to be 196mins, 174.7mins in Valethamate and Drotaverine group respectively. In Multigravida, the mean duration of Active Labor was 176.1mins, 148.2mins in Valethamate and Drotaverine groups respectively. Similar findings were reported by a study done by Ajmera SK et al<sup>36</sup>(2006) which showed the mean duration of active Phase of First stage of Labor to be 284.4mins, 239.5mins, 336.7mins in Valethamate, Drotaverine, Control groups respectively.

Tripti N et al<sup>40</sup> in 2009 also found the mean duration of Active phase of Labor to be less in women given Drotaverine (113.5mins) compared to the Valethamate group (177.4mins).

Madhu C et al<sup>41</sup>(2010) also found there was statistically significant difference in the duration of Labor which was 206.5min in Valethamate group, 183.2mins in Drotaverine group and 245min in Control group.

Another study done by Dahal P et al<sup>43</sup> (2013) showed significant reduction in the duration of

Active Phase of Labor with both Valethamate (254mins) and Drotaverine (178.13mins) on comparison with control group(346.31mins) irrespective of the parity.

Selvaraj SM et al<sup>48</sup>(2016)also found significant reduction in duration of Active phase of Labor with Drotaverine(198mins) than in Valethamate group (252mins) and Control group (383mins).

Similar results were found in the study done by Sharma JB et al<sup>31</sup>(2001), Goswami et ai. Demeter and Blasko et al.

**Table 21** Comparison of mean duration of Second Stage of Labor (in mins) in Primigravidae between the three groups with other studies

Studies	Valethamate	Drotaverine	Control
Present Study N=63	43.57	37.08	43.94
Change de PR <sup>56</sup> (2016) N=60	24.1	21.8	20.7
Aziz M <sup>46</sup> (2015) N=75	22.25	21.17	23.5
Palii SB et al <sup>45</sup> (2013)	44	39.5	-

**Table 22** Comparison of mean duration of Second Stage of Labor (in mins) in Multigravidae between the three groups with other studies

Studies	Valethamate	Drotaverine	Control
Present Study N=87	26.03	30.34	26.71
Change de PR <sup>56</sup> (2016) N=60	18.6	16	20.1
Aziz M <sup>46</sup> (2015) N=75	13.54	14.2	15.45

In the present study in Primigravidae the mean duration of second stage of labor was 43.57(+/-11.52 bSD) in valethamate group, 37.08(+/-12.39SD) minutes in Drotaverine group and 43.94(+/-8.88SD) minutes in control group. In multigravida the mean duration of second stage of labor was 26.03(+/-9.94SD) in valethamate group. 30.34(32.98SD) minutes in drotaverine and 26.71(+/-11.88 SD) minutes in controlgroup.The difference is not statistically significant in between the three groups in both Primigravida and Multigravida.

Change de PR<sup>56</sup>(2016) also found the similar results with mean duration of second stage of labor to be 24.1mins, 21.8mins, 20.7mins in Valethamate, Drotaverine, Control groups respectively in Primigravida. And 18.6mins, 16mins, 20.1mins in Valethamate, Drotaverine, Control respectively in Multigravida.

The results of another study done by Aziz M<sup>46</sup> in 2015 are similar showing the mean duration of second stage of labor to be 22.25mins, 21.17mins, 23.05mins in Valethamate, Drotaverine, Control groups respectively in Primigravida. And 13.54mins, 14.02mins, 15.45mins in Valethamate, Drotaverine, Control respectively in Multigravida. This study is comparable with the study done by Palii SB et al<sup>45</sup>(2013) which reported the mean duration of Second stage of Labor to be 39.5mins in Primigravida, 24.26mins in Second Gravida, 24.5mins in Third gravida in Drotaverine group and in the Valethamate group to be 44mins in Primigravida, 28.8mins in Second Gravida, and 24mins in Third Gravida.

Jogi SR<sup>47</sup> (2015) also found that there is no statistically significant difference between the mean duration of Second stage of Labor in Drotaverine (22.05mins) and Valethamate group(22.49mins).

Similar results were reported by other studies such as Sharma JB et al<sup>31</sup>(2001), AH Khosla et al<sup>33</sup> (2002), Madhu C et al<sup>41</sup>(2010).

**Table 23** Comparison of mean duration of Third Stage of Labor (in mins) in Primigravidae between the three groups with other studies

Studies	Valethamate	Drotaverine	Control
Present Study N=63	6.14	7.66	6.50
Change de PR <sup>56</sup> (2016) N=60	7	8	7.1
Aziz M <sup>46</sup> (2015) N=75	10.25	10.17	10.42

**Table 24** Comparison of mean duration of Third Stage of Labor (in mins) in Multigravidae between the three groups with other studies

Studies	Valethamate	Drotaverine	Control
Present Study N=87	4.65	5.23	5.43
Change de PR <sup>56</sup> (2016) N=60	9.4	7.5	6.63
Aziz M <sup>46</sup> (2015) N=75	9.15	10	9.25

In the present study in Primigravidae the mean duration of third stage of labor was 6.14mins in valethamate group, 7.66 mins in Drotaverine group and 6.50mins in control group.

In Multigravida the mean duration of third stage of labor was 4.65mins in valethamate group,

5.23mins in drotaverine and 5.43mins in control group. The difference is not statistically significant in between the three groups in both Primigravida and Multigravida.

Change de PR<sup>56</sup>(2016) also found the similar results with mean duration of third stage of labor to be 7mins, 8mins, 7.1mins in Valethamate, Drotaverine, Control groups respectively in Primigravida. And 9.4mins, 7.5mins, 6.63mins in Valethamate, Drotaverine, Control respectively in Multigravida.

The results of another study done by Aziz M<sup>46</sup> in 2015 are similar showing the mean duration of third stage of labor to be 10.25mins, 10.17mins, 10.42mins in Valethamate, Drotaverine, Control groups respectively in Primigravida. And 9.15mins, 10mins, 9.25mins in Valethamate, Drotaverine, Control respectively in Multigravida. JogiSR<sup>47</sup> (2015) also found that there is no statistically significant difference between the mean duration of Second stage of Labor in Drotaverine (8.62mins) and Valethamate group (8.92mins).

Similar results were reported by other studies such as Sharma JB et al<sup>31</sup> (2001),Palii SB et al<sup>45</sup>(2013), AH Khosla et al<sup>33</sup>(2002), Madhu C et al<sup>41</sup>(2010).

**Table 25** Comparison of mode of delivery in Primigravidae between the three groups with other studies

Mode Of Delivery	Present Study N=63			Aziz M <sup>46</sup> (2015) N=75		
	Valethamate	Drotaverine	Control	Valethamate	Drotaverine	Control
SVD	90.47	95.83	88.88	96	92	88
Forceps	9.52	4.16	5.55	4	4	8
LSCS	0	0	5.55	0	4	4

**Table 26** Comparison of mode of delivery in Multigravidae between the three groups with other studies

Mode Of Delivery	Present Study N=87			Aziz M <sup>46</sup> (2015) N=75		
	Valethamate	Drotaverine	Control	Valethamate	Drotaverine	Control
SVD	100	100	96.55	92	100	96
Forceps	0	0	3.44	0	0	0
LSCS	0	0	0	8	0	4

In the present study, in Primigravida, 90.47% cases of Valethamate group had Spontaneous Vaginal Delivery, 9.52% had Forceps (Indication

being Fetal Distress for one and Prolonged second stage for another) and no cases underwent LSCS. All Multigravida cases in Valethamate group had Spontaneous Vaginal Delivery.

In Primigravida, 95.83% cases of Drotaverine group had Spontaneous Vaginal Delivery, 4.16% had Forceps (Indication being Fetal Distress) and no cases underwent LSCS. All Multigravida cases in Drotaverine group had Spontaneous Vaginal Delivery.

In the present study, in Primigravidae, only 88.88% cases of Control group had Spontaneous Vaginal Delivery, 5.55% had Forceps (Indication being Prolonged Second Stage of Labor) and 5.55% cases underwent LSCS (Indication being Fetal Distress). In Multigravida, 96.55% cases of Control group had Spontaneous Vaginal Delivery, 3.44% had Forceps (Indication being Fetal Distress) and no cases underwent LSCS.

Hence it can be seen that, the Incidence of operative interference was least in Drotaverine group, but it is not significant.

Similar results were reported by a study done by Aziz M<sup>46</sup> in 2015.

In that study, in Primigravidae, 96% cases of Valethamate group had Spontaneous Vaginal Delivery, 4% had Forceps (Indication for both cases being Fetal Distress) and no cases underwent LSCS. In Multigravida, 92% cases had Spontaneous Vaginal Delivery, 8% had LSCS (Indication being Fetal Distress) and no cases underwent Forceps delivery.

In the same study, among Primigravida, 92% cases of Drotaverine group had Spontaneous Vaginal Delivery, 4% had Forceps (Indication being Prolonged Second Stage) and 4% cases underwent LSCS (Indication being Fetal Distress). In Multigravidae, all cases had Spontaneous Vaginal Delivery and no cases underwent Forceps or LSCS.

In the same study, in Primigravida, only 88% cases of Control group had Spontaneous Vaginal Delivery, 8% had Forceps (Indication being Fetal Distress) and 4% cases underwent LSCS (Indication being Non Progress of Labor). In

Multigravida, 96% cases had Spontaneous Vaginal Delivery, 4% had LSCS (Indication being Fetal Distress) and no cases underwent Forceps delivery.

The results of another study done by Tripti N et al<sup>40</sup> (2009) are similar. 99% of their cases in two groups delivered vaginally. Only one case required LSCS in each group indication being Fetal Distress in Drotaverine group and arrest of dilatation & descent in Valethamate group. Out of 99% vaginal deliveries, 93% were spontaneous, 6% were assisted by Forceps in both the groups. Indication for forceps was the same in both the groups.

Our study is comparable with the study done by Ajmera SK et al<sup>36</sup> (2006), in this study it was observed that in Drotaverine group 96% of women delivered normally, 2.7% required Caesarean Section while 1.3% required Forceps application. In Valethamate Bromide group, 93.3% delivered normally, 4% required LSCS and 2.3% required Forceps application. While in the control group, 94.6% women delivered normally, 2.7% required LSCS and another 2.7% required Forceps application.

Dahal P et al<sup>43</sup> (2013) also observed similar results. In Drotaverine group, all cases had spontaneous vaginal delivery (SVD), no cases required either Forceps or LSCS. In Valethamate group, 96% cases had SVD, 2% cases required Forceps and 2% cases underwent LSCS. In control group, 95% cases had SVD, 4% required instrumental delivery and 1% underwent LSCS.

Khosla AH et al<sup>33</sup> (2003) also observed that the mode of delivery was vaginal in all 300 cases. Ventouse was required in 3 women in Drotaverine group and in Four women each in Valethamate and Control group.

Our study is also supported by the studies done by JogiSR<sup>47</sup> (2015), Jayasree S<sup>44</sup> (2013).

### Side Effects

In the present study, Maternal side effects like Giddiness in 5, Vomiting in 3 and Tachycardia and dry mouth were seen more in Valethamate

group of 20 cases. In Drotaverine group, Giddiness was noted in 4, Vomiting in 1 and Tachycardia and dry mouth in 1 patient. In control group, Giddiness was seen in 1, Vomiting in 2 while Tachycardia in 1 Patient

**Table 27** Frequency of Side Effects in each Group

Side Effect	Valethamate (N=50)	Drotaverine (N=50)	Control (N=50)
Giddiness	5	4	1
Vomiting	3	1	2
Dry mouth, Tachycardia	20	1	1

Hence our study showed no major side effects with the drugs, but the minor side effects like Dry Mouth, Tachycardia was more common in Valethamate group.

In the study done by Aziz M<sup>46</sup>, nausea and vomiting occurred in 4% Epidosin, 8% Drotin and 4% in Control group. None of the patients in Drotaverine group had Tachycardia whereas 12% patients of Valethamate group had Tachycardia and 10% had dryness of mouth.

JogiSR<sup>47</sup> (2015) also found that side effects like Tachycardia (4% in Drotaverine group, 31% in Valethamate group), Dryness of mouth (0% in Drotaverine group, 19% in Valethamate group) were more observed in Valethamate group.

Selvaraj SM et al<sup>48</sup>(2016)also found that dryness of mouth (6% in Drotaverine group, 20% in Valethamate group, 0% in Control group) and Tachycardia (6% each in Drotaverine and Control group , 22% in Valethamate group) was 4 times more in Valethamate group.

Dahal P et al<sup>43</sup>(2013)have also reported that side effects such as dryness of mouth, vomiting, tachycardia were seen more with Valethamate group.

Similar results were reported by AH Khosla et al<sup>33</sup>(2002), K Devinder et al, K Tewari et al and Sharma JB et al<sup>31</sup>(2001). Transient maternal tachycardia was noted in 16% cases receiving Valethamate in studies done by AH Khosla et al<sup>33</sup> (2002) and K Tewari et al., 28% of cases developed transient maternal tachycardia in study done by K Devinder et al.,

Ajmera SK et al<sup>36</sup>(2006), Palii SB et al<sup>45</sup>(2013), Malaysarkar<sup>59</sup>(2001), Sharma JB et al<sup>31</sup>(2001),

Tripti N et al<sup>40</sup>(2009), Change de PR<sup>56</sup>(2016) found Valethamate had more anti-cholinergic side effects than Drotaverine. Our study also proved the same.

**NICU Admission**

In the present study, the neonatal outcome was similar in the three groups. In valethamate group, there was one NICU admission was for neonatal jaundice and one was for birth asphyxia. In the control group, one admissions was for neonatal jaundice,one was for congenital heart disease and one was for birth asphyxia. In drotaverine group there was one nicu admission for neonatal jaundice. However all babies were discharged in good condition and no adverse outcomes were reported.

**Table 28** Comparison of NICU Admission between the three groups in various studies

Drugs	Present Study (N=150)	Dahal P et al <sup>43</sup> (2013)
Valethamate	2	4
Drotaverine	1	2
Control	3	2

Dahal P et al<sup>43</sup>(2013)also reported that fetal outcome was comparable in the three groups. 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 group, 2 in Drotaverine group and 2 in Control group.

Aziz M<sup>46</sup> also found that neonatal complications were more or less same in all the three groups except for one neonatal death in Control group. Birth Asphyxia occurred in 4% in Control group, 2% in Epidosin group and 2% in Drotaverine group. Incidence of neonatal jaundice was 4% in Control group, 4% in Valethamate group and 2% in Drotaverine group.

JogiSR<sup>47</sup>(2015) also found no significant difference in neonatal outcome. No newborn in Drotaverine group had Apgar score <8 at birth but in Valethamate group, 4 newborns had Apgar score <8 at birth, but there were no fetal deaths in the group.

JayasreeS etal<sup>44</sup>(2013) reported no significant association between the incidence of fetal complications in the groups.

Change de PR<sup>56</sup>(2016) also observed that there were no side effects in the neonates in the Control and Drotaverine group. 2 neonates in the Valethamate group had low Apgar score at 1 min but had normal score at 10 min. These neonates also had Tachypnoea which resolved in 24 hours.

### Summary

This study was conducted at Raipur Institute of Medical Sciences, Raipur, from October 2014 to September 2016.

150 Antenatal woman of term gestation were included in the study with 50 patients each in Valethamate, Drotaverine, and Control groups including both primigravidae and multigravidae the three groups were matched statistically in terms of mean age. In both primi and multi, Mean duration of active phase of first stage of labor was significantly less in Drotaverine group (207.08 mins in primi and 138.46 mins in multi) when compared to Valethamate (248.57 mins in primi and 158.96 mins in multi) and control group (370.83 mins in primi and 269.84 mins in multi). Also it was significantly less in Valethamate than in control group.

The difference in the mean duration of second stage of labor between the three groups was not statistically significant in primigravidae (4357 mins in V group, 37.08 mins in D group, 43.94 mins in C group as well as multigravidae (26.03 mins in V group, 23.80 mins in D group and 26.71 mins in C group)

There was no statistically significant difference in the mean duration of third stage of labor between the three groups in both primigravidae (6.14 mins in V group, 6.37 mins in D group, and 6.50 mins in C group) and multigravidae (4.65 mins in V group, 5.23 mins in D group and 5.43 mins in C group)

Mode of delivery was almost similar in the three groups. Both the drugs were not found to increase the rate of instrumental delivery. And the

indication for the same we also similar in the three groups. In the present study one woman required forceps in Drotaverine group (fetal distress) and rest all delivered normally. In valethamate group, two women required forceps (one for prolonged second stage and another for fetal distress). One female required a cesarean section (fetal distress) in control group and one required forceps (prolonged 2<sup>nd</sup> stage)

Although oxytocin augmentation was required in 8 patients of C group, but in only 3 and 2 patients of V and D groups.

No obstetrical complications like cervical tears, postpartum haemorrhage were noted in any of the three groups.

Side effects like dryness of mouth, tachycardia were seen more in the valethamate bromide than in the drotaverine group, which is because of the anti-cholinergic properties of valethamate bromide. Nausea, vomiting and giddiness were seen at a similar rate in both the drug groups as well as the control group.

Neonatal outcome was not affected by these two drugs and was similar in all the groups. all babies went home fine.

Drotaverine and valethamate bromide are comparable in their costs. More frequent dosage (half hourly) of Valethamate bromide is required. Thus, drotaverine appears to be a more cost effective drug.

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