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**Original Research Article**

# Drotaverine hydrochloride and valethamate bromide action in management of labor

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## ABSTRACT

**Background:** Labor duration impacts maternal and perinatal morbidity. Antispasmodics like drotaverine hydrochloride and valethamate bromide are used to shorten labor by facilitating cervical dilation. This study compares the efficacy of these drugs in labor management.
**Methods:** A prospective study was conducted with 200 primigravida women in the active phase of labor. Participants were randomly divided into two groups: Group I received drotaverine hydrochloride (80 mg), and Group II received valethamate bromide (8 mg). Maternal and fetal outcomes, labor progression, and adverse effects were monitored.
**Results:** The mean cervical dilation rate for drotaverine was significantly higher (1.5570 cm/hr) compared to valethamate (1.0840 cm/hr). The first stage of labor was shorter in the drotaverine group (mean 187.200 min) than in the valethamate group (mean 279.850 min). No significant differences were observed in the second and third stages. Vaginal delivery rates were higher with drotaverine (81%) than with valethamate (69%). Tachycardia occurred in 3% of the valethamate group, while no adverse effects were noted with drotaverine.
**Conclusions:** Drotaverine hydrochloride accelerates cervical dilation and shortens labor more effectively than valethamate bromide, with no significant side effects on mother or fetus. It is a safer and more effective option for labor management.

**Keywords:** Antispasmodic, Cervical dilation, Drotaverine, Labor, Primigravida, Valethamate bromide

## INTRODUCTION

Labor and delivery involve intense uterine contractions, cervical ripening, effacement, and dilation, ultimately leading to the fetus and placenta being expelled. One significant factor influencing maternal and perinatal morbidity is the duration of labor. Labor is divided into four stages, typically lasting 12-14 hours in nulliparous women and shorter in multiparous. Active labor is characterized by cervical dilation of more than 4 cm with regular uterine contractions, with normal labor anticipated within 4-6 hours post-threshold. If undelivered within 24 hours or prolonged, complications can arise.[1,2] Uterine contractions and cervical dilation play critical roles in fetal ejection. Dystocia, or abnormal labor progression, is a common cause of prolonged labor, where strong contractions occur without sufficient dilation. Cervical spasms due to circular muscle hyperactivity, worsened by stress, can hinder dilation.[3-5] To address these issues, spasmolytics and spasmoanalgesics are used to facilitate cervical dilation during labor. The ideal antispasmodic should work quickly, not cause uterine inertia, and have minimal adverse effects on both the mother and fetus. The use of antispasmodics in obstetrics to treat cervical spasms was first introduced in 1923 by Von Kries.[6] Though morphine and diazepam have been tested for pain management, they have shown negative maternal and fetal outcomes. Scopolamine and Buscopan are antispasmodic drugs used to shorten labor duration and reduce discomfort.[7,8] Drotaverine hydrochloride, introduced in 1960, is a benzyl isoquinoline derivative that selectively inhibits phosphodiesterase IV at the cervical musculature,

promoting cervical relaxation and dilation. It has minimal side effects in newborns but can cause nausea, vertigo, hypotension, and palpitations in mothers.[9-11] Valethamate bromide (Epidosin), introduced in 1954, is a synthetic anticholinergic ester that relieves cervical spasms through parasympatholytic and musculotropic actions. Though it can cause mild maternal tachycardia, no severe side effects have been reported.[10,12] Both drotaverine and valethamate bromide have been shown to shorten labor by promoting cervical dilation and softening. The goal of this study is to compare the efficacy of these two drugs in labor management.

## METHODS

### *Study design*

This prospective study involved 200 primigravida women in the active phase of labor, each with 4 cm cervical dilation, admitted to the obstetrics department at Al Ameen Medical College, Vijayapur, between September 2022 and June 2024.

A general and systemic examination was performed on all participants, including abdominal assessment to monitor uterine height, frequency, and strength of contractions. Fetal heart rate, rhythm, and regularity were recorded to assess fetal well-being. A vaginal examination was carried out to evaluate cervical dilation, effacement, and station of the presenting part, while pelvic assessment ruled out any pelvic contraction or cephalo-pelvic disproportion.

After informed consent was obtained, participants were randomly divided into two groups. Group I received intravenous drotaverine (80 mg) while in the supine position, with repeat doses administered hourly as needed, up to a maximum of three doses. Group II received intravenous valethamate bromide (8 mg), also with repeated doses if necessary. Both groups were continuously monitored for maternal and fetal well-being, and any abnormalities were managed appropriately. Uterine activity was evaluated every 30 minutes to assess the frequency and duration of contractions, with a particular focus on any changes related to the medications. Vaginal examinations were conducted at labor onset, after administering drotaverine or valethamate bromide, and hourly thereafter.

Cervical status was documented, including the degree of effacement, dilation in centimeters, and cervical consistency. The time of membrane rupture and the position of the presenting part were also noted, as well as the overall time taken for full cervical dilation. Adverse effects such as headache, nausea, vertigo, palpitations, and hypotension were recorded and treated if necessary. Labor progression was documented using a partogram. If labor did not progress within 12 hours, alternative methods were considered. Additional factors recorded included the interval between drug doses, total doses required, delivery method, operative interventions, and the duration of each labor stage. Maternal complications, including blood loss, cervical tears, retained placenta, and postpartum haemorrhage, were also noted. Fetal outcomes were documented, including birth weight, Apgar scores at one and five minutes, and whether the birth was live or stillborn. Both mother and child were monitored for at least 48 hours postpartum.

### *Statistical analysis*

The data obtained from the study were subjected to statistical analysis using SPSS version 20.0 for further evaluation at the significance level of p value=0.05. The data were presented as Mean±standard deviation for continuous variables and frequency for categorical variables. For categorical data, Chi square statistical analysis was done, and for continuous data student's t-test and ANOVA were performed.

## RESULTS

In this study, the distribution of subjects across age groups showed that the majority were from the 21-25 years range, with 93 subjects (46.5%). Regarding the period of gestation, most subjects, 152 (76%), were between 37-40 weeks (Table 1).

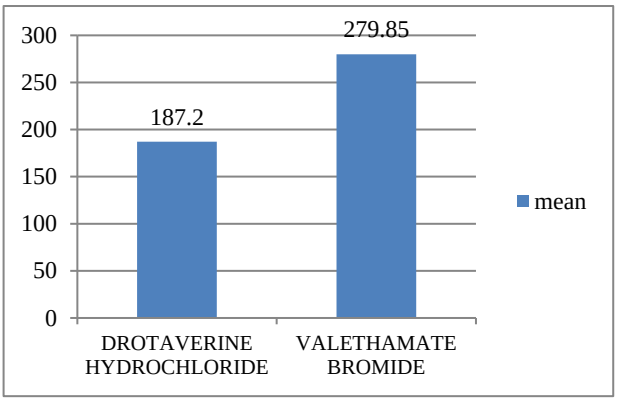


**Figure 1: Comparison of 1st stage duration (active phase) with drug used.**

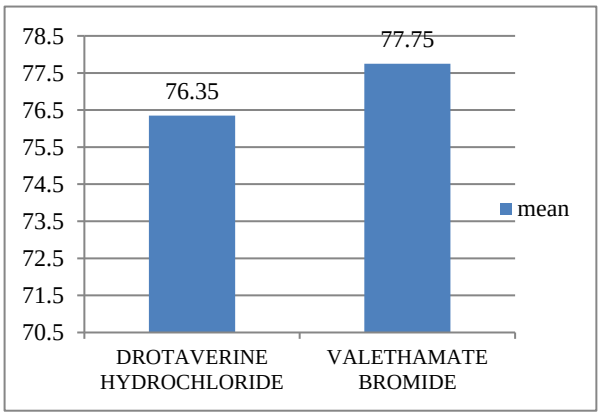


**Figure 2: Comparison of second stage duration with drug used.**

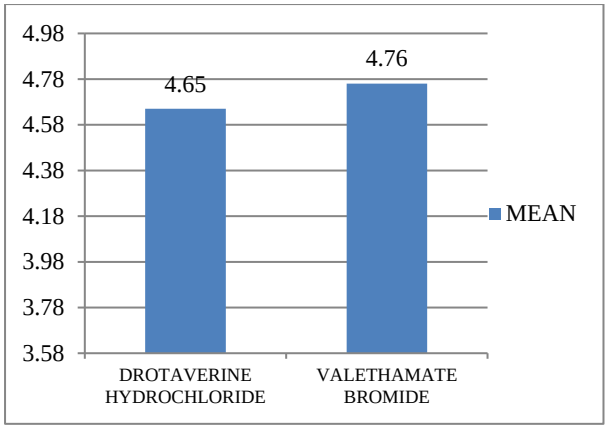


**Figure 3: Comparison of third stage duration with drug used.**

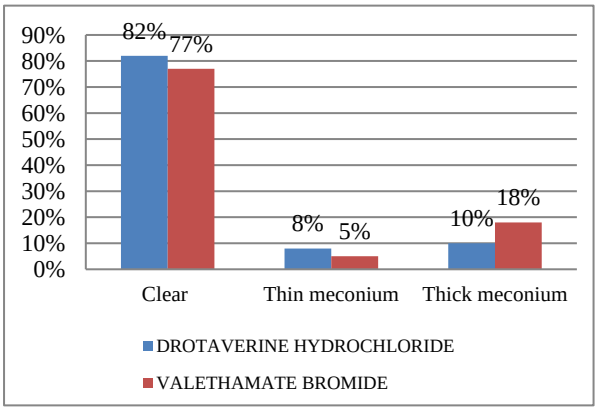


**Figure 4: Comparison of color of liquor with drug used.**

The cervical dilatation in subjects receiving drotaverine hydrochloride had a mean of 1.5570±0.34666, while those receiving valethamate bromide had a mean of 1.0840±0.16374 and this difference was substantial (Table 2). The mean duration of the first stage (active phase) of labor was also compared between the two drugs. The mean for drotaverine hydrochloride was 187.200±48.0336, and for valethamate bromide, it was 279.850±82.760. This difference was highly statistically significant, indicating that the first stage of labor lasted longer in subjects administered valethamate bromide (Figure 1). For the second stage of labor, the mean was 76.3500±17.56453 for drotaverine hydrochloride and 77.750±16.74791 for valethamate bromide.

The results were not statistically significant, though the second stage duration was slightly longer in the valethamate bromide group (Figure 2). Similarly, the mean duration of the third stage of labor was comparable between the two groups, with a mean of 4.6500±.89188 for drotaverine hydrochloride and 4.760±1.04563 for valethamate bromide. This difference was also found to be statistically insignificant (Figure 3).

In terms of delivery outcomes, 81% in the drotaverine group had normal vaginal deliveries, compared to 69% in the valethamate group, a statistically significant difference favoring drotaverine.

Regarding drug dosage, 80% in the drotaverine group required three injections, while 85% in the valethamate group required three injections (Table 3). There were no cases of cervical tear or atonic postpartum hemorrhage in either group (Table 4).

The color of the liquor was clear in 82% from the drotaverine group and 77% from the valethamate group, and statistically insignificant difference was noted (p=0.20) (Figure 4).

Tachycardia occurred in only 3% in the valethamate group, while none in the drotaverine group experienced it. There were no cases of vomiting or dry mouth in either group. NICU admissions occurred in 19% in the drotaverine group and 21% in the valethamate group (Table 5).

**Table 1: Baseline parameters of enrolled patients (N=200).**

| Baseline parameters | | N | % |
|---|---|---|---|
| **Age (in years)** | 15- 20 | 73 | 36.5 |
| | 21-25 | 93 | 46.5 |
| | 26-30 | 34 | 17.0 |
| **Period of gestation** | 37-40 | 152 | 76.0 |
| | >40 | 48 | 24.0 |

**Table 2: Comparison of rate of cervical dilatation among both groups.**

| Drug used | Mean | SD | Mean diff. | P value |
|---|---|---|---|---|
| **Drotaverine hydrochloride** | 1.5770 | 0.34666 | 0.49300 | t=12.859, p<0.001*** |
| **Valethamate bromide** | 1.0840 | 0.16374 | | |

Test used- independent t test, ***: p<0.001 very highly significant

**Table 3: Comparison of mode of delivery and number of injections used among both groups.**

| | | Drotaverine hydrochloride | Valethamate bromide | Total | Chi value | P value |
|---|---|---|---|---|---|---|
| **Mode of delivery** | Normal vaginal | 81<br>81.0% | 69<br>69.0% | 150<br>75.0% | 3.840 | 0.05* |
| | Emergency LSCS | 19<br>19.0% | 31<br>31.0% | 50<br>25.0% | | |
| **Injection given** | 2 | 20<br>20.0% | 15<br>15.0% | 35<br>17.5% | 0.866 | 0.352 |
| | 3 | 80<br>80.0% | 85<br>85.0% | 165<br>82.5% | | |

Test used- chi square, *: p≤0.05 significant, p>0.05 insignificant

**Table 4: Comparison of third stage complications among both groups.**

| Complications | | Drotaverine hydrochloride | Valethamate bromide | Total | Chi value | P value |
|---|---|---|---|---|---|---|
| **Cervical tear** | Yes | 0 | 0 | 0 | -- | -- |
| | No | 100<br>100.0% | 100<br>100.0% | 100<br>100% | | |
| **Atonic postpartum hemorrhage** | Yes | 0 | 0 | 0 | -- | -- |
| | No | 100<br>100.0% | 100<br>100.0% | 100<br>100% | | |

**Table 5: Comparison of maternal and neonatal side effects among both groups.**

| Side Effects | | Drotaverine hydrochloride | Valethamate bromide | Total | Chi value | P value |
|---|---|---|---|---|---|---|
| **Maternal** | | | | | | |
| **Tachycardia** | Yes | 0 | 3<br>3.0% | 3<br>1.5% | 3.046 | .08 |
| | No | 100<br>100.0% | 97%<br>97.0% | 197<br>98.5% | | |
| **Vomiting** | Yes | 0 | 0 | 0 | -- | -- |
| | No | 100<br>100.0% | 100<br>100.0% | 100<br>100.0% | | |
| **Dry mouth** | Yes | 0 | 0 | 0 | -- | -- |
| | No | 100<br>100.0% | 100<br>100.0% | 100<br>100.0% | | |
| **Neonatal** | | | | | | |
| **Admission in NICU** | Yes | 19<br>19.0% | 21<br>21.0% | 40<br>20.0% | 0.125 | 0.72 |
| | No | 81<br>81.0% | 79<br>79.0% | 160<br>80.0% | | |

## DISCUSSION

In this study, the majority of subjects (46.5%) were aged 21-25, with the fewest (17%) in the 26-30 age range, similar to findings by Sharma J et al and others.[13-16] The gestational period for most participants (76%) was 37-40 weeks, consistent with the delivery timing reported in studies by Sharma J et al.[13,14,17-20] The study found a significant difference in cervical dilatation between drotaverine hydrochloride (1.5570±0.34666) and valethamate bromide (1.0840±0.16374), indicating greater dilation with drotaverine. This aligns with earlier research by Shabanam et al, who reported a higher cervical dilation rate with drotaverine (2.05±0.63 vs. 1.79±0.52, p<0.05).[21] Similarly, Jogi SR found a faster dilatation rate in the drotaverine group, consistent with the findings of Tripti and Jyoti.[14,22] In our study, the active phase duration was shorter in the drotaverine hydrochloride group (mean±SD=187.200±48.0336) compared to the valethamate bromide group (mean±SD=279.850±82.760),

with statistical significance. Shabanam et al, similarly reported shorter first stage durations with drotaverine (244.96±96.21) versus valethamate (277.58±100.96).[21] Sinhasane and Nishty and Mandal and Molla also found shorter active phases with drotaverine, supporting our findings.[23,24] Our study found no significant difference in the second stage duration between drotaverine hydrochloride (76.3500±17.56453) and valethamate bromide (77.750±16.74791), though valethamate appeared longer in the graph. Shabanam et al, also reported longer second stage duration for valethamate (54.77±15.91) compared to drotaverine (50.72±16.69).[21] Similar findings were noted by Deshpande H et al and Jogi S

R, with no notable difference between the two drugs.[15,22] In this investigation, the mean±standard deviation for the third stage duration was 4.6500±0.89188 for drotaverine hydrochloride and 4.760±1.04563 for valethamate bromide. Although valethamate appeared longer, the results were not statistically significant. Shabanam et al, reported third stage durations of 5.31±0.88 for drotaverine and 5.56±0.99 for valethamate, with the latter also being longer but statistically insignificant.[21] Similarly, Jogi SR, found no discernible difference between the two drugs.[22] Notably, neither medication resulted in cervical tear or atonic postpartum hemorrhage during the third stage. In situations of dystocia, the standard labor management protocol recommends active labor management.

The drotaverine medication revealed that 81 (81%) of the births were vaginally delivered normally, and 19 (19.0%) were emergency LSCS. The drug valethamate bromide revealed that 31 (31.0%) had emergency LSCS and 69 (69%) had a normal vaginal birth. The outcomes were statistically significant as a result. Soni M et al reported that 96.7% of participants receiving drotaverine and 94% receiving valethamate had normal vaginal births.[16] LSCS was performed on five subjects from the drotaverine group and seven from the valethamate group. Dahal P et al, found that 96% delivered vaginally, with 2% requiring LSCS and 2% instrumental delivery.[25] Shabanam et al noted over 80% spontaneous vaginal deliveries, with 6.6% in the drotaverine group and 10% in the valethamate group requiring LSCS.[21]

The findings align with those of Mandal et al, supporting the conclusions of this study.[18,20,24] In this investigation, we discovered that the maximum number of patients who took the medicine drotaverine hydrochloride (82%) and the greatest number of patients who took the drug valethamate bromide (77%) both had clear liquor color and that there had been no discernible changes to the liquor's hue. Meconium-stained liquor (MSL) was observed in 6-8% of the 100 patients categorised into each group receiving drotaverine and valethamate, according to findings by Deshpande H et al.[15] Drotaverine was utilized in this study in 20 (20%) instances, three injections in 80 (80%) cases, and valethamate bromide in 15 (15%) cases, two injections in 15 (15%) cases and three injections in 85 (85%) cases. In our study, the group receiving drotaverine received fewer injections than the group receiving valethamate. In the trial of Shabanam et al, Injection Drotaverine 40 mg IM every 2 hours were given (for a maximum of three doses), in contrast, Injection Epidosin 8 mg IV (every thirty minutes for a maximum of three doses) in Valethamate bromide group was given.[21] Jogi SR found average number of injections in drotaverine group was 1.7. While it was 2.9 in valethamide, significantly lesser than Drotaverine group.[22] Thus, our study is comparable with the previous studies. The average number of injections for the drotaverine group was 1.7, but the valethamide group had 2.99, according to Jogi SR in the Drotaverine group, a notably lower quantity of injections was administered.[22]

As a result, our findings may be compared to earlier research. In our study, no tachycardia was observed in the drotaverine group, while only 3 (3%) in the valethamate group experienced tachycardia, which was statistically insignificant. Neither group reported vomiting or dry mouth. Previous studies by Sharma J et al and others similarly noted a higher incidence of tachycardia in the valethamate group (9-28%), with no other notable side effects reported.[13,14,20,24,25] Thus, our findings align with earlier research.

In this study, only 19 (19%) of the 100 drotaverine cases and 21 (21%) of the 100 valethamate bromide cases were admitted to the NICU, indicating that neither medication adversely affected the newborns. This supports our findings that the development of cervical smooth muscle dilators enhances labor management. Drotaverine hydrochloride significantly shortens the initial stage of labor and promotes cervical dilation with minimal side effects compared to valethamate bromide. Similar effects on cervical dilation and reduced labor duration were noted by Pai M et al.[26] Additionally, Sharma J et al and Tripti and Jyoti found that valethamate bromide had more adverse cholinergic effects than drotaverine, corroborating our findings.[13,14] Aforementioned studies have shown that drotaverine increases the cervical dilation rate, and our results align with this body of research, demonstrating that the dilation rate in the drotaverine group was significantly faster than in the valethamate bromide group.

## CONCLUSION

Therefore, it can be demonstrated that the duration of the active phase of the initial stage of labor is shortened by drotaverine hydrochloride more successfully than valethamate bromide, with a rise in pace of dilatation of cervix. Better results are obtained by drotaverine without any notable negative effects on the mother or fetus. Since drotaverine has been proven to be a superior medication, it can be used to ease a laboring woman's pain without having a major negative impact on either the mother or the developing fetus.

The study had some limitations, including a small sample size and being conducted at a single institution, which may

affect the generalizability of the findings. Long-term effects on maternal and neonatal outcomes were not assessed. Future studies with larger, multicentric trials are recommended to confirm these results and explore the safety of drotaverine in high-risk pregnancies. Additional follow-up studies could provide further insights into any delayed adverse effects.

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## REFERENCES

1. Prakash P. Rohtagi R. A Comparison of efficacy and side effects of drotaverine hydrochloride and valethamate bromide in augmentation of labour. Int J Health and Clinical Research. 2021;4(22):146-7.
2. Lowe NK. The nature of labor pain. American journal of obstetrics and gynecology. 2002;1;186(5):S16-24.
3. Bryant WM, Greenwell JE, Weeks PM. Alterations in collagen organization during dilatation of the cervix uteri. Surgery, Gynecology & Obstetrics. 1968;1;126(1):27-39.
4. Rao KB. Prolonged and obstructed labour. In:Arulkumaran S, Penna LK, Rao KB editors. The management of labour. 2nd edition, India: OrientLongman Private Ltd; 2005:340-9
5. Palii SB, Akkupalli VL, Maddi S. The Comparative Study of Drotaverine Hydrochloride and Valethamate Bromide in First Stage of Labor. J South Asian Fedaration Obstet Gynaecol. 2013;5(2):52-6.
6. Rohwer AC, Khondowe O, Young T. Antispasmodics for labour. Cochrane Database of Systematic Reviews. 2013(6):009243.
7. O'Driscoll KI, Foley M, MacDonald D. Active management of labor as an alternative to cesarean section for dystocia. Int J Repro Cont Obst Gyn. 1984;1;63(4):485-90.
8. Jayashree S, Ajjammanavar V, Sujatha MS. Comparison of drotaverine and valethamate bromide in first stage of labor. Int J Biol Med Res. 2013;4(2):3215-8.
9. Tile R, Jamkhandi S. To study the efficacy and safety of Drotaverine hydrochloride in augmentation of labour. Obs Rev J Obstet Gynecol. 2019;5(1):77-82.
10. Ahmad S, Rauf B, Shafiq A. Use of Spasfan in labour. J Himont Med. 2002;1:14-8.
11. Srivastava K, Sinha P, Sharma R, Gupta U. A comparative study of the effect of drotaverine hydrochloride with hyoscine butylbromide in first stage of labor. Int J Basic Clin Pharmacol. 2015;4(3):488-91.
12. Gitanjali B. Valethamate bromide. Is there any proof of efficacy and safety for its use in labor. J Pharmacol Pharmaco. 2010;1(1):2-3.
13. Sharma JB, Pundir P, Kumar A, Murthy NS. Drotaverine hydrochloride vs. valethamate bromide in acceleration of labor. Int J Repro Cont Obst Gyn. 2001;1;74(3):255-60.
14. Tripti N, Jyoti J. To compare and evaluate the efficacy and safety of drotaverine and valethamate bromide. J Obstet Gynecol. 2009;1;59(4):324-1.
15. Deshpande HG, Chilakalapalli HR, Shinde MJ, Choudhary S, Patel S, Saha S. Comparative efficacy of drotaverine hydrochloride valethamate bromide effects on cervical dilatation in active phase of labour in primigravida. EJMCM 2023;10:3239-3247.
16. Soni M, Gupta D, Godara S. Drotaverine hydrochloride versus valethamate bromide for cervical dilatation in labour: a comparative study. Int J Repro Cont Obst Gyn. 2020;1;9(5):1986-92.
17. Naga P, Shivanna BS, Subbappa K, Gopal N. Comparative study of efficacy of combination of valethamate bromide and hyoscine with drotaverine hydrochloride on cervical dilatation in active labor. IOSR-JDMS. 2014;13(10):27-9.
18. Kalhon P, Patil AB, Patel R. Efficacy of intramuscular Drotaverine use for cervical dilatation in first stage of labour. Int J Sci Tech. 2015;14(3):670-4.
19. Edessy M, EL-Darwish A, Nasr A, Ali A, El-Katatny H, Tammam M. Different modalities in first stage enhancement of labor. Gen Health Med Sci. 2015;2(1):1-4.
20. Patil AB, Kalhon P, Patel R. Comparative study of drotaverine hydrochloride and valethamate bromide in progress of labor. Inter J Recent Trends Sci Technol. 2015;14(3):678-82.
21. Shabanam, Verma R, Puja. Comparative study of drotaverine hydrochloride and valethamate bromide in management of labour. Int JAMP. 2023;5(3):1423-30.
22. Jogi SR. To compare the efficacy of Drotaverine Hydrochloride and Valethamate Bromide in shortening of the first stage of labour. International Int J Repro Cont Obst Gyn. 2015;1;4(4):1038-44.
23. Sinhasane H, Nishty GM. A comparative study on the efficacy of drotaverine and valethamate on cervical dilatation during labour. Int J Repro Cont Obst Gyn. 2017;1;6(2):423-7.
24. Mandal AK, Molla N. Comparison of efficacy of Drotaverine hydrochloride and Valethamate bromide in the augmentation of labour: a hospital based randomized trial. Int J Repro Cont Obst Gyn. 2018;1;7(4):1579-86.
25. Dahal P, Banerjee B, Uprety DK, Das BP, Thakur A, Agrawal A. Comparative study of efficacy of drotaverine hydrochloride and valethamate bromide with control in first stage of labour. Health Renaissance. 2013;10;11(1):38-42.
26. Pai MV, Sreekumar S, Gupta K, Chatterjee N. Effect of Drotaverine on active phase of labour. Obs and Gynae Today. 2003;8:611-4.

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