Gynecology & Obstetrics
ISSN: 2161-0932

Tarrats et al., Gynecol Obstet (Sunnyvale) 2019, 9:3
DOI: 10.4172/2161-0932.1000500

Research Article Open Access

Hyoscine Butylbromide for Cervical Rigidity in the First Stage of Labor: Randomized Clinical Trial

Laura Tarrats[1*], **Isabel Navarri**[1], **Isabel Paez**[1] **and Sandra Cabrera**[2,3]

[1]*Obstetrics and Gynecology Service, University Hospital Germans Trias i Pujol, Badalona, Canyet Road 08916 Badalona, Barcelona, Spain*

[2]*Nursing Research, Institut Català d´Oncologia Badalona, Canyet Road 08916 Badalona, Barcelona, Spain*

[3]*Department of Fundamental, Medical and Surgical Nursing Science, University of Barcelona, Barcelona, Spain*

***Corresponding author**: Laura Tarrats Velasco, Delivery Ward Midwife, Obstetrics and Gynecology Service, University Hospital Germans Trias I Pujol, Badalona, Canyet Road 08916 Badalona, PhD student, Autonomous University of Barcelona, Spain, Tel: 0034650721780; E-mail: l_tarrats@hotmail.com

Received date: March 12, 2019; **Accepted date**: March 15, 2019; **Published date**: March 21, 2019

Abstract

Background: Midwives and obstetricians may encounter dilations complicated by cervical rigidity, diagnosed during the periodic vaginal examinations performed during labor.

Objective: To assess the effects of hyoscine butylbromide for cervical rigidity in the first stage of labor

Study design: randomized, placebo-controlled, double-blind, parallel, pre-post clinical trial. Pregnant women delivering at University Hospital Germans Trias i Pujol in Badalona, Barcelona between January 2013 and January 2018 were eligible for inclusion. Our calculated sample size target was 70 participants 35 in each group with a 95% confidence level, an alfa and beta level of 5% and 80% power. The intervention group received 40 mg of hyoscine butylbromide intravenously, while controls received a placebo drip. Primary outcomes were: duration (minutes) of the first stage of labor, duration (minutes) from intervention to complete dilation and changes in cervical rigidity. We also collected data on maternal and neonatal variables.

Results: Seventy-one women were included: 47 (66.2%) were nulliparous, and 35 (49.3%) had a spontaneous onset of labor. Fifty-seven (80.3%) women had vaginal deliveries: 37 (52.1%) were eutocic, 7 (9.8%) were assisted by obstetric vacuum, and 13 (18.3%) with forceps/spatulas; 14 (19.7%) were cesarean deliveries following complete dilation. Mean duration of the first stage of labor was 48.3 minutes shorter in the experimental group compared to the control (p=0.287), and mean time from intervention to complete dilation was 63.3 minutes shorter in the experimental group than control group (p=0.084).

Conclusion: dilation time and duration of delivery were lower in women with cervical rigidity who receive hyoscine butylbromide, but differences were not statistically significant.

Keywords: Cervix rigidity; First stage of labour; Hioscine butyl bromide; Midwives

Introduction

In daily practice, midwives and obstetricians may encounter dilations complicated by cervical rigidity, diagnosed during the periodic vaginal examinations performed during labor.

In a previous study of our research group at the University Hospital Germans Trias i Pujol (HUGTiP), we observed a prevalence of cervical rigidity (defined as a non-elastic, constricted cervical ring detected during active labor) in 19.2% of all observed dilations and a positive association between induced labour and cervix rigidity [1,2]. Current induction rates stand at approximately 20% of all labors [3,4], with an upward trend due to clinical guidelines recommending that pregnancy not exceed 41 weeks of gestation [5-7]. Likewise, the appropriate identification of the beginning of the dilation stage (centered, effaced cervix, dilated at least 3 cm; regular uterine contractions, fetal head engaged in the pelvis) is also related to the evolution of labor [8].

Epidural anesthesia is one of the main factors that can produce changes in the tissue characteristics of the cervix at the moment of administration [9,10]. Antispasmodic agents are sometimes used for prevention of delay in labor, despite the fact that the most recent guidelines on intrapartum care advise against these interventions [11].

The cervix is made up of two parts, endocervix and exocervix, which have morphological and functional differences at the mucosal level, but similar stroma [12]. The decision to administer Hyoscine Butylbromide (HBB) during dilation is based on its relaxing action on the smooth genital musculature. The present study aims to analyze the effects of HBB in the presence of cervical rigidity that may slow the correct development of the first stage of labor (dilation) and is not due to previous surgery [13].

Materials and Methods

Aims

To assess the effects of Hyoscine Butylbromide (HBB) for cervical rigidity in the dilation stage of labor.

Methodology

We used a double-blinded, parallel group, pre-post, randomized placebo-controlled clinical trial design. The intervention group of pregnant women received 40 mg HBB intravenously (i.v.). The study took place in the delivery ward of HUGTiP, part of the Catalan Health Institute in Badalona (Catalonia, Spain) in 2013-2018.

Sample

Inclusion, exclusion, and withdrawal criteria are summarized in Table 1.

Inclusion	Exclusion	Withdrawal criteria
Term gestation	Detection of cervical rigidity during active labor	Fetal distress during labor
Singleton		Confirmed by pH testing of fetal head
Low-medium risk pregnancies	Hypersensitivity to any component of the study drug	C-section before complete dilation
Cephalic presentation	Fetal distress during labor confirmed by pH testing of fetal head	The epidural catheter and/or analgesia Up to 30 min before or after HBB administration
Age 18-40 years old	Untreated narrow-angle glaucoma	
Detection of cervical rigidity during active labor	Tachycardia	Missing data in the clinical record
	Myasthenia gravis	Participants required other medication than oxytocic agents, epidural analgesia, prophylactic antibiotics
Written informed consent	Paralytic ileus	
	Mechanical bowel obstruction	
	Megacolon	
	Treatment with tricyclic antidepressants, antihistamines, quinidine, amantadine, disopyramide, dopamine antagonists, β-adrenergic, drugs that could interact with HBB	
	Prior to cervical surgery	
	The epidural catheter and/or analgesia up to 30 min before or after HBB administration	

Table 1: Inclusion, exclusion and withdrawal criteria.

We used Granmo software (version 7.12) to calculate a sample size of 70 participants (35 in each study arm) to detect a minimum difference in dilation time of 60 min (standard deviation [SD] 68.9 min), with an alfa value of 0.05 and beta value of 0.2 in a bilateral contrast. We did not consider attrition during our calculations given that participants were included prospectively until reaching the necessary sample size. We hypothesized that the administration of 40 mg HBB i.v. in laboring women during the dilation stage would reduce the time to dilation by at least 60 min compared to controls, and that these differences would be statistically significant.

Rigour

Participants were selected through non-probabilistic accidental sampling following diagnosis of cervical rigidity during labor. Allocation to the parallel study arms was determined using sealed, opaque, numbered envelopes, which each contained a color-coded card indicating group assignment. Sequence allocation employed a computer-generated (Epidat) random number table.

A midwife not involved in following participants during dilation was responsible for preparing the intervention and placebo fluid bags, which were identical in appearance, and assigning a study code to each.

The birth attendant was blinded to the contents of the fluid bag, as was the participant herself. This double-blinding ensured the impartiality of the assessments.

The independent variable was the administration or not of 40 mg HBB i.v. during the dilation stage.

Participants received a single dose of the drug or placebo following diagnosis of cervical rigidity. Also, the following dependent variables were defined: total duration of dilation (min), time from intervention to complete dilation (min), and the characteristics of the cervix following the intervention (elasticity/rigidity). Other variables are summarized in (Tables 1 and 2).

Intervention characteristics

Upon admittance to the delivery room, the midwives responsible for attending the women during labor gave them written and oral information about the study and invited them to participate if cervical rigidity were detected during the dilation stage.

When cervical rigidity was detected, the diagnosis was confirmed by double examination, and the inclusion/exclusion criteria of the study were assessed.

Our team informed the women of the cervical rigidity and requested their signature on the informed consent form which had been distributed previously. Once we confirmed that they had not received epidural anesthesia in the previous 30 min, we proceeded to administer the intervention:

1. The experimental group received 40 mg HBB i.v, diluted in 100 mL of saline, over 10 min

2. The control group received a placebo drip (100 mL of saline)

Both groups underwent the same procedures for diagnosis of cervical rigidity: the attending midwife detected the characteristics of cervical rigidity and consulted another midwife or obstetrician for a second opinion. If both birth attendants concurred in assessing the cervix as rigid, the diagnosis was accepted.

Women received the intervention immediately after confirmation of cervical rigidity; the next vaginal examination to assess modifications to cervical conditions occurred at 60 min. Subsequent examinations were undertaken according to routine practices over the course of the dilation stage.

Ethical approval

The institutional Ethics Committee for Clinical Research approved the study (HBB V.04-2013), as did the head of Nursing and the supervisors of the Emergency Obstetrics and Gynecology Service. The trial was registered in Europe (EUDRA-CT: 2012-005198-30) and authorized by the Spanish Agency of Medicines and Medical Devices.

All participants gave written informed consent, and the study complied with the ethical standards of the Declaration of Helsinki.

Statistical analyses

All data analyses were carried out using IBM® SPSS® Statistics 24.0 (The International Business Machines Corporation®, New York, NY, USA).

We performed the analysis following a modified intention-to-treat principle, as we excluded from the analysis of the women who underwent a cesarean delivery before completing the dilation stage of labor.

Quantitative variables were expressed as mean (SD), while qualitative and ordered categorical data were described as absolute and relative frequencies in each study arm.

We assessed normality by means of the Shapiro-Wilk test.

The bivariate inferential analysis by study arm was performed using Fisher's exact tests for nominal qualitative variables such as the presence of cervical rigidity, and non-parametric Mann-Whitney U tests for the main analysis of the duration of the dilation stage.

We also evaluated the influence of time on the presence of rigidity, independently of intervention group, using the Mantel test (linear association), and we performed a time-to-event analysis using the Mantel-Cox log-rank test.

Statistical significance was established at 5% (two-tailed).

Results

We included 80 women diagnosed with cervical rigidity during the dilation stage; 9 had a cesarean delivery before dilation was complete, due to either disproportionate pelvic-fetal size (7) or risk to the fetus's well-being (2 women in the control group);

we considered these participants to be lost to follow-up for the trial although all routine labor controls were carried out (Figure 1).

The final sample was made up of 71 women who completed the dilation stage; 80.3% (n=57) had a vaginal delivery, while 19.7% (n=14) delivered via cesarean after dilating to 10 cm. Figure 1 presents the CONSORT participant flow chart. Recruitment was stopped once reached the estimated sample size.

Thirty-six received HBB (20 nulliparous and 16 multiparous), and 35 received placebo (27 nulliparous and 8 multiparous). Participants had a mean age of 29.7 (SD 5.6) years.

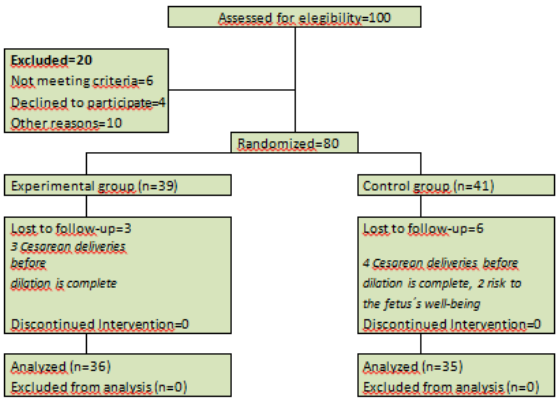

Figure 1: CONSORT flow chart.

Mean gestation was 39.8 weeks. 49.3% (n=35) had gone into labor spontaneously, while the rest were induced. About two-thirds (66.2%, n=47) of the women were nulliparous. At study end, 52.1% (n=37) of the deliveries were normal; 9.8% (n=7) were assisted with vacuum extractor; 18.3% (n=13) with forceps or spatulas; and 19.7% (n=14) were cesarean deliveries. Table 2 shows participants' characteristics by study group.

Variable	HBB Group n (%) / M ± SD	Control group n (%) / M ± SD	p
Age (years)	29.7 ± 5.5	30.2 ± 5.8	0.78
Weeks of gestation	40.0 ± 1.2	39.6 ± 1.2	0.71
Parity:			0.07*
Nulliparous (first dilation)	20 (55.5)	27 (77.1)	
Multiparous (	16 (44.3)	8(22.8)	
Oxytocin augmentation	34 (94.4)	34 (97.1)	0.57
Epidural anesthesia	33 (91.6)	34 (97.1)	0.32
Digital cervix stimulation in examinations	16 (47.1)	20 (58.8)	0.33
Onset of labour:			0.12
Spontaneous	21 (58.33)	14 (40.0)	
Induced	15 (41.67)	21 (60.0)	
Type of birth:			0.66
Eutocic	20 (55.5)	17 (48.5)	
Obstetric vacuum	4 (11.1)	3 (8.5)	
Forceps/spatulas	7 (19.4)	6 (17.1)	
Cesarean delivery	5 (13.8)	9 (25.7)	
*Significance level 5% for Fisher test			

Table 2: Baseline participant characteristics.

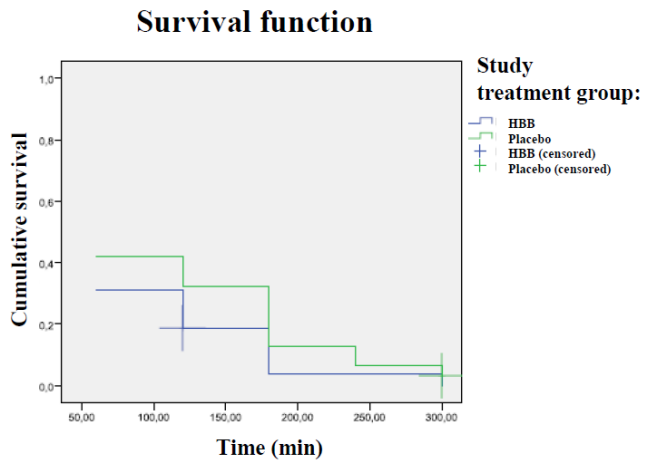

Figure 2: Presence of cervical rigidity over laboring period Time-to-event analysis using the Mantel-Cox log rank test.

Evolution of the Dilation Stage

The total duration of the dilation, as measured in minutes from the beginning of active labor (as judged by the birth attendant) to complete dilation, was on average 48.3 min shorter in the intervention group than in the control group (421.2 min [SD 178.7] versus 469.5 min [SD 200.3]).

Time from intervention (coinciding with the detection of cervical rigidity) to complete dilation was 63.3 min shorter in the experimental group than in the control (238.4 min [SD 138.4] versus 301.7 min [SD 162.8]); p=0.084.

Figure 2 shows the evolution of the cervical rigidity over the course of the labor. Participants in the HBB group presented a larger decrease in the persistence of cervical rigidity compared to the control group, although the difference was not statistically significant p=0.194.

In the analysis of cervical rigidity over labor progression, we observed a linear relationship in both groups; cervical rigidity decreased significantly as laboring went on (experimental: p=0.017; control: p<0.001).

The HBB group showed a more dramatic decrease in cervical rigidity (Figure 3).

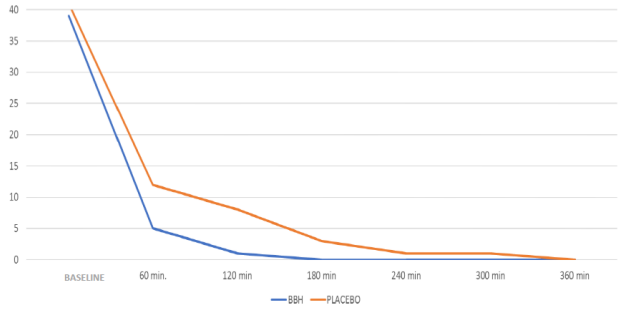

Figure 3: Association between cervical rigidity and time during labor Evaluation of influence of time on the presence of rigidity, independently of intervention group, using the Mantel test (linear association).

No adverse events occurred in the intervention group.

In the neonates, no differences were found regarding fetal heart rate variability and reactivity pre and post-intervention,

Apgar scores between study groups, the risk of fetal distress or in admittance to the neonatal intensive care unit (NICU) (Table 3).

Variable	HBB (n=36)	Control(n=35)	P
	n (%) / M ±SD	Vn (%) / M ± SD	
Pre-treatment FHR	134.94 ± 9.2	132.14 ± 44.6	0.21*
Post-treatment FHR	134.65 ± 8.7	139.57 ± 8.6	0.23*
Correct variability and reactivity pre and post treatment	31 (93.94)	35 (100)	0.14**
Risk of fetal distress	10 (27.78)	7 (20.00)	0.44**
Admission to NICU	1 (2.78)	1 (2.86)	0.98**
Birth weight	3417.1 ± 419.3	3253.4 ± 460.4	0.70*

FHR: Fetal Heart Rate; NICU: Neonatal Intensive Care Unit

*T-test

**Chi-squared

Table 3: Neonatal variables and study group.

Comments

In their updated guidance on intrapartum care, the WHO advises against the routine use of antispasmodic agents to ease dilation [11]. The use of HBB as a dilation easier is an off-label use of this drug.

In our delivery ward, the use of HBB to ease dilation is selective and has a specific purpose: in this case to improve the tissue conditions of a rigid cervix which is not the result of previous surgery. In the reviewed literature, no other clinical trial regarding HBB administration in case of the rigid cervix in the first stage of labor was found.

The reviewed trials assessed the effects of HBB as dilation easier. Samuels et al. [14] designed a double-blind Randomized Clinical Trial (RCT), finding a mean difference of 72 min in the duration of the dilation between groups. Kirim et al. [15] performed another double-blind RCT, administering 20 mg HBB i.v. in a single dose in the intervention group. That trial found a statistically significant difference of 57 min in the total duration of dilation between groups.

We did not observe any adverse events in the laboring women or in the neonates. HBB can produce side effects such as dry mouth, maternal tachycardia, sight accommodation difficulty, flushing, and urinary retention, as Maged et al. [16] stated in their study (in which one study arm received 40 mg i.v. HBB). As these side effects are implicit in HBB administration, in our study all participants were told to warn the attendant midwife in case side effects occurred but were not recorded to be analyzed as variables. Maternal vital signs (blood pressure, heart rate, and temperature) were assessed with the periodicity established for all labors in our ward. No fetal tachycardia occurred. Fetal well-being is assessed with cardiotocography (CTG) in all labors.

Other studies with similar designs have also reported results favoring HBB as a dilation easer [17-20], while only one clinical trial had results that were unfavorable to HBB [21], which they administered as a dose of 20 mg upon dilation of at least 4 cm and always following the performance of an amniotomy. Their results show a longer dilation stage in the experimental group than in the controls (4.1 [SD 1.8] versus 3.4 [SD 1.6]; $p<0.05$). Trialists also found increased admittances in the NICU and a higher rate of cesarean deliveries in the experimental group, although these differences were not statistically significant.

Aggarwal et al. [22] assessed the effects of 40 mg i.v. HBB as both a dilation easer and analgesic, reporting a significant reduction in pain (35.6%) in the HBB group as well as a significant decrease in the duration of the dilation stage.

Gupta et al. [23], and Fardiazar et al. [24] studied the effect of atropine versus HBB as accelerators and analgesics during labor; in the HBB group, the dilation stage was significantly shorter, and there were also fewer adverse events reported than in the atropine group. Sarbhjit et al. [25] compared three different antispasmodic drugs for cervical dilation, with their results favoring HBB over the other two arms.

The results of our study show a reduction of 48.3 min in the total duration of dilation in the experimental group compared to the control ($p=0.287$). The difference between groups lengthens to 63.3 min ($p=0.084$) when measuring time from intervention to complete dilation. In their study, Samuels et al. [14] found a difference between groups of 72 min in the total duration of dilation stage, while in Kirim et al.'s [15] study the mean difference in duration of dilation was 51 min; both differences were statistically significant.

Another relevant result is the fact that almost twice as many women in the control group had a cesarean delivery compared to the experimental group (n=9 versus n=5, respectively). In the reviewed literature, only Aldahhan et al. [21] found more cesareans in the HBB group. In any case, these differences were not statistically significant in any of the studies performed to date, including ours.

We assessed differences in cervical rigidity systematically by means of vaginal examination in all included women 60 min after administering treatment; we observed a faster dilation in the HBB group over this hour, and the control group also required more vaginal examinations over the total dilation stage, which coincides with the greater persistence of cervical rigidity in this group.

Limitations

The study sample was heterogeneous in terms of parity between groups. This significantly higher proportion of nulliparous women in the control group could have affected the total duration of dilation.

Vaginal examination is a diagnostic method that is difficult to contrast. In the examples found of studies that attempt to classify different degrees of cervical rigidity based on silicone models, authors point out in their discussion that silicone is not similar enough to human tissue to develop an adequate classification system [26]. In our trial, we used a double examination as a method of diagnostic contrast. As a university hospital, this practice occurs frequently so that residents can learn to examine the cervix with the guidance of another experienced professional.

There are many factors that operate simultaneously and synergistically during labor, including factors such as the choice of setting and the type of labor [27], a correct diagnosis at the beginning of labor [28], continuous professional support and care [29], and the application of pain relief measures [27-30].

Finally, we note that we did not record maternal constants when treatment was administered because HBB can produce moderate tachycardia, so assessing maternal heart rate would have broken the blinding.

Conclusion

The results obtained do not show statistically significant differences that would support the systematic use of HBB in women with cervical rigidity; the clinical differences between groups may allow consideration of selective use of HBB in cases requiring intervention to ease dilation for reasons such as persistent cervical rigidity.

Acknowledgment

We thank the pregnant women who participated in our study, as well as Dolors Roca, Sergio Alonso, Isabel Andrés, and delivery ward midwives at HUGTiP for their continued support and help. This project was widely supported by Institut Germans Trias i Pujol (IGTP) and HUGTiP (University Hospital Germans Trias i Pujol).

Conflict of Interest Statement

The authors report no conflicts of interest in this work.

Funding Statement

This study was supported with a Talents research scholarship provided by the HUGTiP and the Germans Trias I Pujol Institute (IGTP); Autonomous University of Barcelona (UAB).

References

1. Downe S, Gyte GML, Dahlen HG, Singata M (2013) Routine vaginal examinations for assessing progress of labour to improve outcomes for women and babies at term. Cochrane Database Syst Rev15: CD010088.
2. Tarrats L, Cabrera S (2014) Cervix rigidity in first stage of labour: Prevalence and influence in the labour process. Matronas Prof 15: 98-104.
3. Moore J, Kane Low L (2012) Factors that influence the practice of elective induction of labour: What does evidence tell us? J Perinat Neonatal Nurs 26: 242-250.
4. Caughey AB, Sundaram V, Kaimal AJ, Cheng YW, Gienger A, et al. (2009) Maternal and neonatal outcomes of elective induction of labor. Evid Rep Technol Assess 176: 1-257.
5. Miller NR, Cypher RL, Foglia LM, Pates JA, Nielsen PE, et al. (2015) Elective induction of labor compared with expectant management of nulliparous women at 39 weeks of gestation: A Randomized controlled Trial. Obstet Gynecol 126: 1258-1264.
6. Little SE (2017) Elective Induction of Labor: What is the impact? Obstet Gynecol Clin North Am 44: 601-614.
7. Induction of labour, NICE guidelinev (2008).
8. Robson M (2013) The diagnosis, treatment and audit of poor progress in labour (oral comunication). ECIC: 1st European Congress on Intrapartum Care. Ámsterdam.
9. Toledano RA, Leffert L (2018) Neuraxial analgesia for labor and delivery (including instrumented delivery).
10. Rajappa GC, Anandaswamy TC, Pattadi TJ, Swarup A (2017) Cervical dilatation in parturient receiving neuraxial analgesia: Comparison of epidural analgesia alone with combined spinal epidural analgesia. J Obstet Anaesth Crit Care 7: 43-46.
11. World Health Organization (2018) WHO recommendations: intrapartum care for a positive childbirth experience.
12. Corton MM, Leveno KJ, Bloom SL, Spong CY, Dashe JS, et al. (2014) Williams Obstetrics (24th ed). United States of America: Mc Graw-Hill Education.
13. Jolley JA, Wing DA (2008) Pregnancy manegement after cervical surgery. Obstet Gynecol 20: 528-533.
14. Samuels LA, Christie L, Roberts-Gittens B, Fletcher H, Frederick J, et al. (2007) The effect of hyoscine butylbromide on the first stage of labour in term pregnancies. BJOG 114: 1542-1546.
15. Kirim S, Asicioglu O, Yenigul N, Aydogan B, Bahat N, et al. (2015) Effect of intravenous hyoscine-N-butyl bromide on active phase of labor progress: a randomized double-blind placebo controlled trial. J Matern Fetal Neonatal Med 28: 1038-1042.
16. Maged AM, Mosaad M, AbdelHak AM, Kobt MM, Salem MM, et al. (2017) The effect of hyoscine butylbromide on the duration and progress of labor in primigravidae: A randomized controlled trial. J Matern Fetal Neonatal Med. 31: 2959-2964.
17. Sirohiwal D, Dahiya K, De M (2005) Efficacy of hyoscine-N-butyl bromide (Buscopan) suppositories as a cervical spasmolytic agent in labour. Aus N Z J Obstet Gynaecol 45: 128-129.
18. Makvandi S, Tadayon M, Abbaspour M (2011) Effect of hyoscine-N-butyl bromide rectal suppository on labor progress in primigravid women: Randomized double-blind placebo-controlled clinical trial. Croat Med J 52: 159-163.
19. Akleh HE, Al-Jufairi ZA (2010) Effect of hyoscine-N-butyl bromide (Buscopan) in accelerating first stage of labor. J Bahrain Med Soc 22: 103-107.
20. Sekhavat L, Karbasi SA, Fallah R, Mirowliai M (2012) Effect of hyoscine butylbromide first stage of labour in multiparus women. Afr Health Sci 12: 408-411.
21. Aldahhan F, Alwaeely F, Raheen F (2011) The evaluation of the effect of Buscopan on the duration of labour. Bas J Surg 17: 25-29.
22. Aggarwal P, Zutshi V, Batra S (2008) Role of hyoscine N-butyl bromide (HBB, buscopan) as labor analgesic. Indian J Med Sci 62: 179-184.
23. Gupta B, Nellore V, Mittal S (2008) Drotaverine hydrochloride versus hyoscine-N-butylbromide in augmentation of labor. Int J Gynaecol Obstet 100: 244-247.
24. Fardiazar Z, Niknami F, Mashayekhi S, Ghojazadeh M (2013) Hyoscine-N-butylbromide versus atropine as labour accelerant and analgesic: A randomized clinical trial. Pak J Biol Sci 16: 443-445.
25. Sarbhjit K, SKB Parmjit K, Surinder B (2013) To compare the effect of camylofin dihydrochloride (anafortin) with combination of valethamate bromide (epidosin) and hyoscine butyl-N-bormide (buscopan) on cervical dilation. J Clin Diagn Res 7: 1897-1899.
26. Machui O, Blucher U, Dudenhausen JW (1996) How objective is clinical determination of cervix consistency? Z Geburtshilfe Neonatol 200: 155-160.
27. Bolten N, Jonge A, Zwagerman E, Zwagerman P, Klomp T, et al. (2016) Effect of planned place of birth on obstetric interventions and maternal outcomes among low-risk women: a cohort study in the Netherlands. BMC Pregnancy Childbirth 16: 329.
28. Mikolajczyk R, Zhang J, Grewal J, Chan L, Petersen A, et al. (2016) Early versus late admission to labor affects labor Progression and risk of cesarean section in nulliparous women. Front Med (Lausanne) 3: 26.
29. Hodnett ED, Gates S, Hofmeyr GJ, Sakala C (2012) Continuous support for women during childbirth. Cochrane Database Syst Rev (10): CD003766.
30. Steel A, Sibbritt D, Broom A, Gallois C, Frawley J , et al. (2015) Managing the pain of labour: Factors associated with the use of labour pain management for pregnant Australian women. Health Expect 18: 1633-1644.