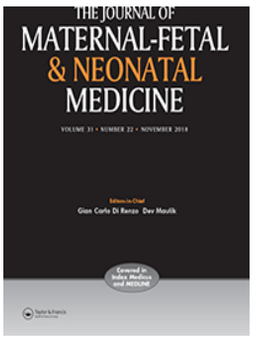

The Journal of Maternal-Fetal & Neonatal Medicine

ISSN: 1476-7058 (Print) 1476-4954 (Online) Journal homepage: http://www.tandfonline.com/loi/ijmf20

The effect of hyoscine butylbromide on the duration and progress of labor in primigravidae: a randomized controlled trial

Ahmed Mohamed Maged, Medhat Mosaad, Ahmed M. AbdelHak, Mohamed M. Kotb & Maged M. Salem

To cite this article: Ahmed Mohamed Maged, Medhat Mosaad, Ahmed M. AbdelHak, Mohamed M. Kotb & Maged M. Salem (2018) The effect of hyoscine butylbromide on the duration and progress of labor in primigravidae: a randomized controlled trial, The Journal of Maternal-Fetal & Neonatal Medicine, 31:22, 2959-2964, DOI: 10.1080/14767058.2017.1359828

To link to this article: https://doi.org/10.1080/14767058.2017.1359828

Accepted author version posted online: 24 Jul 2017.
Published online: 02 Aug 2017.

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE
2018, VOL. 31, NO. 22, 2959–2964
https://doi.org/10.1080/14767058.2017.1359828

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

The effect of hyoscine butylbromide on the duration and progress of labor in primigravidae: a randomized controlled trial

Ahmed Mohamed Maged, Medhat Mosaad, Ahmed M. AbdelHak, Mohamed M. Kotb and Maged M. Salem

Department of Obstetrics and Gynecology, Kasr Aini Hospital, Cairo University, Cairo, Egypt

ABSTRACT

Objective: To assess the effect of hyoscine butylbromide (HBB) on duration of the first stage of labor in primigravdae.

Methods: A case–control study conducted on 120 primigravida at term admitted in active labor were divided into three equal groups. A single dose of the drug (placebo or HBB 20 mg or HBB 40 mg) was injected intravenously slowly to groups A, B, and C. The duration of the first stage was calculated from the time of cervical dilatation of three to four centimeters in active labor until a fully dilated cervix was observed.

Results: The duration of first stage was significantly shorter in women receiving 20 and 40 mg of HBB when controlled to control women (187.73 ± 20.92, 186.41 ± 19.40 versus 231.39 ± 33.14 min). There was no significant difference between the three study groups regarding duration of the second stage (36.76 ± 9.98, 35.72 ± 9.97 and 37.55 ± 10.57, respectively, $p > .05$), number of cases delivered by cesarean section (12.5%, 12.5%, and 15%, respectively, $p > .05$) and Apgar score of the neonates ($p > .05$). There was no significant difference between the three study groups regarding occurrence of side effects named dry mouth (7.5%, 12.5%, and 5%, $p > .05$), flushing (2.5%, 5% and 0%, $p > .05$), tachycardia (2.5%, 2.5%, and 2.5%, $p > .05$), or urinary retention (2.5%, 0%, and 0%, $p > .05$).

Conclusion: Intravenous injection of HBB decreases the duration of active phase of labor in primigravidae with no side effects.

ARTICLE HISTORY
Received 7 April 2017
Accepted 23 July 2017

KEYWORDS
Augmentation of labor; hyoscine butylbromide; normal labor

Introduction

Parturition can be arbitrarily divided into four overlapping phases that correspond to the major physiological transitions of the myometrium and cervix during pregnancy [1]. These phases of parturition include (1) a prelude to it, (2) the preparation for it, (3) the process itself, and (4) recovery [2].

The first stage begins when spaced uterine contractions of sufficient frequency, intensity, and duration are attained to bring about cervical thinning or effacement. This labor stage ends when the cervix is fully dilated – about 10 cm – to allow passage of the term-sized fetus. The first stage of labor, therefore, is the stage of cervical effacement and dilatation [2].

The progress of labor in nulliparas has particular significance because curves reveal a rapid change in the slope of cervical dilatation rates between 3 and 5 cm. Thus, cervical dilatation of 3–5 cm or more, in the presence of uterine contractions, can be taken to reliably represent the threshold for active labor.

The mean duration of active-phase labor in nulliparas was 4.9 h. But the standard deviation of 3.4 h is large, hence, the active phase was reported to have a statistical maximum of 11.7 h [3].

Indeed, rates of cervical dilatation ranged from a minimum of 1.2 up to 6.8 cm/h. The ideal management of labor and delivery requires two potentially opposing viewpoints on the part of clinicians. First, birthing should be recognized as a normal physiological process that most women experience without complications. Second, intrapartum complications, often arising quickly and unexpectedly, should be anticipated [4].

According to Orji (2008), the WHO partograph is similar for nulliparas and multiparas. Labor is divided into a latent phase, which should last no longer than 8 h, and an active phase. The active phase starts at 3 cm dilatation, and progress should be no slower than 1 cm/h A 4-h wait is recommended before intervention when the active phase is slow [5]. Lavender et al. [6] randomized 3000 nulliparous women to labor interventions at 2 h versus 4 h as recommended by WHO.

CONTACT Ahmed Mohamed Maged prof.ahmedmaged@gmail.com 481, King Faisal Street Haram, Giza, Egypt

More than 30 years ago, O'Driscoll et al. [7] pioneered the concept that a disciplined, standardized labor management protocol reduced the number of cesarean deliveries for dystocia. Their overall cesarean delivery rate was 5% in the 1970s and 1980s with such management [7]. The approach is now referred to as active management of labor. Two of its components – amniotomy and oxytocin – have been widely used.

Wei et al. [8] in a Cochrane database review found a modest reduction in cesarean delivery rates when active management of labor was compared with standard care. Frigoletto et al. [9] reported another randomized trial with 1934 nulliparous women at Brigham and Women's Hospital in Boston. Although they found that such management somewhat shortened labor, it did not affect the cesarean delivery rate [9]. These observations have since been reported by many others [10].

Oxytocin has amino acid homology similar to arginine vasopressin. Because of this, it has significant antidiuretic action, and when infused at doses of 20 mU/min or more, renal-free water clearance decreases markedly. If aqueous fluids are infused in appreciable amounts along with oxytocin, water intoxication can lead to convulsions, coma, and even death [11].

The American College of Obstetricians and Gynecologists recommends the use of amniotomy to enhance progress in active labor, but cautions that this may increase the risks of infection and maternal fever [12].

When necessary obstetricians use cervical ripening agents to decrease the duration of labor. Intravaginal misoprostol (prostaglandin E1 analogue) and dinoprostone (prostaglandin E2) are the most commonly used agents for cervical ripening [13].

Hyoscine-*n*-butylbromide is a derivative of hyoscine which is extracted from leaves of the Dubosia tree found mainly in Australia. It is known by its spasmolytic action and has been arose since 1951 [14].

Hyoscine butylbromide (HBB) belongs to the parasympatholytic group of drugs and is a semisynthetic derivative of scopolamine. It is an effective antispasmodic drug without the untoward side effects of atropine as it does not cross the blood brain barrier therefore no central action is seen. It is a quaternary ammonium derivative, which exerts a spasmolytic action on the smooth muscle of the gastrointestinal, biliary, and genitourinary tracts [15].

It acts primarily by blocking the transmission of neural impulses in the intraneural parasympathetic ganglia of abdominal organs, apparently inhibiting cholinergic transmission in the synapses of the abdominal and pelvic parasympathetic ganglia, thus relieving spasms in the smooth muscles of gastrointestinal, biliary, urinary tract, and female genital organs, especially the cervico-uterine plexus, thus aiding cervical dilatation [16].

The aim of this study is to assess whether the intravenous injection of hyoscine butylbromide is effective in hastening cervical dilatation, thus shortening the duration of the first stage of labor in primigravidae.

Materials and methods

This is a prospective double-blind case–control study conducted at Kasr Alainy medical school at Cairo University during the period from July 2015 to December 2016. After approval of local ethical committee, 120 patients were recruited to the study with their ages between 18 and 35 years, all were primigravidae with gestational age between completed 37–41 weeks and 6 d carrying uncomplicated cephalic singleton pregnancy with occipito-anterior position. All had established spontaneous active labor (defined as the presence of at least three regular uterine contractions over 10 min with cervical dilatation 3–4 cm) with cervical effacement not less than 50% with intact amniotic membranes. Women with indications of elective cesarean section, medical disorders associating pregnancy as pregnancy induced hypertension and gestational Diabetes or spontaneous rupture of membranes were excluded from the study. Exclusion criteria included women with contraindications for hyoscine butylbromide as known allergy to hyoscine or other atropinics (e.g., atropine, scopolamine), myasthenia gravis, megacolon, or glaucoma and those who underwent epidural anesthesia, oxytocin induction, or augmentation.

Women who meet the inclusion criteria were asked to participate in the study and an informed written consent was obtained from each patient after explaining thoroughly the aims, risks, and benefits of the study.

All participants were subjected to complete history, General and abdominal obstetric examination to check adherence to inclusion and exclusion criteria. Vaginal examination was done and included evaluation of cervical dilatation, effacement and position, state of fetal membranes, presenting part, position of fetal head, and pelvic adequacy.

Obstetric ultrasound was done using Medison X6 ultrasound (Samsung Medison, Seoul, South Korea) machine equipped with a 4–7-MHz transabdominal probe with the woman in slightly left tilted supine

position to avoid supine hypotension to confirm the viability, gestational age, estimated fetal weight, placental site and grade, and fetal heart rate.

All women were randomized equally using automated web-based randomization system into three groups. Group I included 40 pregnant women received 20 mg hyoscine butylbromide (1 ml HBB +1 ml saline) intravenously. Group II included 40 pregnant women received 40 mg hyoscine butylbromide intravenously. Group III included 40 pregnant women received 2 ml of normal saline intravenously as a placebo.

Women were admitted when active phase of labor starts defined as the presence of at least three regular uterine contractions over 10 min with cervical dilatation 3–4 cm with cervical effacement not less than 50% [17].

A single dose of the drug (placebo, HBB 20 mg or HBB 40 mg) was injected intravenously slowly. Labor was monitored. Vaginal examination was conducted every 2 h. The duration of the first stage was calculated from the time of cervical dilatation of three to four centimeters in active labor until a fully dilated cervix was observed. If the initial progress of labor (as assessed through partographs) was unsatisfactory, then, oxytocin augmentation was initiated. Those patients were excluded from the study.

The primary outcome parameter was the duration of first stage of labor. Other outcomes were duration of the second stage of labor, mode of delivery, maternal adverse effects, and neonatal outcome.

Statistical methods

Data were coded and entered using the statistical package SPSS version 23 (SPSS Inc., Chicago, IL). Data were summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test. For comparing categorical data, Chi-square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. p Values less than .05 were considered as statistically significant.

Sample size calculation was done using the comparison of duration of first stage of labor between parturient mothers given hyoscine butylbromide (G1) and those who were not given any drug (G2). As reported in previous publication [18], the mean ± SD of first-stage duration in G1 was 186.8 ± 125.6 min, while in G2, it was 260.4 ± 120.9 min. Accordingly, we calculated that the minimum proper sample size was 39 patients in each arm to be able to reject the null hypothesis with 95% power at $\alpha = 0.05$ level using one-way analysis of variance test. Sample size calculation was done using G*Power software version 3.1.2 for MS Windows, Franz Faul, Kiel University, Kiel, Germany.

Table 1. Characteristics of the study population.

	Group I (20 mg HBB)	Group II (40 mg HBB)	Group III (control)	p value
Age (years)	24.15 ± 3.82	24.87 ± 3.74	24.43 ± 3.73	>.05 NS
Height (cm)	162.65 ± 5.72	162.65 ± 5.72	163.50 ± 4.67	>.05 NS
Weight (kg)	78.65 ± 8.62	78.65 ± 8.62	78.98 ± 9.02	>.05 NS
GA (weeks)	38.95 ± 1.02	38.95 ± 1.02	39.12 ± 1.05	>.05 NS

Data are presented as mean ± SD.

Results

There was no significant difference between the three study groups regarding age, weight, height or gestational age (Table 1). The duration of first stage was significantly shorter in women receiving both doses of HBB when controlled to control women (Table 2).

There was no significant difference between the three study groups regarding the duration of second stage, neonatal birth weight, number of cases delivered by cesarean section and Apgar score of the neonates (Table 2).

There was no significant difference between the three study groups regarding occurrence of side effects named dry mouth, flushing, tachycardia, or urinary retention (Table 3). The women excluded from the study and the causes of exclusion are shown in Table 4.

Discussion

The management of normal labor is both an art and a science. Prolongation of labor is one such dilemma that every obstetrician tries to avoid. The ultimate aim of the obstetrician is to accomplish the delivery in the shortest possible time without compromising maternal and fetal safety. For decades, health providers have worked to manage labor actively and safely, with the goal of shortening the duration of painful labor. Reduction of cesarean sections and other fetal and maternal complications is also an important aspect of labor management [19].

Prolonged labor is one of the most important risk factors for perinatal compromise. The two major factors that determine duration of labor are uterine contractility and rate of cervical dilation [20].

Table 2. Labor duration and neonatal outcome among the study groups.

	Group I (20 mg HBB)	Group II (40 mg HBB)	Group III (control)	*p* value		
				I and II	I and III	II and III
Active phase of 1st stage duration (min)	187.73 ± 20.92	186.41 ± 19.40	231.39 ± 33.14	>.05	<.001	<.001
2nd stage duration (min)	36.76 ± 9.98	35.72 ± 9.97	37.55 ± 10.57		>.05	
Fetal weight (g)	3239.39 ± 332.08	3170.31 ± 264.53	3221.21 ± 336.12		>.05	
Cases delivered with Cesarean section[a]	5 (12.5%)	5 (12.5%)	6 (15%)		>.05	
Apgar 1 min	7.1 ± 0.55	7.2 ± 0.51	7.2 ± 0.78		>.05	
Apgar 5 min	8.2 ± 0.6	8.1 ± 0.5	8.1 ± 0.55		>.05	

Data are presented as mean ± SD.
[a]Data are presented as number (percentage).

Table 3. Side effects.

	Group I (20 mg HBB) (%)	Group II (40 mg HBB) (%)	Group III (control) (%)	*p* value
Dry mouth	3 (7.5)	5 (12.5)	2 (5)	>.05 NS
Facial flushing	1 (2.5)	2 (5)	0 (0)	>.05 NS
Tachycardia	1 (2.5)	1 (2.5)	1 (2.5)	>.05 NS
Urine retention	1 (2.5)	0 (0)	0 (0)	>.05 NS

Data are presented as number (percentage).

Table 4. Women excluded and causes.

	Group I (20 mg HBB) (%)	Group II (40 mg HBB) (%)	Group III (control) (%)	*p* value
Exclusion	7 (17.5)	8 (20)	7 (17.5)	>.05 NS
Causes of exclusion				
ROM	3 (42.8)	4 (50)	3 (42.8)	>.05 NS
Fetal distress	2 (28.5)	2 (25)	1 (14.2)	>.05 NS
Failure of progression	1 (14.3)	1 (12.5)	2 (28.5)	>.05 NS
Obstructed	1 (14.3)	1 (12.5)	1 (14.2)	>.05 NS

Data are presented as number (percentage).

Spasmolytic drugs are frequently employed to overcome cervical spasm and thus reduce the duration of labor. One of these spasmolytics is hyoscine-*n*-butylbromide which exerts a spasmolytic action on the smooth muscle of the gastrointestinal tract, biliary, and genitourinary tracts [21]. Our study found that administration of HBB in 20 or 40 mg has significantly decreased the duration of first stage of labor without exerting such effect on the second and third stages of labor.

On one hand, the physiological explanation of that is the primary site of action of HBB which is the cervix without effect on uterine contractility. That is very important as enhancement of uterine contractions that shorten the second stage is exposing both the parturient women and her fetus to risks especially injuries. On the other hand, if it exerted an inhibitory action on uterine activity, it can expose the woman to hazards of atonic postpartum hemorrhage and retained placenta [18].

The study was done on age group ranging from 18 to 35 years old, patients aging less than 18 years or more than 35 years were excluded from our study as pregnancy in this age group consider high risk pregnancy [22].

Patients with occipitoposterior position were excluded as it is associated with prolonged first and second stages of labor [23] Qahtani and Hajeri [15] conducted a randomized, double-blinded, controlled trial on 97 primigravid term pregnant women in spontaneous labor received either hyoscine butylbromide or a placebo intramuscularly once the women entered the active phase of labor. The mean duration of the first stage in the control group was 215 min, compared with 165 min in the study group, representing a decrease of 23.3% (p value = .001). There were no significant changes in the duration of the second (p value = .063) or third (p value = .0618) stages of labor [15].

Kirim et al. [24] performed a randomized, double-blinded, controlled trial done on healthy primigravid and multigravid women in spontaneous labor at term. A total of 80 patients were divided into two equal groups to either a single dose of 20 mg (1 ml) of HBB or placebo (1 ml saline) intravenously. The mean duration of the first stage of labor was 191.1 ± 43.06 min in the primigravid patients of the HBB group, while it was 248.2 ± 66.1 min in the placebo group, a statistically significant difference of 57 min (p value < .001). The mean duration of the first stage of labor was 170.1 ± 50.8 min in the multigravid patients of the HBB group, while it was 224.06 ± 53.7 min in the placebo group (a difference of 54 min, p value < .001). There was no significant change in the times for the second and third stages of labor. There were no significant differences in terms of Apgar scores noted at 1 and 5 min, prepartum and postpartum hemoglobin levels and birth weight. No adverse maternal and fetal effects were observed in both HBB and placebo groups [24].

Sekhavat et al. [18] conducted a single-blinded randomized clinical trial study on 188 multiparas women in early active phase of labor divided into two groups: the hyoscine group (n = 94) received 20 mg (1 ml) of hyoscine and the control group (n = 94)

received 1 ml of normal saline which was given as placebo, intravenously. The duration of the first stage was 186.8 ± 125.6 min versus 260.4 ± 120.9 min (p value = .001) and the duration of second stage of labor was 20.0 ± 8.1 min versus 25.8 ± 9.4 min (p value = .03) in the hyoscine group versus controls, respectively. The frequency of cesarean section and mean of neonatal Apgar score at minutes of one and five was not different in both groups. No serious adverse events were seen in the two groups [18].

The difference in results related to second stage may be acquired from the nature of participants as multigradiva may respond in a different way when compared with primigravida.

Our study is an important randomized controlled, double-blinded study limited to primipara women who are more suspected to abnormal progress of labor and subjected to more hazards of prolonged labor. Our intervention led to shortening of the duration of first stage of labor. That is unquestionably beneficial as such shortening of duration alleviates the need for more doses of analgesics with its potential fetal and neonatal effects and lower the cost of labor. Shortened labor is associated with lower risk of chorioamnionitis, puerperal, and neonatal sepsis that is associated with prolonged labor. It also decreased the risk of postpartum hemorrhage which is markedly increased after prolonged labor. Also shortened labor raises maternal tolerability to vaginal delivery decreasing the risk of cesarean section resulted from maternal exhaustion or psychological troubles associated with labor pain especially in developing areas without high availability of epidural analgesia. We think that will be also associated with less postpartum depression which is needed to be evaluated in future studies.

We also observed no effect on the rate of cesarean section among the study groups. However, we do believe that this finding is related to small sample size and if the trial is repeated with large sample size, decreased rate of cesarean will be imminent.

Fetuses with limited reserve or those with diminished liquor and women with medical disorders can tolerate uterine contractions for a limited time and we think that will decrease the rate of cesarean section in these high risk pregnancy.

We also found that HBB has no effect on the second and third stages of labor. That is also beneficial as the hastened second stage will be associated with increased risk of maternal and fetal birth injuries.

In conclusion, intravenous injection of hyoscine butylbromide helps to decrease the duration of active phase of labor in primigravidae with no side effects on either the mother or the neonate. We recommend the small dose (20 mg) intravenously as there was no significant changes with higher dose.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] Word RA, Li XH, Hnat M, et al. Dynamics of cervical remodeling during pregnancy and parturition: mechanisms and current concepts. Semin Reprod Med. 2007;25(1):69–79.

[2] Cunningham FG, Leveno KJ, Bloom SL, et al. Physiology of labor. In: Cunningham FG, Williams JW, editors. William's obstetrics. 24th ed. New York (NY): McGraw-Hill; 2014. p. 408–432 [Chapter 21].

[3] Friedman EA. Primigravid labor: a graphicostatistical analysis. Obstet Gynecol. 1955;6(6):567–589.

[4] Cunningham FG, Leveno KJ, Bloom SL, et al. Normal labor. In: Cunningham FG, Williams JW, editors. William's obstetrics. 24th ed. New York (NY): McGraw-Hill; 2014. p. 433–454 [Chapter 22].

[5] Orji E. Evaluating progress of labor in nulliparas and multiparas using the modified WHO partograph. Int J Gynecol Obstet. 2008;102(3):249–252.

[6] Lavender T, Alfirevic Z, Walkinshaw S. Effect of different partogram action lines on birth outcomes: a randomized controlled trial. Obstet Gynecol. 2006;108(2):295–302.

[7] O'Driscoll K, Foley M, MacDonald D. Active management of labor as an alternative to cesarean section for dystocia. Obstet Gynecol. 1984;63(4):485–490.

[8] Wei S, Wo BL, Xu H, et al. Early amniotomy and early oxytocin for prevention of, or therapy for, delay in first stage spontaneous labour compared with routine care. Cochrane Database Syst Rev. 2009;2:CD006794.

[9] Frigoletto FD Jr, Lieberman E, Lang JM, et al. A clinical trial of active management of labor. N Engl J Med. 1995;333(12):745–750.

[10] Brown HC, Paranjothy S, Dowswell T, et al. Package of care for active management in labour for reducing caesarean section rates in low-risk women. Cochrane Database Syst Rev. 2008;4:CD004907.

[11] Cunningham FG, Leveno KJ, Bloom SL, et al. Induction and augmentation of labor. In: Cunningham FG, Williams JW, editors. William's obstetrics. 24th ed. New York (NY): McGraw-Hill; 2014. p. 523–534 [Chapter 26].

[12] American College of Obstetricians and Gynecologists. Dystocia and augmentation of labor. Practice Bulletin, Reaffirmed 2013. 2003;49 (December).

[13] Norwitz ER, Robinson JN, Repke JT. Labor and delivery, obstetrics: normal and problem pregnancies. 3rd ed. New York: Churchill Livingstone; 2003.

[14] Tytgat GN. Hyoscine butylbromide: a review of its use in the treatment of abdominal cramping and pain. Drugs. 2007;67(9):1343–1357.
[15] Qahtani NH, Hajeri FA. The effect of hyoscine butylbromide in shortening the first stage of labor: a double blind, randomized, controlled, clinical trial. Ther Clin Risk Manage. 2011;7:495–500.
[16] Weiser T, Just S. Hyoscine butylbromide potently blocks human nicotinic acetylcholine receptors in SH-SY5Y cells. Neurosci Lett. 2009;450(3):258–261.
[17] Norwitz ER, Schust DJ, Fisher SJ. Implantation and the survival of early pregnancy. N Engl J Med. 2001; 345(19):1400–1408.
[18] Sekhavat L, Karbasi SA, Fallah R, et al. Effect of hyoscine butylbromide first stage of labour in multiparus women. Afr Health Sci. 2012;12(4):408–411.
[19] López-Zeno JA, Peaceman AM, Adashek JA, et al. A controlled trial of a program for the active management of labor. N Engl J Med. 1992;326(7):450–454.
[20] Hofmeyr GJ. Obstructed labor: using better technologies to reduce mortality. Int J Gynecol Obstet. 2004;85(1):S62–S72.
[21] Samuels LA, Christie L, Roberts-Gittens B, et al. The effect of hyoscine butylbromide on the first stage of labour in term pregnancies. BJOG. 2007;114(12): 1542–1546.
[22] Samiya M, Samina M, Blade A. High risk pregnancy and correlation to neonatal outcome. Indian J Med Sci. 2008;5(1):75–80.
[23] Ponkey SE, Cohen AP, Heffner LJ, et al. Persistent fetal occiput posterior position: obstetric outcomes. Obstet Gynecol. 2003;101(5 Pt 1): 915–920.
[24] Kirim S, Asicioglu O, Yenigul N, et al. 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. 2015;28(9):1038–1042.