



Original Article

Effect of hyoscine butyl-bromide on the duration of active phase of labor: A randomized-controlled trial



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ABSTRACT

Objective: Hyoscine butyl bromide (HBB) is known for its antispasmodic action and has been in use for over five decades, there is however no consensus on its effectiveness in the labor process. The aim of this study was to determine the effect of HBB on the duration of the active phase of labor.

Materials and methods: A randomized double-blind placebo-controlled clinical trial involving 160 parturient who received either intravenous Hyoscine butyl-bromide (20 mg in 1 ml; n = 80) or intravenous normal saline (1 ml, n = 80). The mean duration of active phase of labor was compared between the two groups.

Results: The observed mean duration of the active phase of labor was significantly shorter ($P = 0.001$) in the Hyoscine butyl-bromide group (365.11 ± 37.32 min, range = 280–490) than in the Placebo group (388.46 ± 51.65 min, range = 280–525). There was no significant difference between the two groups in the mean duration of the second and third stages of labor (20.46 ± 10.46 vs. 23.38 ± 18.95 min, $P = 0.43$ and 8.96 ± 4.34 vs. 9.23 ± 5.92 min, $P = 0.75$, respectively). The mean 1-min APGAR scores were also comparable (8.08 ± 1.54 vs. 7.64 ± 1.60 , $P = 0.08$). The mean postpartum blood loss was significantly less in the Hyoscine butyl-bromide group (303 ± 96.52 vs. 368 ± 264.19 ml, $P = 0.04$).

Conclusion: Hyoscine butyl-bromide was effective in shortening the duration of the active phase of labor. It was also associated with significantly less postpartum blood loss.

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Introduction

The duration of active phase of labor is an important determinant of maternal and fetal complications associated with parturition [1]. In particular; prolonged labor has been linked with significant maternal and neonatal morbidity [2].

Hyoscine N-butyl-bromide (HBB) is a derivative of hyoscine, which is extracted from the leaves of the Dubosia tree found mainly in Australia [3]. It has been in use for over 50 years, for treatment of dysmenorrhea, pelvic spasm (e.g during hysterosalpingography), abdominal cramps, hypersalivation and motion sickness [4–6]. HBB acts by inhibiting cholinergic neuro transmission in the abdominal and pelvic parasympathetic ganglia, thus relieving spasm in the smooth muscles of gastrointestinal, biliary, urinary tract and female genital organs, especially the cervix and lower uterine segment; a

phenomenon that may cause cervical dilatation and effacement. Uterine contractions are however not affected by hyoscine and its derivatives [4].

Hyoscine butyl-bromide, unlike atropine and hyoscine (scopolamine), does not cross the blood–brain barrier; it therefore has no central action. This may be the reason why the frequency and severity of side effects on the sweat, salivary glands, eyes and the heart is less when HBB is compared to atropine at therapeutic doses [4,7]. It has been used to shorten the duration and reduce the blood loss of medically induced abortion [8].

Interventions to make the labor process shorter, have continually generated interest among obstetricians with debate on the benefit of antispasmodics still raging on, as literature is replete with conflicting reports from studies [4,5,9,10]. Definite conclusions of the effects of hyoscine butyl-bromide on the duration of active phase of labor are yet to be made from meta-analyses. The reasons for these discrepancies are mostly from methodological issues; especially in reports from studies between women of different parities [11]. In addition, most of the available studies were,

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conducted outside Africa. The resolution of this uncertainty is much more important in Sub-Saharan Africa, where prolonged and obstructed labor is still a major contributor to maternal mortality and morbidity [2].

The present study aimed at determining the effect of hyoscine butyl-bromide on the duration of the active phase of labor as well as the fetomaternal outcomes such as intra-partum blood loss and the neonatal APGAR scores.

Materials and methods

This was a randomized double-blind, placebo-controlled trial conducted in the Department of Obstetrics and Gynecology of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC) located in Ile-Ife, Osun state, South-Western Nigeria. Data were obtained from March to December 2014. Published reports from the institution had revealed caesarean section, labor induction and labor augmentation rates of 10.6%, 18% and 13.2% respectively [12–14].

Participants were parturient aged 18–35 years, with singleton pregnancies in vertex presentation and in active phase (cervical dilatation of 4 cm) of spontaneous labor at term (37–41 weeks gestation), without chronic or pregnancy-induced illnesses. Exclusion criteria were: grand multiparity (defined as parturient who have carried 5 or more pregnancies beyond 28 weeks which is the age of viability in Nigeria [15]), previous uterine scar, caesarean section, presence of any contraindication to vaginal delivery, cervical cerclage, pre-labor rupture of fetal membranes, maternal pyrexia and allergy to pentazocine, hyoscine or their excipients. Patients with history suggestive of, or diagnosed previously to have glaucoma, myasthenia gravis, obstructive uropathy, Down's syndrome, asthma, cardiac, liver or renal disease, persistent gastro-oesophageal reflux disease, severe constipation, persistent diarrhea, ulcerative colitis, seizure disorder or psychiatric illness were also excluded from the study.

The sample size was determined based on the primary outcome variable which was the mean duration of the active phase of labor. In a study on the effects of hyoscine butyl bromide on the duration of labor, Al Qahtani [6] reported a mean duration of active phase of labor of 190 ± 75 min among parturient who received intravenous HBB and 251 ± 92 min in women who did not receive HBB. These values were applied in the calculation of sample size using the formula for comparison of means [16]. Type II error margin for this study was set at 0.1, implying a power of 90%. A minimum difference in mean duration of active phase of labor of 45 min was assumed, for the effect to be attributable to the HBB administered. Thus, with 10.6% (published caesarean section rate at OAUTHC) [10] added for attrition, a total of 160 participants were recruited for the study (80 subjects in each group).

Patient recruitment was done after obtaining a written informed consent. The parturient were then examined and the findings recorded in the study proforma. Randomization was achieved using the permuted block randomization method. A computer generated random number sequence was used to achieve this. Both the investigators and the subjects were blinded as to the subject's allocation to receive HBB or placebo.

The intervention drugs were dispensed in sealed brown paper envelope packets, which were prepared at the hospital pharmacy. One set of packets contained 1 ml (20 mg) of Hyoscine butyl-bromide (Pemasol[®], Jiangsu Huayang Pharma Co. Ltd. Jiangsu China.) and the other set contained 1 ml of 0.9% normal saline (placebo). Both liquids are colorless, and were each pre-drawn into 2 ml syringes. Each packet was prepared at patient recruitment and stored in a refrigerator until use or discarded after 24 h when

unused. The content of each packet was administered intravenously as a single dose by the midwife or doctor, when cervical dilatation reached 4 cm observed by vaginal examination, which was considered as the reference point for the beginning of active phase of labor [13,14].

Amniotomy was performed for all participants in established labor whose fetal membranes were still intact at cervical dilatation of 4 cm. Labor in each parturient was monitored with the WHO partograph. Analgesia (Pentazocine 30 mg intramuscularly) was administered to all participants after amniotomy, before cervical dilatation reached 6 cm (to avoid neonatal respiratory depression).

Oxytocin augmentation was initiated where the uterine contractions were not adequate (i.e. less than 3 contractions in 10 min and/or contractions lasting less than 40 s in duration). Intervention by instrumentation or caesarean section was dictated by obstetric indications; data of such participants were not included in the final analysis. The same randomization code was re-assigned and intervention administered to the next consecutive consenting parturient who met the selection criteria. The third stage of labor was actively managed in all participants according to the International Confederation of Midwives/International Federation of Gynaecology and Obstetrics (ICM/FIGO) protocol [17].

After delivery of the baby and immediate clamping of the umbilical cord, a BRASS-V drape (BRASS-V drape[®], Excellent Drapes, Moogambigai, Madurai, India) was spread underneath each parturient and the upper level of the content of the drape's collecting pouch was read against its calibration to determine blood loss. Subsequent blood loss up till 2 h postpartum was measured by application of sanitary pads (Comfit[®], Femina Hygienical Products, Port-Harcourt, Nigeria) of known weight (20 g each) to the perineum. These pads were re-weighed 2 h postpartum and blood loss estimated from the pads' weight gain thus: 1 g \approx 1 ml. The parturients' vital signs were also recorded postpartum and patients whose clinical condition remained stable were transferred to the postnatal ward. In the event of persistent bleeding, subsequent management was in accordance with the departmental protocol for the management of primary postpartum hemorrhage. Primary postpartum hemorrhage was defined as bleeding from the genital tract after delivery of the baby in excess of 500 mls or blood loss in excess of 10% of the antenatal packed cell volume or any blood loss, sufficient to cause a derangement in the cardiovascular status of the patient [24].

Capillary blood samples were obtained on admission, and 24 h after delivery for hematocrit estimation to determine change in hematocrit. Participants were monitored closely for features of adverse reactions such as maternal tachycardia, dry mouth, pruritus, rash and difficult swallowing. Emergency treatment for anaphylactic reaction was made available. The accoucheur completed a proforma detailing the duration of labor during the first and second stages; maternal complications and neonatal conditions at birth (Apgar score and birth weight). The data obtained were processed using SPSS version 15.0 (SPSS Inc, Chicago; IL). Univariate and bivariate analysis was done, with the Chi-square test and the Fisher exact test used where appropriate. The student t-test was used for comparison of means in independent samples. The 95% confidence interval was used and the level of statistical significance set at p-value of <0.05.

Ethical approval was obtained from the research and ethics committee of the OAUTHC Ile-Ife (Protocol number ERC/2012/12/05). The study was also registered with the Pan African Clinical Trial Registry (PACTR) with unique identification number-PACTR201403000779211. The study protocol is available at www.pactr.org.

Results

The participants were recruited over a 9-month period (March–December 2014). A total of 160 parturient (Fig. 1), had their data included in the analysis (Hyoscine butyl bromide $n = 80$, Placebo $n = 80$). Six parturient (3 had Caesarean section and 1 had vacuum extraction in the Hyoscine butyl bromide group; 1 had Caesarean section and 1 refused trial drug in the placebo group), were replaced and their data excluded from analysis, giving a total number of recruited participants $n = 166$. Thus the total dropout rate was 6/166 (3.61%), while the dropout rate due to caesarean section was 4/166 (2.41%).

The participants were comparable with respect to baseline obstetric bio-data including antenatal clinic booking status [Table 1].

The mean duration of active phase of labor was significantly shorter in the HBB group (365.11 ± 37.32 min, range = 280–490) than in the control (placebo) group (388.46 ± 51.65 min, range = 280–525), [mean difference 23.35 min, 95% CI -37.43 to -9.27, $P = 0.001$]. However, no significant differences were observed in the durations of the second and third stages of labor (20.46 ± 10.46 vs. 23.38 ± 18.95 min, $P = 0.43$ and 8.96 ± 4.34 vs.

9.23 ± 5.92 min, $P = 0.75$) respectively, between the 2 groups [Table 2].

Further analysis of the 2 major parity groups with respect to behavior and outcome in labor, revealed that this reduction in duration of the active phase of labor between the HBB and placebo groups was much more significant in the multipara ($P = 0.02$) than among primigravidae ($P = 0.04$), not shown in table.

With Oxytocin-augmented labor; although a significant difference in duration of active phase of first stage of labor between the HBB and placebo groups was observed among the multipara ($P = 0.001$), this reduction in duration was not statistically significant between the HBB and placebo groups in primigravidae ($P = 0.32$). HBB was not found to exert any statistically significant difference (compared to placebo) on the mean duration of active phase of non-augmented labor in both primigravidae ($P = 0.07$) and multipara ($P = 0.94$) [Table 3].

The mean estimated blood loss was lower in the HBB compared to placebo group (303 ± 96.52 vs. 368 ± 264.19 ml, mean difference 65.25 ml, 95% CI of -127.36 to -3.14, $P = 0.04$). Significantly more cases of primary postpartum hemorrhage (PPH) occurred in the placebo group compared to the HBB group ($P = 0.03$). The situation

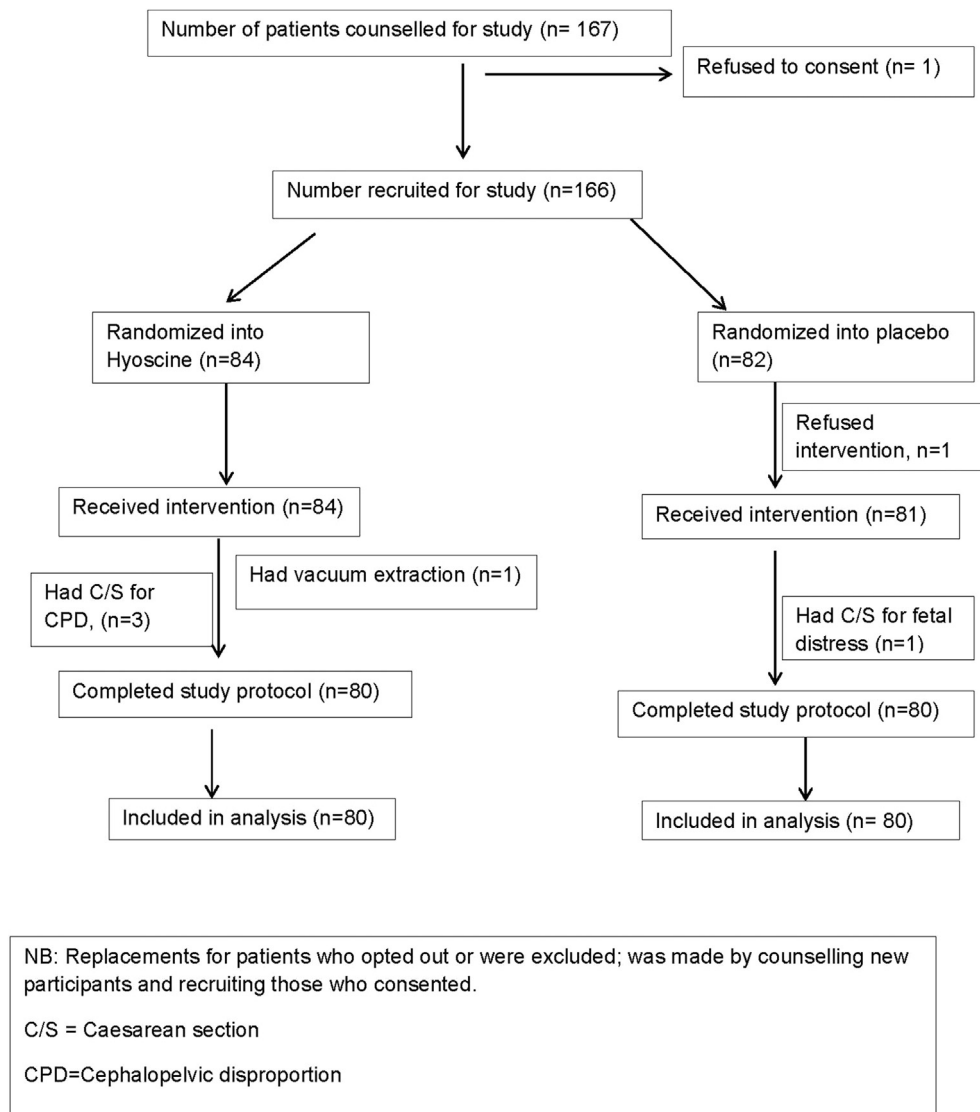


Fig. 1. Consort flow chart.

Table 1
Socio-demographic Characteristics of the participants.

Parameter	Study groups Mean \pm SD (R) ^a		P-value	95% CI	
	HBB ^b	Placebo		Lower	Upper
Mean age (years)	28.03 \pm 4.79 (18–38)	28.33 \pm 5.34 (18–42)	0.71	–1.88	1.28
Median parity	1(2)	1(2)			
BMI (Kg/m ²)	27.49 \pm 3.21 (20.0–33.8)	27.81 \pm 3.55 (21.0–36.9)	0.55	–1.38	0.74
GA (weeks)	38.60 \pm 1.23 (37–41)	38.81 \pm 1.38 (37–41)	0.31	–0.62	0.20
Birth weight (Kg)	3.03 \pm 0.32 (2.3–4.2)	3.11 \pm 0.35 (2.5–4.1)	0.14	–0.19	0.03
ANC ^c Booking					
Yes	69	70	0.82		
No	11	10			

^a Range.^b Hyoscine Butyl-Bromide.^c Ante Natal Clinic.**Table 2**
Mean duration of the different stages of labor between the hyoscine butyl-bromide and the placebo groups.

Stage of Labor	Group	Duration (mins ^a) mean \pm SD	Range	Mean difference	95% CI		P value
					Lower	Upper	
Active phase	HBB	365.11 \pm 37.32	280–490	23.35	–37.43	–9.28	0.001
	Placebo	388.46 \pm 51.65	280–525				
Second stage	HBB	20.46 \pm 10.46	5–48	1.91	6.70	2.87	0.43
	Placebo	22.38 \pm 18.95	5–120				
Third stage	HBB	8.96 \pm 4.34	3–20	0.26	1.88	1.36	0.75
	Placebo	9.23 \pm 5.92	3–38				

^a Minutes.**Table 3**
Mean duration of active phase between the Hyoscine butyl-bromide and the placebo groups, with respect to augmentation of labor.

Type of labor (n ^a)	Study Group (n ^a)	Duration (mins ^b) mean ± SD	Range	Mean difference	95% CI		P value
					Lower	Upper	
Augmented (90)							
Primigravidae (41)	HBB (18)	386.06 ± 37.62	300–490	13.34	−40.36	13.68	0.32
	Placebo (23)	399.39 ± 47.92	320–525				
Multipara (49)	HBB (25)	357.56 ± 31.91	292–401	38.73	−67.09	−10.37	0.01
	Placebo (24)	396.29 ± 60.83	296–524				
Non augmented (70)							
Primigravidae (26)	HBB (14)	368.43 ± 33.31	298–401	29.24	−61.37	2.90	0.07
	Placebo (12)	397.67 ± 43.64	348–490				
Multipara (44)	HBB (23)	358.39 ± 41.64	280–480	1.01	−26.37	24.35	0.94
	Placebo (21)	359.40 ± 40.42	280–450				

^a Number of participants.^b Minutes.

is however different when requirement for blood transfusion is considered; as no significant difference was observed between the 2 study groups ($P = 0.12$) in this regard [Table 4].

The observed mean APGAR scores at 1 min (8.08 ± 1.54 vs. 7.64 ± 1.60 , $P = 0.08$) and 5 min (9.54 ± 1.09 vs. 9.40 ± 1.09 , $P = 0.35$) were also comparable between the HBB and the placebo groups [Table 5].

Dry mouth and tachycardia were the only side effects that occurred in both groups and were attributable to the intervention drugs. No statistically significant difference was found between parturient who received HBB and those received placebo, when comparing these side effects ($P = 0.57$). No ocular, urologic or neurologic manifestations occurred throughout the study.

Discussion

The finding in this study of a shorter duration of the active phase of labor with the use of HBB is in consonance with some earlier

reports [4,5]. Active management protocols have traditionally placed more emphasis on primigravidae and low-parity parturient because of higher rates of dysfunctional labor [18]. This has consequently produced higher and relatively more liberal rates of oxytocin-augmentation of first stage of labor in this group of women, hence the need to deepen the scope of research to address these potential confounders.

In oxytocin-augmented labor, a significant reduction in duration of active phase of the first stage was observed between the HBB and placebo groups among multipara but not among primigravidae. Al-Khishali observed that HBB reduced the duration of first stage of labor among multipara in Iraq, a distinction was however not made between oxytocin augmented labor in that study [19]. In un-augmented labor, HBB did not produce any significant difference in the duration of labor when compared to placebo, among both multipara and primigravidae in the present study. These observations may be due to the fact that slow progress of labor among primigravidae is mostly due to uterine inertia [20] and oxytocin-

Table 4

Estimated blood loss, occurrence of Postpartum Hemorrhage and Blood Transfusion between the Hyoscine butyl-bromide and placebo groups.

Parameter	Group (n ^a)	Mean ± SD	Range	Mean difference	95% CI		P value
					Lower	Upper	
EBL ^b (ml ^c)	HBB (80)	303 ± 96.52	150–780	65.25	–127.36	–3.14	0.04
	Placebo (80)	368 ± 264.19	150–2300				
Hematocrit change (%)	HBB (80)	–1.77 ± 2.04	–10 to 0	0.24	–1.27	2.76	0.50
	Placebo (80)	–2.01 ± 2.35	–11 to 0				
PPH ^d	HBB (80)	Placebo (80)					
Yes (n = 9)	1	8					0.03
No (n = 151)	79	72					
Blood Transfusion	HBB (80)	Placebo (80)					
Yes (n = 4)	0	4					0.12
No (n = 156)	80	76					

^a Number of parturient.^b Estimated Blood Loss.^c Millilitres.^d Post-Partum Hemorrhage.**Table 5**

The neonatal APGAR scores and Occurrence of side effects between the Hyoscine butyl-bromide and placebo groups.

Parameter	Group (n ^a)	Mean ± SD	Range	Mean difference	95% CI		P value
					Lower	Upper	
APGAR at 1 min ^b	HBB (80)	8.08 ± 1.54	3–10	0.44	0.05	0.93	0.08
	Placebo (80)	7.64 ± 1.60	3–10				
APGAR at 5 min ^b	HBB (80)	9.54 ± 1.09	6–10	0.15	–0.15	0.43	0.35
	Placebo (80)	9.40 ± 1.09	6–10				
Side effects (n ^a)	HBB	Placebo			0.55	0.58	0.57
Dry mouth (31)	18	13					
Skin rash (1)	0	1					
Maternal tachycardia (8)	4	4					
Fetal tachycardia (3)	1	2					

^a Number of participants.^b Minutes.

augmentation would invariably correct this dystocia in most primigravid parturient. It is also well established that HBB has no effect on uterine contractions; its actions in labor are mainly on the cervix, as an antispasmodic agent [4]. Thus labor in primigravidae was not significantly affected by HBB; whereas in multipara, dystocia is often due to other issues apart from uterine inertia [21]. One of these issues is probably the thickened cervix or cervical spasm, which may have been worsened or caused by the administered oxytocin in multipara who had augmented labor in the placebo group, but was prevented or relieved by the concomitantly administered intervention in the HBB group. This effect of oxytocin in causing spasm at the level of the cervix and lower uterine segment has also been reported in some studies [9,22]. In consonance with reports from earlier studies, these observations also suggest that routine oxytocin-augmentation for multipara with slow progress may not be justified without considering other factors such as the cervix, fetal malposition and the pelvis [21]. This effect of HBB in significantly reducing the duration of oxytocin-augmented first stage of labor in multipara, can also be considered as a safety mechanism among this group of women; as the duration of myometrial exposure to oxytocin and the oxytocin dose required may be less, thereby reducing the risk of uterine rupture from prolonged exposure to, or higher doses of oxytocin [23].

The durations of the second and third stages of labor were similar in the study groups. This is in agreement with earlier published reports [4,5]. Makvandi et al., using rectally administered HBB was however able to demonstrate a significant reduction in the duration of second stage of labor [16]. HBB reduces spasm at the level of the cervix and the lower uterine segment but has no effect on uterine contractions, that are required for the propulsive phase of the second stage of labor [4,9].

In contrast to earlier reports [5,6,16], significantly less postpartum blood losses were observed in the HBB group compared to placebo. The finding of a significant effect of HBB among multipara who had oxytocin augmentation of labor may be a possible explanation. Oxytocin augmentation, high parity and longer duration of labor (all causing myometrial fatigue) are recognized risk factors for increased postpartum blood loss and PPH [24]. Shorter durations of labor (due to HBB) may be protective. However, the occurrence of primary PPH requiring blood transfusion was similar in both groups.

The neonatal APGAR scores at 1-min and 5-min were comparable in both groups; a finding which is also in agreement with earlier reports [4,16]. There was no significant difference in the occurrence of dry mouth and tachycardia (which are recognized side effects of HBB) [6,7] between the intervention and placebo groups. This is in consonance with earlier reported safety of the HBB in the labor process [5,19]. It is important to note that although all patients with cervical dilatation ≤ 6 cm had Pentazocine analgesia, maternal excitement in labor and pain (especially close to the second stage) may also be causes of tachycardia [6,17,20].

In conclusion, Hyoscine butyl bromide was effective in reducing the duration of active phase of labor, especially in multipara who had oxytocin-augmented labor. It was also associated with significantly less postpartum blood loss. There was however, no significant difference in the durations of the second and the third stages of labor and neonatal APGAR scores. There was also no significant occurrence of adverse drug reaction attributable to HBB administered in the active phase of labor. Thus HBB may be selectively administered, especially to multipara undergoing labor augmentation with oxytocin.

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Conflict of interest

The authors have no conflicts of interest relevant to this article.

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References

- [1] Neilson JP, Lavender T, Quenby S, Wray S. Obstructed labour. *Br Med Bull* 2003;67:191–204.
- [2] Melah GS, El-Nafaty AU, Massa AA, Audu BM. Obstructed labor: a public health problem in Gombe, Gombe state. *Niger J Obstet Gynaecol* 2003;23:369–73.
- [3] Tytgat GN. Hyoscine butylbromide a review of its use in treatment of abdominal cramping and pain. *Drugs* 2007;67:1343–57.
- [4] Aggarwal P, Zutshi V, Batra S. Role of hyoscine N-butyl bromide as labor analgesic. *Indian J Med Sci* 2008;62(5):179–84.
- [5] Samuels LA, Christie L, Roberts-Gittens B, Fletcher H, Frederick J. The effect of hyoscine butylbromide on first stage of labor in term pregnancies. *BJOG* 2007;114(12):1542–6.
- [6] Al Qahtani NH, Al Hajeri F. The effect of hyoscine butylbromide in shortening the first stage of labor: a double blind, randomized, controlled clinical trial. *Ther Clin Risk Manag* 2011;7:495–500.
- [7] Tewari K, Jabeen R, Sabzposh MA, Rabbani T. Comparison of hyoscine-butylbromide and valethamate bromide in shortening the duration of labor. *Indian Med Gaz* 2003;137:15–9.
- [8] Javadi EH, Ghaffari S, Movahed F, Javadi A, Mashrabi O. The effect of adding hyoscine to vaginal misoprostol on shortening the time of abortion induction. *Afr J Pharm Pharmacol* 2013;7(2):46–9.
- [9] Clark SL, Simpson KR, Knox E, Garite TJ. Oxytocin: new perspectives on an old drug. *Am J Obstet Gynecol* 2009;200(1):35.1–6.
- [10] Ehigiegba AE, Adeyemo IS. Uterine rupture in labor: a continuing obstetric challenge in developing countries- the Benin experience. *J Biomed Sci* 2006;5(1):44–50.
- [11] Rowher AC, Khondowe O, Young T. Antispasmodics for labor (review). *The cochrane collaboration*. John Wiley and Sons Ltd; 2013.
- [12] Okonofua FE, Makinde ON, Ayangade SO. Yearly trends in Caesarean section and caesarean morbidity at Ile-Ife, Nigeria. *Trop J Obstet Gynaecol* 1988;1(1):31–5.
- [13] Loto OM, Fadahunsi AA, Kolade CO. Safety and efficacy of misoprostol for induction of labor in a semi-urban hospital setting. *J Obstet Gynecol* 2004;24(6):638–40.
- [14] Orji EO, Fatusi AA, Makinde ON, Adeyemi AB, Onwudiegwu U. Impact of training on the use of partograph on maternal and perinatal outcome in peripheral health centers. *J Turkish-German Gynecol Assoc* 2007;8(2):148–52.
- [15] Eze JN, Okaro JM, Okafor MH. Outcome of pregnancy in the grandmultipara in enugu, Nigeria. *Trop J Obstet Gynaecol* 2006;23:8–11.
- [16] Kirkwood BR, Sterne JAC, editors. *Essential medical statistics*. 2nd ed. Massachusetts: Blackwell Science Ltd; 2003. p. 420.
- [17] International Confederation of Midwives, International Federation of Gynaecology and Obstetrics. Prevention and treatment of postpartum haemorrhage. New advances for low resource settings. Joint statement, Call to Action. ICM/FIGO. 2006. Available at: <http://www.who.int/pmnch/events/2006/figo2006statementeng.pdf>. [Accessed 10 August 2016].
- [18] Sheiner E, Levy A, Feinstein U, Hallak M, Mazor M. Risk factors and outcome of failure to progress during the first stage of labor: a population based study. *Acta Obstet Gynecol Scand* 2002;81:222–6.
- [19] Al-Khishali HA, Rasheed FA, Hussein SA. The effect of 20 mg hyoscine butylbromide on normal labor in Iraqi primi- and multi-gravida women. *J Adv Sci Res* 2012;3(4):70–3.
- [20] Ness A, Goldberg J, Berghella V. Abnormalities of the first and second stages of labor. *Obstet Gynecol Clin N Am* 2005;32:201–20.
- [21] Odendaal HJ. Is the unsafe use of oxytocin in South Africa contributing to our high prevalence of perinatal asphyxia? *Obstet Gynaecol Forum* 2002;12:1.
- [22] Orhue AAE. Induction of labor. *Trop J Obstet Gynaecol* 1997;14(1):1–14.
- [23] Aboyeji AP, Ijaiya MD, Yahaya UR. Ruptured uterus; a study of 100 consecutive cases in Ilorin, Nigeria. *J Obstet Gynaecol Res* 2001;27(6):341–8.
- [24] Selo-Ojeme DO. Primary postpartum hemorrhage. *J Obstet Gynaecol* 2002;22:463–9.