EFFECT OF HYOSCINE BUTYL BROMIDE ON THE DURATION OF ACTIVE PHASE OF LABOUR IN EKITI STATE, NIGERIA; A RANDOMISED CONTROLLED TRIAL

ABSTRACT

Background: Active management of labour is aimed at reducing the duration of labour without adverse effects on the mother and the foetus. The cervix consists majorly of fibrous tissues and smooth muscles with a rich supply of autonomic nerves which may play a role in cervical dilatation. Therefore, efforts are ongoing to explore the possible effect of smooth muscle relaxation property of hyoscine butyl bromide in facilitating cervical dilatation and shortening the active phase of labour.

Objectives: To determine the effect of hyoscine butyl bromide on the duration of active phase of labour in Ekiti State, Nigeria.

Study Design: A randomised, double-blind controlled trial comparing the effect of intravenous hyoscine butyl bromide to placebo on the duration of active phase of labour and it involved two groups namely; parturient who received 20mg intravenous hyoscine butyl bromide and parturient who received 5mls of intravenous normal saline as placebo.

Methodology: A total of 272 parturient who satisfied the inclusion criteria were recruited for the study by systematic sampling. These were equal number of 136 participants each who received 20mg intravenous hyoscine butyl bromide and who received 5mls of intravenous normal saline as placebo. They were matched for gestational age and social status. The results were analysed using SPSS version 24 with appropriate tables and figures generated.

Results: The mean duration of active phase of labour in hyosine butyl bromide group was 270.2±90.6 minutes compared to 303.6±94.5 minutes in placebo group (p value = 0.005). The estimated blood loss between the study and placebo groups who had vaginal delivery were (216.8±92.0 ml versus 210.0±66.4 ml; p value = 0.513) while that of those who had caesarean section were (454.2±109.7 ml versus 523.5±183.8 ml; p value = 0.254). The neonatal outcomes among study and placebo groups relative to 1 minute were (p value = 0.280) and 5 minute (p value = 0.238) APGAR scores. The neonatal admission into intensive care unit for hyosine butyl bromide group babies was 13.2% while that of placebo group babies was 14.7%; p value = 0.726.

Conclusion: Intrapartum administration of intravenous hyoscine butyl bromide to parturient shortens the duration of active phase of labour.

INTRODUCTION

The duration of active phase of labor is a crucial determinant of maternal and foetal outcomes associated with parturition[1]. Importantly, prolonged labour is associated with significant maternal and neonatal morbidity that are not limited to maternal exhaustion, puerperal infections and postpartum haemorrhage[2]. Active management of labour has been shown to be beneficial[3]. It reduces the occurrence of prolonged labour and the duration of labour with little or no adverse effects on the mother and the foetus[2]. Among the interventions in active management of labour are use of analgesics, oxytocics, and smooth muscle relaxants[4].

Hyoscine N-butyl-bromide (HBB); a derivative of hyoscine is an extract from the leaves of Dubosia tree found majorly in Australia[5]. It has found its use in the treatment of dysmenorrhoea, pelvic spasm (e.g during hysterosalpingography), abdominal cramps and motion sickness for over 50 years[4,6,7]. HBB relieves spasm in the smooth muscles of gastrointestinal, biliary and urinary tracts and as well female genital organs, especially the cervix and lower uterine segment[4]. It acts by inhibiting cholinergic neuro transmission in the abdominal and pelvic parasympathetic ganglia. This property may enhance cervical dilatation and effacement. It however does not affect uterine contractions because uterine contractions originate from the cornual end of the uterus[4].

Hyoscine butyl bromide (HBB) belongs to the parasympatholytic group of drugs and is a semi-synthetic derivative of scopolamine. It is an effective antispasmodic drug without the deleterious side effects of atropine[8]. Due to the quaternary ammonium structure, hyoscine butyl bromide does not cross the blood-brain barrier; hence, it is not associated with central nervous system side effects that are occasionally seen with other hyoscine compounds like atropine and hyoscine (scopolamine)[8]. This may be responsible for less frequency and severity of side effects on sweat glands, salivary glands, eyes and the heart when HBB is compared to atropine at therapeutic doses[4,9]. It has been used to shorten the duration and reduce the blood loss of medically induced abortion[10].

Interventions to make duration of labour shorter have continually generated interest among Obstetricians with debate on the benefit of antispasmodics still unsettled, as literature is replete with conflicting reports from studies; hence, consensus has not been reached on its role in active management of labour. Several clinical trials have described the effects of HBB on labour progress and some reported that the mean duration of the first stage of labour was significantly shorter in

HBB group than that in the placebo group[6,11-16]. Other studies have shown conflicting results[17,18]. Trevino et al and Barau et al. found no significant differences in the mean duration of active phase of labour between HBB and placebo groups[17,18]. In addition, most of the available studies were conducted outside Africa and this actually shows a knowledge gap which this study will provide answer to. The resolution of this conundrum is more important in sub-Saharan Africa, where prolonged and obstructed labour are still major contributors to maternal morbidity and mortality[19]. This study aims to determine the effect of hyoscine butyl bromide on the duration of active phase of labour in Ekiti State, Nigeria.

METHODOLOGY

Study Area: The study was conducted in the Departments of Obstetrics and Gynaecology of Federal Teaching Hospital, Ido Ekiti and the State Specialist Hospital, Ikole Ekiti both in Ekiti State, Nigeria. These are referral centers for primary and secondary health centres in Ekiti State and the neigbouring States. Antenatal booking records of the two hospitals showed a total of 7,295 patients annually and average delivery rate of 6,544 per year.

Study Population: The study population were pregnant women at term gestation who satisfied the inclusion criteria and were admitted in active phase of labour at the study area.

Inclusion Criteria: Pregnant women in active phase of labour with singleton pregnancy at ≥ 37 weeks gestational age, cephalic presenting fetus and normal fetal heart rate.

Study Design: The study was a randomised, double-blind controlled trial comparing the effect of intravenous hyoscine butyl bromide to placebo on the duration of active phase of labour and it involved two groups namely; parturient who received 20mg intravenous hyoscine butyl bromide and parturient who received 5mls of intravenous normal saline as placebo.

Study Tool: The study tool was data collection sheets.

Sample Size: The sample size was 272 comprising 136 eligible participants who received 20mg intravenous hyoscine butyl bromide and 136 eligible participants who received 5mls of intravenous normal saline as placebo. It was determined by a previously validated formula for randomised controlled trial[20].

Sampling Technique: The sampling method was systematic sampling. First, pregnant women were screened to determine those who satisfied the inclusion criteria. Second, the eligible participants were randomized using a computer generated random numbers.

Randomissation and Blinding: The Pharmacy unit that is attached to the maternity complex of the Federal Teaching Hospital, Ido-Ekiti and that of State Specialist Hospital, Ikole Ekiti were involved in the double-blinding. This was to ensure that both the primary care givers and the patients were not able to differentiate the content of each ampoule. The Pharmacists that were involved in this study were trained in the blinding procedure.

Study number and groups were predetermined. Random numbers were generated from 1 to 272 using computer generated random numbers to cover the entire sample size of 272. Study groups allocation was done using blocks of four to assign patients into study groups A or B. The groups were sequentially matched with the generated random numbers from serial number 1-272. This yielded 136 participants in each group. The control group received placebo while the study group received 20mg hyoscine butyl bromide. Allocated groups were placed in consecutively numbered and sealed opaque envelopes.

Two hundred and seventy-two units of the research drugs i.e., 272 ampoules of 1ml (10mg) hyoscine butyl bromide and 272 ampoules 1ml each of sterile normal saline injection with similar appearance, equal volume and in similar glass bottles were supplied to the pharmacy unit to cover the study population of 272 parturient. The bottle labels were masked with masking tapes by the pharmacist so that research assistants would not be able to read the labels on the drugs. Also, two 5ml syringes and needles were packed alongside the research drugs inside each of the serially numbered envelopes and were labeled as either drug A or drug B; A being the study drug and B being the placebo. Serially numbered stickers from 1 to 272 were affixed to each of the drug envelopes.

Since parturient in Federal Teaching Hospital, Ido-Ekiti accounted for 42% of study population in year 2019, 42% (114) of the hyoscine butyl bromide and placebo were retained at Federal Teaching Hospital, Ido-Ekiti, while 58% (158) of it were used at State Specialist Hospital, Ikole Ekiti. One hundred and fourteen drug envelopes; i.e, envelope numbered one to 57 containing hyoscine butyl bromide and normal saline were retained in Federal Teaching Hospital, Ido-Ekiti, while the remaining 158; i.e, envelope numbered 58 to 136 of both hyoscine butyl bromide and

normal saline were used at State Specialist Hospital, Ikole Ekiti and were delivered to their Pharmacy department for onward use.

Patients Recruitment: Having obtained informed consent to participate in the study from eligible participants the antenatal records for booked participants were reviewed for co-existing medical conditions and history of the index pregnancy, while the conditions were determined during clerking of the unbooked patients. Gestational ages of participants who were sure of their last menstrual period were calculated from it; thereafter, a first trimester ultrasound scan was reviewed when available to ascertain the estimated gestational age. History taking, physical examination and routine investigations were carried out as part of protocol in the labour ward unit. All patients were questioned about the presence or absence of adverse reactions related to the use of the medications.

All participants had clinical obstetric examination to exclude the presence of any exclusion criteria immediately before commitment to the treatment allocation. Initial vaginal examination was done by the research assistant in the labour ward to ascertain that the cervix was between 4cm and 9cm dilated. Intravenous hyoscine butyl bromide (20mg statum) or sterile normal saline injection was administered to all parturient who fulfilled the study criteria at admission and their cervical status were assessed four hourly. Management of the labour followed the departmental protocol using a partograph and parturient who required augmentation of labour had it as per departmental protocol. The findings were documented and transferred to the data collection sheet. The research assistants were four residents doctors who were trained about the study protocol (such as the contents of the information sheet, consent form, data collection sheet and also sample collection) daily for one week before commencement of the study. Duration of active phase of labour is the period between admission into the labour ward (when cervix is at least 4cm dilated) and when the cervix becomes fully dilated.

Data Collection: Informed consent was obtained from each participants and the antenatal records for booked participants and history of the index pregnancy were reviewed, while similar information were determined during clerking of the unbooked patients. Gestational ages of participants who were sure of their last menstrual period were calculated from it; thereafter, a first trimester ultrasound scan was reviewed when available to ascertain the estimated gestational age. History taking, physical examination and routine investigations were carried out as part of protocol

in the labour ward unit. All participants had clinical obstetric examination and initial vaginal examination was done by the research assistant in the labour ward to ascertain that the cervix was between 4cm and 9cm dilated. Intravenous hyoscine butyl bromide (20mg statum) or sterile normal saline injection was administered to all parturient at admission and their cervical status were assessed four hourly. Management of the labour followed the departmental protocol using a partograph and parturient who required augmentation of labour had it as per departmental protocol. All the findings including labour and postpartum events were documented and transferred to the data collection sheets.

Data Analysis: The data were analyzed using the Statistical Package for Social Sciences (SPSS) software version 24. Categorical variables were expressed as absolute numbers and percentages and the differences in means analyzed using the Chi square test or Fisher exact test as appropriate, while continuous variables were presented as means with standard deviations and the differences analysed with the Student *t* test. The level of significance was set at $p \leq 0.05$. Results were presented using tables and figures.

Ethical Consideration: An institutional approval for this study were obtained from the Ethical Review Committees of Federal Teaching Hospital, Ido-Ekiti and State Specialist Hospital, Ikole Ekiti. Informed written consent was obtained from each participant after adequate counselling and the data obtained from the study were treated with confidentiality and used solely for the purpose of the study.

RESULTS

Table 1: Socio-demographic characteristics of the participants

Variable	**HBB group n (%) N = 136**	**Placebo group n (%) N = 136**	**Chi-square**	**p - value**
Age			4.017	0.260
20-24	28 (20.6)	29 (21.3)		
25-29	52 (38.2)	45 (33.1)		
30-34	46 (33.8)	42 (30.9)		
35-39	10 (7.4)	20 (14.7)		
Mean age ± SD	*28.5 ± 4.3*	*29.0 ± 4.7*	*-0.933*[t]	*0.352*
Religion			1.563	0.458
Christianity	112 (82.4)	108 (79.4)		
Islam	23 (16.9)	28 (20.6)		
Traditional	1 (0.7)	0 (0.0)		
Educational status			1.990	0.575
None	1 (0.7)	0 (0.0)		
Primary	13 (9.6)	10 (7.4)		
Secondary	54 (39.7)	50 (36.8)		
Tertiary	68 (50.0)	76 (55.9)		
Occupation			2.613	0.624
Civil servant	56 (41.2)	58 (42.6)		
Farming	19 (14.0)	24 (17.6)		
Trading	34 (25.0)	24 (17.6)		
Housewife	12 (8.8)	12 (8.8)		
Artisan	15 (11.0)	18 (13.2)		
Parity				
Primiparous	58 (42.6)	44 (32.4)	3.075	0.080
Multiparous	78 (57.4)	92 (67.6)		
Booking status			0.952	0.329
Booked	129 (94.9)	125 (91.9)		
Unbooked	7 (5.1)	11 (8.1)		
Mean GA in weeks ± SD	*39.0 ± 1.3*	*38.5 ± 3.5*		

HBB- Hyoscine butyl bromide; t - Students' t-test

Table 1 showed the socio-demographic characteristics of participants in both study groups. The largest age group for both groups was 25-29 years which accounts for 34.8% (52) in HBB group and 33.1% (45) in placebo group. The mean age of women that received HBB was 28.5 ± 4.3 years, while the mean age for those that received placebo was 25 ± 4.7 years (p value = 0.352); showing no statistically significant difference in the ages between the two groups. There was no statistically significant difference in terms of parity of participants. In the HBB group, 58 (42.6%) of participants were primiparous and seventy-eight (57.4%) were multiparous; while in the placebo group, 44 (32.4%) were primiparous and 92 (67.6%) were multiparous, (p value = 0.080). Difference in the booking status was not significant as 129 (94.9%) and 125 (91.9%) of parturient in both groups were booked, (p value = 0.329). The mean gestational age of participants was 39

± 1.3 weeks in HBB group and 38.5 ± 3.5 weeks in the placebo group. The differences in the socio-demographic parameters were not statistically significant as p values for all the variables were > 0.05.

Table 2: Comparism of mean duration of labour among the two groups

Variable	HBB group	Placebo group	t test	p-value
Active phase (min)	**n=124**	**n=119**		
Mean ± SD	*270.2 ± +90.6*	*303.6 ± 94.5*	*-2.810*	***0.005***
Presenting cervical dilatation				
4 - 5cm	n = 98	n = 82		
(Mean ± SD)	*296.0 ± 72.2*	*350.4 ± 64.2*	*-5.298*	***<0.001***
6 - 7cm	n = 23	n = 32		
(Mean ± SD)	186.7 ± *84.3*	212.9 ± *55.5*	-1.395	0.169
8 - 9cm	n = 3	n = 5		
(Mean ± SD)	69.0 ± *0.0*	115.0 ± *32.2*	-2.395	0.054
Second stage (min)	**n=124**	**n=119**		
Mean ± SD	*19.0 ± 6.4*	*20.9 ± 8.9*	*-1.978*	***0.049***
Third stage (min)	**n=124**	**n=119**		
Mean ± SD	*6.4 ± 2.8*	*7.2 ± 6.4*	*-1.172*	*0.242*

Table 2 compared the mean duration of labour among the HBB and placebo groups. The mean duration of active phase of labour in HBB group was 270.2 ± 90.6 minutes, while in control group was 303.6 ± 94.5 minutes; t = 2.810, (p value = 0.005) which was statistically significant. A sub-categorization of the mean duration of active phase of labour relative to the cervical dilatation showed a significance for women at 4 - 5 cm cervical dilatation with mean duration of 296.0 ± 72.2 minutes for HBB and 350.4 ± 64.2 minutes for placebo group with (p value < 0.001). The difference in duration of active phase of labour in parturient who presented during 6 – 7 cm and 8 – 9 cm cervical dilatation was not statistically significant, (p values = 0.169 and 0.054) respectively. The mean duration of second stage of labour in HBB group was 19.0 ± 6.4 minutes and 20.9 ± 8.9 minutes for placebo group; t = 1.978, (p value = 0.049). The difference in mean duration of second stage of labour was statistically significant. The mean duration of third stage of labour in HBB group was 6.4 ± 2.8 minutes and 7.2 ± 6.4 minutes for the placebo group; t = 1.172, (p value = 0.242), the difference was not statistically significant.

Table 3: The mean duration of active phase compared between HBB and placebo groups with respect to augmentation of labour.

Type of labour	Study Group (n)	Duration (mins) Mean±SD	t test	p value
Augmented	**HBB (n = 32)**	**327.2 ± 84.7**		
			0.475	**0.636**
	Placebo (n = 38)	**317.1 ± 91.3**		
Primipara	HBB (n = 19)	349.8 ± 95.4	-0.768	0.448
	Placebo (n = 13)	373.1 ± 63.9		
Multipara	HBB (n = 13)	294.1 ± 53.8	0.223	0.825
	Placebo (n = 25)	288.0 ± 90.7		
Non-augmented	**HBB (n = 92)**	**250.4 ± 84.3**	**-3.418**	**0.001**
	Placebo (n = 81)	**297.2 ± 95.9**		
Primipara	HBB (n = 36)	255.2 ± 50.7	-5.093	**<0.001**
	Placebo (n = 28)	341.6 ± 84.2		
Multipara	HBB (n = 56)	247.3 ± 100.5	-1.417	0.157
	Placebo (n = 53)	273.8 ± 94.1		

Table 3 compared the mean duration of active phase of labour in the two groups with need for augmentation of labour. In the group that had augmentation of labour, the mean duration of active phase was 327.2 ± 84.7 minutes in HBB group and 317.1 ± 91.3 minutes in the placebo group. The difference in this duration was not statistically significant, (p value = 0.636).

In the group that did not have augmentation of labour, the mean duration of labour was 250.4 ± 84.3 minutes among the HBB group and 297.2 ± 95.9 minutes among the placebo group. This difference was statistically significant, (p value = 0.001). This significance was attributable to the primiparous women (HBB group lasted 255.2 ± 50.7 minutes and placebo group lasted 341.6 ± 84.2 minutes, p value < 0.001).

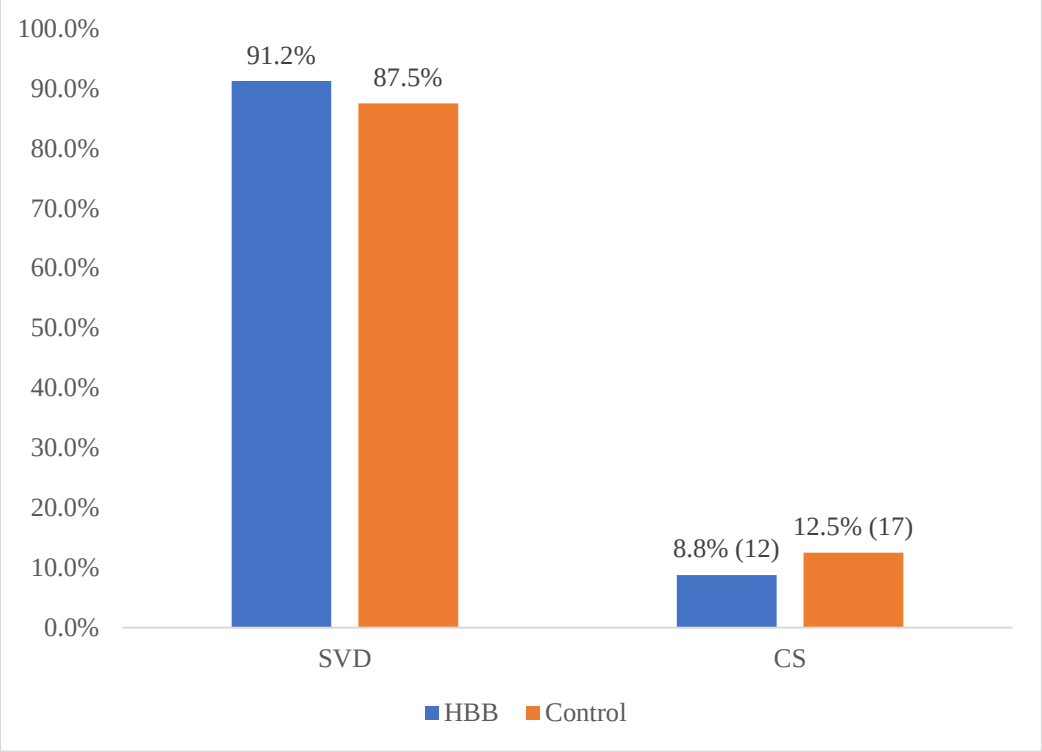

Figure 1: Route of Delivery (χ^2 = 0.965, p=0.326)

Figure 1 compares the mode of delivery between HBB and placebo groups. In the HBB group, 91.2% of participants had vaginal deliveries, while 8.8% had Caesarean section. In the placebo group, 87.5% of participants had vaginal deliveries, while 12.5% had Caesarean section. These differences were not statistically significant, (p value = 0.326).

Table 4: Indications for Caesarean Section compared between HBB and placebo groups

Variable	**HBB (Group A)**	**Placebo (Group B)**		
	n (%)	**n (%)**	**Chi**	**p-value**
	n = 12	**n = 17**	**square**	
Indications for Caesarean Section				
Suspected foetal distress	5 (41.7)	7 (41.2)	2.318	0.677
Cephalopelvic disproportion	4 (33.3)	5 (29.4)		
Abruptio placenta	2 (16.7)	1 (5.9)		
Maternal request	0 (0.0)	2 (11.8)		
Cervical dystocia	1 (8.3)	2 (11.8)		

Table 4 showed indications for Caesarean section among the parturient. Twenty-nine parturient (10.7% of the study population) had Caesarean section; 12 (8.8% of the HBB group) and 17 (12.5% in the placebo group). In the HBB group, 4.7% of the Caesarean sections done were on account of suspected foetal distress; 33.3% were on account of cephalopelvic disproportion, 6.7% on account of abruptio placenta, while the remining 8.3% were on account of cervical dystocia.

In the placebo group, 4.2% of the Caesarean sections were on account of suspected foetal distress, 29.4 % were on account of cephalopelvic disproportion, 5.9% were on account of abruptio placenta, 11.8% were on account of maternal request and the remining 11.8% were on account of cervical dystocia. There was no statistically significant difference in terms of indications for Caesarean section (p value = 0.677).

Table 5: Mean Estimated Blood Loss compared between HBB and placebo groups with respect to mode of delivery

Mode of delivery	Study Groups (n)	EBL (ml) Mean±SD	t test	p value
SVD				
	HBB (n = 124)	216.8 ± 92.0	0.656	0.513
	Placebo (n = 119)	210.0 ± 66.4		
Primipara	HBB (n = 55)	209.5 ± 85.7	0.785	0.434
	Placebo (n = 41)	197.6 ± 52.4		
Multipara	HBB (n = 69)	222.6 ± 97.0	0.434	0.655
	Placebo (n = 78)	216 ± 72.1		
Caesarean Section				
	HBB (n = 12)	454.2 ± 109.7	-1.165	0.254
	Placebo (n = 17)	523.5 ± 183.8		
Primipara	HBB (n = 3)	483.3 ± 76.4	-1.768	0.152
	Placebo (n = 3)	566.7 ± 28.9		
Multipara	HBB (n = 9)	444.4 ± 121.0	-0.930	0.363
	Placebo (n = 14)	514.3 ± 202.3		

Table 5 compared the mean estimated blood loss in HBB and placebo groups with respect to mode of delivery. In the group that had vaginal delivery, the mean estimated blood loss in the HBB group was 216.8 ± 92.0 mls, while it was 210.0 ± 66.4 mls in the placebo group. This difference was not statistically significant (p value = 0.513). Analysis along parity was done, and the difference in the means were also not statistically significant. Among the group that has Caesarean section, the mean estimated blood loss in the HBB group was 454.2 ± 109.7 mls, while it was 523.5 ± 183.8

mls in the placebo group. The difference in means was not statistically significant, (p value = 0.254). Analysis along parity was done, and it showed that mean blood loss was not significantly affected by parity.

Table 6: Mean Change in packed cell volume compared between HBB and placebo groups with respect to mode of delivery

Mode of delivery	Study Groups (n)	Change in PCV (%) Mean±SD	t test	p value
SVD				
	HBB (n = 124)	1.42 ± 0.94	0.032	0.974
	Placebo (n = 118)	1.42 ± 1.03		
Primipara	HBB (n = 55)	1.65 ± 0.87	-0.877	0.383
	Placebo (n = 41)	1.80 ± 0.78		
Multipara	HBB (n = 69)	1.23 ± 0.96	0.141	0.888
	Placebo (n = 77)	1.21 ± 1.09		
Caesarean Section	HBB (n = 10)	2.30 ± 1.42	-0.571	0.573
	Placebo (n = 16)	2.63 ± 1.41		
Primipara	HBB (n = 2)	2.50 ± 0.71	-1.414	0.293
	Placebo (n = 2)	3.50 ± 0.70		
Multipara	HBB (n = 8)	2.25 ± 1.58	-1.414	0.293
	Placebo (n = 14)	2.50 ± 1.45		

Table 6 showed the mean difference in packed cell volume between HBB and placebo groups with respect to mode of delivery. Among the group that had vaginal delivery, mean change in packed

cell volume was 1.42 ± 0.94 % in the HBB group, while it was 1.42 ± 1.05 % in the placebo group; (p value = 0.974). Parity of the parturient did not significantly impact change in packed cell volume. In the group that had vaginal delivery, the mean change in packed cell volume was 2.30 ± 1.42 % in the HBB group, while it was 2.63 ± 1.41 % in the placebo group. These differences were not statistically significant (p value = 0.573). Parity of parturient did not significantly affect change in packed cell volume.

Table 7: Neonatal outcome among study participants

Variable	**HBB group N = 136 Median**	**Placebo group N = 136 Median**	**MWU**	**p-value**
APGAR scores				
1st minute	8	8	8589.500	0.280
5th minute	9	9	8546.000	0.238
10th minute	**n = 7**	**n = 5**		
	8	8	14.000	0.237
NICU	**n (%)**	**n (%)**	χ^2	**p-value**
Admitted	18 (13.2)	20 (14.7)	0.122	0.726
Not admitted	118 (86.8)	113 (85.3)		
Indication for admission	**n = 18**	**n = 20**		
Mild birth asphyxia	3 (16.7)	6 (30.0)	6.735	0.151
Moderate birth asphyxia	6 (33.3)	1 (5.0)		
Neonatal hypoglycemia	2 (11.1)	2 (10.0)		
Presumed sepsis	7 (38.9)	9 (45.0)		
Respiratory distress syndrome	0 (0.0)	2 (10.0)		

Mann-Whitney U Test

Table 7 compared neonatal outcome between HBB and placebo groups. Among the neonates in the HBB group, the median APGAR score was 8 at first minute, 9 at fifth minute. Seven of the newborns required resuscitation up till 10th minute, with the median APGAR score of 8 at 10

minutes. Among the neonates in the placebo group, the median APGAR score was 8 at first minute, 9 at fifth minute, while five of them needed resuscitation till 10th minute; with the median APGAR score of 8 at 10 minutes. The differences in their APGAR scores were not statistically significant as p values were > 0.05.

In the HBB group, 18 (13.2%) of the newborns were admitted into the neonatal intensive care units, while 118 (86.8%) did not require admission. In the placebo group, 23 (16.9%) of the neonates required admission, while the remaining 113 (83.1%) did not require admission. The difference in need for admission into the neonatal intensive care unit was not statistically significant (p value = 0.726).

DISCUSSION

The participants in this study were comparable in terms of age, gestational age and parity across both groups. This showed that the randomisation process was effective in selecting comparable participants in each group thereby eliminating bias in the selection process as expected in a randomisation process. Therefore, the possible interference of difference in socio-demographic factors as a confounding variable was not significant.

This study showed that hyoscine butyl bromide significantly reduces the mean duration of active phase of labour; the difference in duration of active phase of labour between the two study groups being 33 minutes. It also demonstrated a significant reduction in the duration of second stage of labour, amounting to 1.9 minutes. However, there was no statistically significant difference in the duration of third stage of labour. These findings are due to the fact that HBB reduces spasm at the level of the uterine cervix and the lower uterine segment, but it has no effect on uterine contractions that are required for the propulsive phase of the second stage of labor[4,21]. The effect hyoscine butyl bromide has on the durations of the first and second stages of labour was similar to the findings of Sekhavat et al[22], who found a 74 minute reduction in the duration of active phase of labour between the two groups. This similarity may be because both studies shared similar designs. The magnitude of reduction in the duration of active phase in their study on the other hand was much more than this present study; this may be because their subjects were all multipara and are expected to have shorter labour durations, unlike this present study that enrolled both multipara and primipara. Effect of hyoscine butyl bromide on the active phase of labour appears to be most useful in parturient that had the drug between 4 - 5 cm cervical dilatation as opposed to ones that presented

after 5 cm cervical dilatation, in whom there was no significant difference in the mean durations of their active phase. This finding could not be corroborated with the reviewed literatures, as investigators analysed active phase of labour together, irrespective of cervical dilatation at enrolment into the study.

Hyoscine butyl bromide shortened the duration of active phase of labour in both primipara and multipara in this study though the difference was not statistically significant. This finding was similar to that of Imaralu et al[14] and Ibrahim et al[20]. Though these two studies were double and single blinded respectively, their findings were consistent with the theory that hyoscine butyl bromide acts primarily as a cervical antispasmodic agent, and does not impact on uterine contractions. However, this finding was in contrast to that of Al-Khishali et al[23], who reported that HBB shortens the duration of first stage of labour in multiparous women more than in primiparous. Factors that may be responsible for this sharp contrast in findings could be because of racial and geographical differences. While this present study shared racial and geographical similarities with those of Imaralu et al and Ibrahim et al, Al-Khishali was Iraqi in origin.

It was observed in this study that augmentation of labour blunts the effect of HBB on duration of active phase of labour, as there was no significant difference between the HBB and placebo groups that had augmentation of labour. However, its effect on duration of active phase of labour in parturient who did not have augmentation of labour was significant. Sub-categorisation of the augmented group into primiparous and multiparous revealed that this statistical significance was attributable to the primiparous women. Hence, HBB appeared particularly useful in primiparous women with adequate uterine contractions. This could probably be because the sub-set of primiparous women in this study that had uterine inertia had been managed effectively by augmentation of labour, leaving the ones with purely cervical spasm of the sub-set benefitting from the HBB administration. This finding was similar to that of Imaralu et al[14]. The duration of labour in their work was similarly shorter in parturient that did not require augmentation of labour, but they reported that the statistical significance was in favour of multiparous as opposed to the finding in the present study. On the other hand, Mohaghegh and co-workers[24] in their systematic review concluded that there was no significant difference between those who had augmentation of labour and those that did not. Factors responsible for these divergent findings could not be ascertained; but it could be because this study and the one by Imaralu et al were both hospital-based and the

subjects were blacks, as opposed to the systematic review by Mohaghegh et al who had a global review of randomised clinical trials on the topic.

There was no statistically significant difference in the mode of deliveries between hyoscine butyl bromide and placebo groups. This demonstrates that HBB does not increase the rate of Caesarean section, and the finding was similar to that of Qahtani et al[25] and Mohaghegh et al[24].

In agreement with other reports[6,7,17], there was no statistically significant difference in the estimated blood loss between the HBB and placebo groups. It showed that the smooth muscle relaxing action of HBB does not affect contractility of the myometrium. However, Imaralu et al[14] had contrasting finding. In their study, they found that mean estimated blood loss was lower in the HBB group compared to the placebo group by as much as 63 mls. This difference could be due to the fact that they used gravimetric method to estimate blood loss post-partum, but this present work used clinical method for its estimation. Gravimetric method could be more accurate in blood estimation, but contribution of liquor to the weight of the under-pads could be a confounding factor to gravimetric method.

Hyoscine butyl bromide did not affect the packed cell volume of the participants significantly. The mean differences in post-delivery packed cell volume were similar across the two groups. Parity and route of delivery were also shown not to have significant impact in packed cell volume of the parturient. This finding further corroborates the earlier result which showed that there was no significant difference in the estimated blood loss and further confirms that HBB does not cause post-partum haemorrhage. These findings are comparable with those of other researchers[6,7,17]; though Imaralu et al[14] had a different finding.

Requirement for blood transfusion across the two groups was similar. Out of the four parturient that had PPH in the HBB group, two needed to be transfused with blood. In the same vein, out of eight parturient in the control group that had PPH, only three were transfused with blood. This finding agreed with other similar studies[14,26].

Hyoscine butyl bromide did not affect the immediate neonatal outcome in this study. The median Apgar score at first and fifth and tenth minutes were the same in both groups. There was no difference in the neonatal admission in the intensive care unit in both groups. The number and

indications for neonatal admissions in both groups were comparable. Different studies have shown no difference in neonatal outcome between HBB and placebo groups[14,17,25].

CONCLUSION: Intrapartum administration of intravenous hyoscine butyl bromide to parturient shortens the duration of active phase of labour.

RECOMMENDATIONS

1. Administration of intravenous hyoscine butyl bromide to all pregnant women in active phase of labour is recommended in order to reduce the incidence of prolonged labour and its attending complications.
2. A larger multi-centre study on the subject matter is recommended to fully justify the findings in this study.

Disclaimer (Artificial intelligence)

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Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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Details of the AI usage are given below:

1.

2.

3.

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