EFFECT OF HYOSINE NEBUTYLBROMIDE IN THE DURATION OF LABOUR IN TERM PREGNANCIES IN NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL NNEWI SOUTH EAST NIGERIA

A

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BY

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I attest that I will supervise this project.

Thanks

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Abstract

Background: labour is ideally a joyous experience but can be associated with fetomaternal complications when prolonged thus any safe measure to prevent prolonged labour is a well development for both the parturients and care givers.

Objectives: To evaluate the effect of hyoscine n-butyl bromide (HBB) on the duration of the first stage of labour in term pregnancies in NAUTH Nnewi.

Methods: This is a double blind randomized trial involving 124 parturients who presented to the Labour ward of Nnamdi Azikiwe university teaching hospital at term in active phase of labour. They were randomly given an intramuscular injection of either 40mg of HBB or 2mls of water for injection as a placebo. The effect of HBB on duration of the stages of labour, maternal and neonatal complications were then evaluated.

Results: The mean duration of the first stage of labour was noted to be shorter in HBB group for both the primigravidas (246.56±21.86 against 391.81±56.57 minutes for control) and for multiparous (205.88±17.80 against 323.83±15.99 for control). There were no significant change in the duration of second and third stages of labour for classes of parturients in both groups. There no significant changes in the mode of delivery or in maternal or neonatal outcome in both groups of parturients. Conclusions: Hyoscine n-butyl bromide is effective in reducing the first stage of labour without adverse maternal or neonatal outcome.
CHAPTER ONE

INTRODUCTION

Labour is characterised by the onset of painful, regular uterine contractions of progressively increasing frequency and intensity associated with progressive cervical effacement and dilatation with the descent of the presenting part leading to delivery of the fetus and placenta per vaginam. Ideally this is a joyous experience but may sometime turn sour when prolonged.

Prolonged labour is said to occur when the spontaneous active phase of first stage of labour (which is from cervical dilatation of greater than or equal to 4cm) exceeds the duration of over 12 hours for all parturient at term irrespective of age parity or race, this is due to the rate of cervical dilatation of slower than normal 1cm per hour and is associated with maternal and fetal morbidity and mortality from maternal exhaustion, post partum hemorrhage, sepsis, fetal asphyxia and fetal distress. Therefore any obstetrics measure to shorten the duration of labour without jeopardizing fetomaternal status is warranted.

The progress of labour is assessed by checking for uterine contraction which is normally about 3 contractions in ten minutes, progressive effacement and dilatation of cervix (which is at the rate of 1cm per hour when normal) and the descent of the presenting part. Thus cervical dilatation is one of the determinants of the duration of labour. Many factors may affect the rate of cervical dilatation. These factors include initial state of the cervix, parity, cephalopelvic disproportions and the intensity of the uterine contractions. Therefore facilitating cervical dilatation will invariably shorten the progress of labour.

Cervical ripening expressed as a remodeling of the cervical connective tissue has been proven to be necessary for an uncomplicated vaginal delivery. Recent
biochemical evidence also suggests that the cervix could obstruct labour by a sustained spasm due to insufficient connective tissue remodeling. While various immunohistochemical studies concentrate upon collagen type remodeling and stabilization, it is a known fact that up to 1015% of the non pregnant cervices is constituted by smooth muscles fibres. Studies have also shown that besides a decrease in fibrous connective tissue in the cervix at term, there is an increase in the proportions of smooth muscle fibers which also become dissociated and hypertrophic and are aligned in a particular direction.

These studies relating to the presence of smooth muscles in the cervix logically support the use of antispasmodics and smooth muscle relaxants in helping the cervix to dilate. Hyoscine butyl bromide is a smooth muscle relaxant with unique mechanism of action. It is a spasmolytic drug that acts by competitive antagonism to acetyl choline at post ganglionic parasympathetic nerve ending. It is adduced to reduce the duration of labour by accelerating cervical dilatation without major side effects. However various other methods have been used to reduce the duration of labour like amniotomy, intravaginal administration of relaxin, cervilaxin in conjunction with oxytocin, drotavarine hydrochloride, valethemate bromide and hyoscine butyl bromide (HBB).

HBB belongs to the anticholinergic group of drugs and is a semi-synthetic derivative of scopolamine. It inhibits the muscarinic action of acetyl choline on structures innervated by post-ganglionic cholinergic nerve as well as on smooth muscles that responds to acetyl choline but lack cholinergic innervations. Therefore, it has spasmolytic actions on smooth muscles organs but the uterus is not affected. It is hypothesized that Hyoscine-Nbutyl bromide reduces the duration of the first stage of labour by overcoming cervical spasm and promoting cervical dilatation. Based
on these intrinsic characteristics of HBB, It remains an antispasmodic widely used in labour rooms to hasten cervical dilatation and has been shown to be effective in reducing duration of first stage labour without any associated apparent adverse maternal or neonatal outcome\textsuperscript{11}. Thus, its antispasmodic property could be an effective intervention and treatment strategy in obstetrics practice in decreasing the incidence of prolonged labour\textsuperscript{2}.

HBB is marketed under the trade name buscopan\textsuperscript{14} and is on the World Health Organisation (WHO) list of essential medicines\textsuperscript{15}.

Several studies have reported on the use of hyoscine-n-butyl bromide given during labour to reduce or prevent pain and to prevent prolonged labour, with results ranging from being very beneficial and safe\textsuperscript{3,11} to conferring some harmful effect or no benefit\textsuperscript{12}. Some of the studies have argued that Buscopan crosses the placenta and may cause fetal tachycardia, however the fetus apparently is not affected and fetal respiration is not depressed\textsuperscript{16}. One study argued that it causes depression of the central nervous system of the neonate if given before the onset of labour and also contribute to neonatal haemorrhage due to reduction in vitamin k dependent clotting factor in the neonate\textsuperscript{17} however majority of the studies did not find any adverse fetal outcome\textsuperscript{3,11,13}.

To the best of my knowledge, no study on the effects of Buscopan in labour has been published in Nigeria. The aim of this study is to determine the effect of Buscopan on duration of labour and on fetal as well as maternal outcome in Nnamdi Azikiwe University Teaching Hospital, Nnewi, Southeast Nigeria.
CHAPTER TWO
LITERATURE REVIEW

The simplest objective of every pregnancy remains the safe delivery of a healthy baby to a healthy mother but this simple objectives may not be achieved in cases of prolonged labour due to the fetomaternal complications associated with it\(^1\). The uterine contractions in labour may induce painful distress in the mother and may also lead to reduction in placental blood flow which in combination with head compression can lead to hypoxia\(^1\). This is usually tolerated by the uncompromised fetus but in the cases of prolonged labour, these changes will induce distress in the fetus, so to reduce this scourge of obstetrics practice, active management of labour (a policy to reduce rate of prolonged labour) was proposed\(^18\) and has been shown to reduce the duration of first stage of labour with its safety proven in randomized controlled clinical trials involving 3000 women\(^11\).

Hyoscine-N-Butylbromide (HBB) is a quaternary compound derived from Dubosia tree found mainly in Australia\(^13\) and it does not cross the blood brain barrier readily so central effects are rare\(^11\) it is a competitive antagonist of acetylcholine at the muscarinic receptors\(^13\). It has a selective blocking action on the intramural parasympathetic ganglia especially the cervico-uterine plexus aiding analgesia and cervical dilatation without affecting uterine contractions\(^13\). It can be given orally, rectally or intravenously. HBB has low bioavailability (<1%) after oral administration and low protein binding with a half life of about 5 hours and molar mass of 360.467g/mol\(^20\), and is rapidly distributed into the tissues after intravenous administration (t1/2 29 minutes).\(^20\) Its chemical formula is \(C_{21}H_{30}N_4\). It is mainly excreted by the kidney (50%) and through the rectum\(^20\). Animal studies with rats and rabbits has shown no evidence of teratogenicity and no adverse effect on fertility\(^19\).
Studies have shown the various uses and modes of actions of hyoscine butyl bromide in the field of obstetrics and its use to shorten labour event has been studied by many in both randomized and non randomized control trials using various routes of drug administration, It was found that most of its prompt actions occurred with parenteral and suppository routes and the optimal time of administration was at cervical dilatation of above 3cm and no significant side effects was observed with up to 30mg dose. The majority of the studies upheld the efficacy and safety of HBB in shortening of the first stage of labour with no side effect to the fetus or mother\textsuperscript{3,11,21}, while few others showed no benefit\textsuperscript{28}. One study showed that HBB may reduce rate of cervical dilatation thus predisposing to prolong labour\textsuperscript{12}.

**STUDIES ON EFFECT OF HYOSCINE-N-BUTYL BROMIDE (HBB) IN LABOUR**

The effect of HBB in labour has been studied in both primigravida\textsuperscript{11,21,22} and multiparous women\textsuperscript{23,24,25}. In a prospective randomized control trial using 104 primigravida\textsuperscript{s}, Aggarwal et al showed that HBB shortens the active phase of labour\textsuperscript{21} with mean duration of labour of 3 hours 46 minutes among HBB group against 8 hours 16 minutes in the control, however the principal investigator in this study who prepared the drug and the placebo also allocated the women to the test and the control groups and this could be a source of bias in their study. In this present study, both the investigators and the patients were blinded and a pharmacist who was not part of the study was involved in the preparation of the drug and the placebo. Makvandi et al in their randomized double blind placebo controlled trial in Iran involving 130 primigravida\textsuperscript{s}\textsuperscript{22} supported the above findings with rate of cervical dilation of 2.6cm/h in HBB group and 1.5cm/h in the control group(p<0.001). This is also comparable to a study in Saudi Arabia by Nourah et al in a randomized double blind study with 97 primigravida showed mean duration of labour of 165 and 215
minutes in study and control groups respectively, a 23.3% \((p= 0.001)\) reduction in the duration of first stage of labour\(^{11}\).

In a single-blind randomized control trial done in Iran with 188 multiparous women, Sekhavat et al also demonstrated that HBB is effective in shortening active phase of labour in the multiparous\(^{23}\) which was also confirmed in a work by Samuels et al in a randomized double blind controlled trial using 129 women (both primigravidas and multiparous)\(^{24}\) which is in line with the work of Sirohiwal (using 200 women) showing effectiveness of HBB in shortening first stage of labour in both primigravidas and multiparous women\(^{25}\) and this was supported by Kirim et al in their study which showed a statistically significant difference in the first stage of labour of 57 minutes \((p<0.001)\) between primigravidas on HBB compared to control and 54 minutes between multiparous on HBB compared to the control\(^{26}\). Wegar et al working in Iraq showed that HBB decreases the duration of first stage of labour significantly only in multiparous women\(^{27}\). However, this is at variance with the work by Fouad et al in Iraq which showed that women treated with HBB has significantly lower rate of cervical dilatation at one hour when compared with control and thus concluded that HBB increases the duration of the first stage of labour when compared with the control\(^{12}\) while the work by Kennedy showed that HBB has no effect on duration of first stage of labour\(^{28}\). The findings by Kennedy could be due to the administration of the drug at cervical dilatation of 2-3cm which is at latent phase of labour. Latent phase administration of HBB has been shown to decrease labour progress by reducing uterine tension\(^{27}\). In this present study, HBB was administered in active phase of labour at cervical dilatation of greater than 3cm.

STUDIES COMPARING HBB AND OTHER ANTISPASMODICS IN LABOUR
HBB has also been compared to other antispasmodics in shortening the active phase of labour. Fardiazar et al compared HBB and atropine in a single blind randomized clinical trial using 120 women and showed that HBB is preferable to atropine in reducing the length of first stage of labour\textsuperscript{29}. This is in contrast to the study by Gupta et al comparing the efficacy and the side effects of drotaverine hydrochloride and HBB which showed that both have no role in labour augmentation\textsuperscript{30}. A meta-analysis by Rohwer et al accessing the effects of antispasmodics in labour in terms of pregnancies showed low quality evidence that antispasmodics reduces the duration of first stage of labour\textsuperscript{2}. The study evaluated twenty-one trials. Antispasmodics used included valemethane bromide, hyoscine butyl bromide, drotaverine hydrochloride, rociverine and camylofin dihydrochloride\textsuperscript{2}. Most of the studies analyzed included antispasmodic as part of their package of active management of labour. Thirteen trials reported on the duration of first stage of labour, which was significantly reduced by an average of 74.34 minutes when antispasmodics were administered. Mean difference (MD) -74.34 minutes, 95% Confidence interval (CI) -98.76 to -49.93. Seven studies reported on the total duration of labour, which was significantly reduced by an average of 85.51 minutes (MD-85.51 minutes, 95% CI -121.81 to 49.20). Six studies had data for the outcome, rate of cervical dilatation\textsuperscript{2}. Administration of antispasmodic significantly increased the rate of cervical dilatation by an average of 0.61cm/hour and no serious neonatal adverse events were reported\textsuperscript{2}. Venkata in his study with 200 women with term pregnancies in active phase showed that the effect of HBB and Valathemate bromide (epidosin) are comparable in reducing the length of first stage of labour in both primigravidas and multiparous\textsuperscript{31}, however oxytocin was also administered to some of the women during the study and may have affected the outcome of the study therefore I excluded those that received oxytocin augmentation in this particular study. Raghavan in United Kingdom also concluded that both HBB and valethamate are effective in reducing the duration of the first stage of labour\textsuperscript{32}. The action of HBB in
reducing the length of first stage of labour was also shown in the work by Reynavillasmil et al\textsuperscript{33} to be comparable to that of oxytocin, Guerresi et al while comparing the influence of spasmolytic treatment and amniotomy on delivery time concluded that HBB has no appreciable effect on the dilatation of cervix and delivery times\textsuperscript{34}. Some of the works also showed that HBB can in addition reduce pain in labour\textsuperscript{29}. Aggarwal et al showed up to 36\% reduction in pain\textsuperscript{21}.

STUDIES ON THE EFFECT OF HBB IN LABOUR BY DIFFERENT ROUTES OF ADMINISTRATIONS.

The effect of HBB in the duration of active phase labour has been studied using intravenous injections, intramuscularly or as rectal suppository. Nourah et al in their study used the intramuscular route\textsuperscript{11} of administration to demonstrate the effectiveness of HBB in reducing first stage of labour which is in contrast to the work by Kennedy which while using the intramuscular/subcutaneous route showed no effect when HBB was given in labour\textsuperscript{28}. This as was noted earlier may be due to the administration of HBB at a cervical dilatation of 2-3cm in the work by Kennedy while Nourah et al in their study administered HBB at 3-4cm cervical dilatations. Kennedy in their work also used nitrous oxide as labour analgesia in the study which may have affected the uterine contractions\textsuperscript{28} thus we avoided nitrous oxide as labour analgesia in this study. Sekhavat et al used the intravenous route of administration in their study to show that HBB is effective in reducing the duration of labour\textsuperscript{23}. In the study by Sekhavat however, the women in the intervention group were not blinded to the study so in this present study, both the women and the care givers were blinded to the study. The same route of administration was used in the randomized trial by Samuels et al with similar results\textsuperscript{24} , Fardizar et al in comparing HBB and atropine as labour accelerant and analgesic in a randomized trial used same intravenous route\textsuperscript{29} and got comparable result and Aggarwal et al in their randomized trial in India also used same route with comparable route\textsuperscript{21}, Kirim et al
and Reyna-Villasmil et al also used the intravenous route of administration\textsuperscript{26,33}. All the above studies showed the efficacy of HBB in reducing active phase of labour duration despite the route of administration. However this is in contrast to the work by Foud et al using same route of administration but showed that HBB is ineffective and can prolong labour duration\textsuperscript{12}.

In a non randomised controlled trial by Sirohiwal et al HBB was used as a rectal suppositories\textsuperscript{25} and similar route was used in the work by Makvandi with comparable result\textsuperscript{22}. Venkata also used rectal suppository while comparing the effect of HBB with Epidosin on cervical dilatations and got comparable result\textsuperscript{31}. Ahmed working in Egypt administered HBB rectally and got similar results\textsuperscript{35}.

COMPLICATIONS OF HBB USE IN LABOUR

Maternal complications were absent in all but few of these studies which showed that HBB is not only effective but safe in labour\textsuperscript{11,21}. Nourah et al showed no maternal adverse effect in their study\textsuperscript{11}, which agrees with the work by Agarwal et al which also showed no maternal adverse effect when HBB is used in labour\textsuperscript{21}. This is similar to the result of the work by Sekhavat et al\textsuperscript{23}. Sirohiwal also showed no maternal adverse effect in their study\textsuperscript{25} and this agrees with the studies by Samuels et al, Makvandi et al, Kirim et al and Venkata\textsuperscript{22,24,26,31}. However this is in contrast to the work by Fouad et al which suggested that HBB can prolong the first stage of labour and thus may pose some maternal risk\textsuperscript{12}.

There were no significant difference in the total blood loss after delivery and rate of caesarean section when HBB is used to shorten the first stage of labour when compared to control. Nourah et al showed no difference in caesarean section rate between the study group and the control\textsuperscript{11} and this agrees with the study by Aggarwal et al showing comparable mode of delivery between the HBB arm of their
study and the control\textsuperscript{21}. Sekhavat et al also showed no increase in the caesarean section rate when HBB is used to shorten labour duration\textsuperscript{23}. In their non randomized control trial, Sirohiwal et al showed no increase in the incidence of operative deliveries when HBB is used in labour\textsuperscript{25}. Samuels et al showed slight but statistically insignificant increase in caesarean section rate between the HBB group and the control group (6.7 versus 4.3\%)\textsuperscript{24}. In contrast, Fouad et al showed a significant increase in the frequency of caesarean section in HBB group of their study (21\%) compared to the controls (4\%)\textsuperscript{12}. The indication for the caesarean sections were however not recorded\textsuperscript{12}.

**EFFECT OF HBB ON FETAL OUTCOME**

Fetal outcome was also shown to be good with the use of HBB to shorten the first stage of labour as demonstrated by no significant difference between the apgar scores of the woman in HBB arm of the majority of the studies and those in the control arm. Sekhavat et al showed no difference in the mean neonatal apgar score at one and five minutes in both HBB group and the control group\textsuperscript{23} which is comparable to the study by Nourah et al\textsuperscript{11}, Aggarwal et al also revealed no documented adverse effects on the fetus\textsuperscript{21}. This is in agreement with the findings in the study by Samuels et al\textsuperscript{24}. Sirohiwal et al also showed no significant difference in Apgar scores at 1 and 5 minutes between the HBB group and their controls\textsuperscript{24} and this was supported by Makvandi et al and Kirim et al\textsuperscript{22,26}. However, this is in contrast to the study by Fouad et al which showed a slight increase in fetal heart rate though it agrees with overall non significant change in apgar score at 1 and 5 minutes between study group and their control\textsuperscript{12}. The work by Fouad et al also noted no significant increase in admission to the neonatal intensive care unit\textsuperscript{12}.
STUDIES ON EFFECT OF HBB ON SECOND AND THIRD STAGES OF LABOUR

All the studies but few showed that HBB has no effect in the duration of second and third stages of labour. Sirohiwal et al showed no difference in the duration of second and third stages of labour between the HBB group and the control groups. This is comparable to the work by Samuel et al and Gupta et al. Foud et al noted no significant change in the second stage of labour between the two groups which agrees with the work by Kirim et al, in contrast Makvardi et al in their work observed shorter duration in second stage (p< 0.01) in HBB group compared to the control group, they also suggested that the longer duration of second stage in the control group may be due to longer duration of first stage in that group leading to maternal tiredness and thus poor bearing down effort. Additionally, a study by Sekhavat et al came to similar conclusion of observed shorter duration of second stage of labour in HBB arm compared to the control arm of the study, Ahmed in Egypt also observed shorter second stage after the administration of HBB in labour while the work by Hanaa et al in Iraq showed that HBB also effectively shorten second and third stages of labour.

NEED FOR THIS STUDY

The scourge of prolonged labour is well pronounced in an environment such as ours so any safe and effective method to prevent prolonged labour will help to prevent the complications associated with it.

The efficacy and safety of HBB as shown in this study is a welcome development in our environment, because of the availability of HBB, its low cost and its lack of major side effects will promote its use in labour by both the doctors and the midwives. However more multicentre studies will be needed to further prove the effect of HBB in labour.
CHAPTER THREE

JUSTIFICATION FOR THE STUDY

Management of prolong labour represents a challenging area in the daily obstetrics practice. Prolong labour is associated with maternal exhaustion, post partum haemorrhage, sepsis, fetal asphyxia and distress thus active management of labour was proposed so as to eliminate the morbidity and mortality associated with prolonged labour.

For active management of labour, good uterine contractions and simultaneous cervical dilatation and softening is required. But in spite of good uterine contractions, cervical dilatation may be hampered due to inhibitory impulse in the form of spasm. Therefore, the treatment of prolonged labour is a highly desirable goal of intrapartum care both from the prospective of maternal and fetal wellbeing and for the provider of birth services. Management of prolonged labour entails shorter exposure to pain, anxiety and distress and would thus translate into a major improvement in maternal satisfaction with child birth experience.

Several methods have been used for management of prolonged labour including amniotomy and oxytocis. Amniotomy can cause infections and can be combined with oxytocin for better results while oxytocin can cause hyper stimulations, water intoxications, vomiting, diarrhoea, fetal distress and neonatal jaundice. Additionally, oxytocin when used in active management of labour is associated with uterine rupture when used injudiciously by health care givers. Therefore any simpler, cheap and readily available alternative without the above complications like hyoscine n-butyl bromide is a welcome development as the findings of this study corroborated its effectiveness. One recent Cochrane review by Rohwer et al concluded that more randomized controlled studies are needed to evaluate effect of antispasmodics on the duration of labour².
HBB as proven in this study to shorten duration of labour will provide the required effective, cheap and readily available alternative that will be relatively free of complications, which can be used in a low resource setting like ours. Additionally, there is no such published study on the effectiveness of HBB in the duration of labour in Nigeria.
CHAPTER FOUR AIM AND SPECIFIC OBJECTIVES

Aim:

To evaluate the effect of hyoscine n-butyl bromide (HBB) on the duration of the first stage of labour in term pregnancies in Nnewi, South-east Nigeria.

Specific objectives:

1. To determine the duration of the first stage of labour following administration of HBB versus placebo.
2. To determine the duration of second stage of labour following administration of HBB versus placebo.
3. To determine the rate of operative deliveries after administration of HBB versus placebo.
4. To determine the rate of adverse fetal outcome following administration of HBB versus placebo

HYPOTHESIS

Hyoscine - n-butyl bromide shortens the duration of first stage of labour without adverse maternal or fetal side effects.
CHAPTER FIVE
SUBJECTS AND METHODS

Study area

The study was conducted in Nnamdi Azikiwe University Teaching Hospital, Nnewi. This teaching hospital provides a 24-hour specialty care. Most of the deliveries and evaluations are made by midwives and resident doctors with consultant supervision.

Study period

The study was undertaken within four months.

Study design

The study was a double blind randomized controlled clinical study. Pregnant women with term pregnancies who consent to the study were randomly assigned to take a dose of intravenous Hyoscine n-butyl bromide or placebo.

OUTCOME MEASURES

Primary outcome measures were the duration of the first and second stages of labour. Secondary outcome measures were the rate of caesarean sections, instrumental deliveries and the apgar scores at one and five minutes.

Sample size and sampling technique

This was determined using the formula $d = \frac{\Delta}{SD^{30}}$ where $\Delta$ = standardized difference

Target difference

$SD = $ Standard deviation
A Target difference of 60 minutes was used and SD of 68.9 from a similar study (double blind randomized control trial) by Samuels et al because the study was done among women of Afrocaribbean ethnicity.

\[ d = \frac{60}{68.9} \]
\[ d = 0.87 \]

A nomogram (appendix 4) for the calculation of sample size was then used to get the required sample size at a p value of 0.05 and a power of 90%. Thus from the above method the required sample size was determined to be 112 women.

To correct for attrition arising from consent withdrawal and or from obstetrics or medical conditions in the exclusion criteria with the expectation of 10% attrition rate, the formula \( N = \frac{n}{1-q} \) where \( N \) is the final sample size, \( n \) is the initial sample size and \( q \) is the expected attrition.

\[ N = \frac{112}{1-0.1} \]
\[ N = \frac{112}{0.9} \]
\[ N = 124. \]

Therefore 124 women will be recruited (62 parturients per arm of the study)

**Study population**

This were all consenting pregnant women seen in the labour ward during the period of the study and who meet the inclusion criteria, until the calculated sample size was reached.

**Inclusion criteria**
Only women who give informed consent, age of 18 years or older, pregnant women with term pregnancy that came in spontaneous established labour.

**Exclusion criteria**

Exclusion criteria include those women that refused consent, those with any contraindication to vaginal delivery and those with medical illness like hypertension, diabetics, pre eclampsia.

**Data collection**

Ethical clearance was obtained from NAUTH Ethics committee. Trained resident doctors including the researcher were involved in the collection of data from the patients immediately after arriving at the labour ward for delivery. The information were collected using patients case files and partographs.

**Study procedure**

Women who met the inclusion criteria and present in a spontaneous labour at term were randomized to receive either Hyoscine n-butyl bromide (HBB) or water for injection after explaining the study aim to them and consent form signed. A pharmacist was involved in the preparation of the HBB and the placebo (water for injection). The pharmacist under aseptic conditions prepared 124 syringes. Sixty two of which will contain 40mg of HBB and the other sixty two will contain 2mls of water for injection. This was prepared in batches of four and be kept in the fridge with fresh batches prepared only when the former is exhausted. The pharmacist randomly assigned numbers to the syringes and only the pharmacist knew the content of the syringes and only decoded the numbers to the researcher at the end of the study.
The women received either 40mg (2mls) of HBB intramuscularly or placebo (2mls of water for injection). Both fluids are colourless and thus indistinguishable. This was given after history and examination confirmed spontaneous labour at cervical dilation of >3cm. Further management of the patient were as per labour ward protocol. The duration of the first, second and third stages of labour as well as the mode of delivery, maternal adverse effect and apgar scores were recorded on the partograph and were used to analyze the result.

Data and statistical analysis

Data after correction were checked for completeness, tabulated and analyzed using the statistical program SPSS (Statistical program for social sciences) version 20. Proportions were compared by Chi-square where appropriate and the statistical significance of $P$-value will be $P<0.05$.

A bivariate analysis was done using chi square test for difference of proportions between cases and controls for categorical variables and results showed in odds ratio (OR) and respective confidence intervals. A multivariate analysis was run using logistic regression backward conditional model to control the confounding effect independent determinants.

Ethical consideration

Due approval was gotten from the NAUTH ethics committee. The nature of the study was carefully explained to the women and their informed consent (consent form-appendix 1) were obtained before being recruited into the study. The rights of the patient to participate or withdraw from this study were fully honoured without any adverse consequence to the patient.
**Beneficence to participants**

No patients participating in this study was made to pay for any of the procedures. The results obtained from this study will help in the formulation of evidenced-based policies for better management of women in labour.

**Non maleficence to participants**

There was little or no inconvenience that arose from participating in the study.

**Justice**

Method of patients selection was scientifically objective and ensured fairness such that random sampling was used.

**Incentives to patients**

The cost of the research was entirely borne by the researcher. The subjects and the investigators were not paid.
RESULTS

One hundred and twenty four women from different educational and occupational background who consented to the study were enrolled. Sixty two of them received the drug while the remaining sixty two received water for injection as a placebo.
The women were comparable in age and gestation with a minimum age of 21 and maximum of 42. A mean age of 30.7 and median of 32 with a standard deviation of 6.03. Their cervical dilatation findings of about 4-5cm was also comparable.
Figure 2 shows educational status of the patients.

Fig 3 shows the Occupations of the patients.
Fig 4 Shows the marital status of the parturients
Table 1 shows the mean age of the parturient

<table>
<thead>
<tr>
<th>N</th>
<th>Valid</th>
<th>124</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>30.7419</td>
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<tr>
<td>Median</td>
<td></td>
<td>32.0000</td>
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<tr>
<td>Std. Deviation</td>
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<td>6.03765</td>
</tr>
<tr>
<td>Minimum</td>
<td></td>
<td>21.00</td>
</tr>
<tr>
<td>Maximum</td>
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<td>42.00</td>
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</table>

Table 2. Demographic characteristics of the parturients

<table>
<thead>
<tr>
<th>Parity</th>
<th>Age group (in years)</th>
<th>control</th>
<th>drug</th>
<th>Total</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Primigravida</th>
<th>20-24</th>
<th>12(23.07)</th>
<th>15(28.84)</th>
<th>27(51.92)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25-29</td>
<td>10(19.23)</td>
<td>10(19.23)</td>
<td>20(38.46)</td>
</tr>
<tr>
<td></td>
<td>30&amp;above</td>
<td>2(3.84)</td>
<td>3(5.76)</td>
<td>5(9.61)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24</td>
<td>28</td>
<td>52</td>
</tr>
<tr>
<td>Multigravida</td>
<td>25-29</td>
<td>6(8.33)</td>
<td>5(6.94)</td>
<td>11(15.28)</td>
</tr>
<tr>
<td></td>
<td>30&amp;above</td>
<td>32(44.44)</td>
<td>29(40.28)</td>
<td>61(84.72)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>38</td>
<td>34</td>
<td>72</td>
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</tbody>
</table>

Table 3 shows mean age of participants in the two groups

<table>
<thead>
<tr>
<th>Control</th>
<th>Drug</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=62</td>
<td>N=62</td>
<td></td>
</tr>
<tr>
<td>MEAN AGE</td>
<td>30.79±6.02</td>
<td>30.69±6.10</td>
</tr>
</tbody>
</table>

Table 4 shows the mean age of participants based on parity

<table>
<thead>
<tr>
<th>Primigravida</th>
<th>Multigravida</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=52</td>
<td>N=72</td>
<td></td>
</tr>
<tr>
<td>MEAN AGE OF PARTICIPANTS(in years)</td>
<td>25.17±3.65</td>
<td>34.76±3.80</td>
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</table>

Table 3 Gestational age of participants
<table>
<thead>
<tr>
<th>Parity</th>
<th>Gestational age in weeks</th>
<th>Drug</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primigravida</td>
<td>36.00</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>37.00</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>38.00</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>39.00</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>40.00</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Multigravida</td>
<td>37.00</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>38.00</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>39.00</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>40.00</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>

*Fishers exact test

The mean duration of first stage of labour in primigravidas was $391.81 \pm 56.57$ minutes in the control and $246.56 \pm 21.86$ in the HBB group showing a significant decrease of $145.2$ minutes ($p=0.001$) while the mean duration of first stage of labour in the multiparous women were $323.83 \pm 15.99$ in the control group and $205.88 \pm 17.80$ in the HBB group which is about a decrease $117.65$ minutes which was statistically significant ($p$ value=$0.002$)

of labour in both the control and the HBB group for both the primigravida and multiparous.
In the primigravida the second stage duration was 30.46±2.43 minutes in the control and 28.14±4.05 minutes in the HBB group (p=0.531) while the third stage duration was 10.40±1.07 in the control and 9.86±1.11 minutes in the HBB group (p=0.081)

The durations of the second of labour in the multiparous women were 21.81±1.82 minutes in the control and 19.57±5.02 in the test group (p = 0.541) while the third stage was 11.03±0.53 in the control and 9.69±1.03 in the group (p=0.814) respectively.

Table 4: The Duration of labour in the parturients

<table>
<thead>
<tr>
<th>Parity</th>
<th>Stages of labour</th>
<th>Control Duration of labour in minutes</th>
<th>Drug Duration of labour in minutes</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primigravida</td>
<td>First stage</td>
<td>391.81±56.57</td>
<td>246.56±21.86</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30.46±2.43</td>
<td>28.14±4.05</td>
<td>0.531</td>
</tr>
<tr>
<td></td>
<td>Second stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Third stage</td>
<td>10.40±1.07</td>
<td>9.86±1.11</td>
<td>0.081</td>
</tr>
<tr>
<td>Multigravida</td>
<td>First stage</td>
<td>323.83±15.99</td>
<td>205.88±17.80</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21.81±1.82</td>
<td>19.57±5.02</td>
<td>0.541</td>
</tr>
<tr>
<td></td>
<td>Second stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Third stage</td>
<td>11.03±0.53</td>
<td>9.69±1.03</td>
<td>0.814</td>
</tr>
</tbody>
</table>

There was no significant difference between in mode of delivery between the control and the HBB group for both classes of parturient in the study. (as shown in Table 5)

Among the primigravidas, 21(40.4%) parturient in the control had spontaneous vaginal delivery while 25 women(40.1%) in the test group had spontaneous vaginal
five parturient had abdominal delivery due to cephalopelvic disproportion, three (5.8%) of which were from the control and two (3.8%) from the test group (p = 0.989). A parturient (1.9%) in the test group had assisted vaginal delivery with ventose due to poor maternal effort.

Thirty-seven multiparous (51.4%) women in the control group and thirty-four (47.2%) in HBB group delivered by spontaneous vertex delivery (p = 0.785), While one woman (1.4%) in control group had abdominal delivery due to cephalopelvic disproportion (0.888)

**Table 5: Mode of delivery across both groups**

<table>
<thead>
<tr>
<th>Parity Mode</th>
<th>ofControl</th>
<th>Drug</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primigravida SVD</td>
<td>21</td>
<td>25</td>
<td>0.786</td>
</tr>
<tr>
<td>Ventose</td>
<td>0</td>
<td>1</td>
<td>0.987*</td>
</tr>
<tr>
<td>CS</td>
<td>3</td>
<td>2</td>
<td>0.989*</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>multigravida SVD</td>
<td>37</td>
<td>34</td>
<td>0.785</td>
</tr>
<tr>
<td>CS</td>
<td>1</td>
<td>0</td>
<td>0.888*</td>
</tr>
<tr>
<td></td>
<td>38</td>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>

*Fishers Exact test

SVD: Spontaneous vertex delivery.
There were no significant statistical difference between the APGAR scores of neonates delivered by both classes of parturient in both the control and the test group. (See Table 6) One neonate (1.9%) in the test group among the primigravidas and one (1.4%) in control group (p=0.786) among the multiparous women (p=1.00) had a score of <7 at one minutes. 28 neonates (53.8%) in the control had Apgar score of greater than 7 at five minutes against 23 neonates (46.1%) in the HBB group (p=0.876). Among the multiparous, 38 neonates (52.8%) in the control and 34 neonates (47.2%) had Apgar score >7 at five minutes (p=0.887)

### Table 6: Apgar score at 1minute

<table>
<thead>
<tr>
<th>PARITY</th>
<th>APGAR</th>
<th>control</th>
<th>drug</th>
<th>P value</th>
</tr>
</thead>
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<tr>
<td></td>
<td>SCORE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>@1minute</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primigravia</td>
<td>&lt;7</td>
<td>0</td>
<td>1</td>
<td>0.786</td>
</tr>
<tr>
<td></td>
<td>≥7</td>
<td>28</td>
<td>23</td>
<td>0.876</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>28</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Multigravia</td>
<td>&lt;7</td>
<td>1</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>≥7</td>
<td>37</td>
<td>34</td>
<td>0.887</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>38</td>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>

### Table 7:APGAR SCORE at 5minutes
There were no significant difference in the incidence of maternal complications in both classes of parturients. Three primigravidas (5.8%) complained of nausea in the HBB group against one (1.9%) complaint in the control group (p = 0.786). There was also one (1.9%) complaint of vomiting in the control group against two (3.8%) in the test group (p = 0.867) and one (1.9%) complaint of tachycardia among the HBB group and none in the control (p = 0.543).

Among the multiparous there was four (5.6%) incidences of nausea and vomiting in the parturient in HBB group compared to one (1.4%) in the control group (p = 0.604).

Table 8: maternal complications

<table>
<thead>
<tr>
<th>Parity</th>
<th>Complications</th>
<th>Drug</th>
<th>control</th>
<th>P value</th>
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<tbody>
<tr>
<td>Primigravida</td>
<td>Nausea</td>
<td>3</td>
<td>1</td>
<td>0.786*</td>
</tr>
<tr>
<td></td>
<td>vomiting</td>
<td>2</td>
<td>1</td>
<td>0.867</td>
</tr>
<tr>
<td></td>
<td>tachycardia</td>
<td>1</td>
<td>-</td>
<td>0.543*</td>
</tr>
<tr>
<td>multigravida</td>
<td>Nausea</td>
<td>3</td>
<td>1</td>
<td>0.604*</td>
</tr>
<tr>
<td></td>
<td>vomiting</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSIONS

This present study was carried out in among primigravidas and multiparous women in active phase of labour which is a strong advantage of the study since it helped to establish its effect in both classes of parturients. The use of HBB in labour is widespread all over the world and was even suggested and introduced in Saudi Arabia by midwives.

This present study showed that HBB can shorten the duration of first stage of labour in both primigravida and multiparous women and this is comparable to a similar study by Samuels et al, Sirohiwal et al and Kirim et al. However this is at variance with the work by Wegar et al which showed that HBB is effective only in the multiparous. Kennedy postulated that HBB has no effect on the duration of labour and this may be due to administration of the drug by Kennedy at latent phase of labour. In this present study, Buscopam was administered during the active phase of labour.

This study also showed that HBB has no effect in second and third stages of labour and this is at variance with the work by Makvandi et al and Sekhavat et al who observed shorter duration of labour in HBB arm of their study. But our study agrees with the work by Samuels et al, Sirohiwal et al and Gupta et al. The lack of effect on the second and third stages of labour may be due to activity of HBB which is mainly on the smooth muscle of the cervix with little or no effect on the uterus when administered in active phase of labour. This obviates the fear of rapid second stage especially in multiparous which may result in maternal and neonatal complications such as cervical tears and tentorial tears.

This study also revealed no significant difference in the mode of delivery for women on HBB arm of the study and control and This observation compares with the findings in the study by Nourah et al. Maternal complications and neonatal outcome were also showed not to be statistically different in this study which is similar to the studies by Nourah et al, Aggarwal et al and Sekhavat et al.

This study supports the Effectiveness of Hyoscine –n-Butyl bromide in reducing the durations of a first stage labour with a good safety profile. Clinically this could help in formation of labour ward protocols.
The strength of this study lies in the fact that it is a double blind randomized control trial and it was carried on both primigravidas and multiparous there by showing its effectiveness in both classes of parturients. However it has a limitation of been conducted in a tertiary centre and with small sample size thus may not be a through representation of the populace. There was no long time follow up of the neonates for possible determination of any deficit later in life and there was difficulty in determining the exact time of full cervical dilation in the parturients.

CONCLUSION

From the result of this study which compares with that of other previous studies, it can be concluded that Hyoscine n butyl bromide is effective in reducing the duration of the first stage of labour without any significant maternal or neonatal adverse effect. This is the first study of this topic in our institution, it is suggested that more studies be conducted in other institutions in Nigeria in other to further explore the useful role of buscopan in active phase of labour.

REFERENCES


12. Aldahhan FH, Alwaee FA, Raheem F. The Evaluation of the effect of buscopan (Hyoscine-n-butyl bromide) on the duration of labour. Bas J of
18. O’Driscoll K, Stronge JM, Minogue M. Active management of labour.
http:/www.drugs.com/uk/pdf/leaflet/273646.pdf
2011; 52(2):159-63.


APPENDIX 1

40

Proforma for the study on Effect of Hyoscine n-butyl bromide in the duration of labour in term pregnancies in NAUTH Nnewi.

Hospital Number..............................................................

Age..................................................................................

Parity..............................................................................

Gestational Age............................................................

Time of active phase.....................................................

Time of full cervical dilation..........................................  

Time of Delivery............................................................

Estimated blood loss....................................................

Mode of delivery

Spontaneous vaginal Delivery........................................

Caesarean Section........................................................

Assisted (instrumental) Vaginal Delivery.......................  

Apgar scores at

1 minute...........................................................................
APPENDIX 2: THE CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

The purpose of this consent form is to provide you with the information you need to consider in deciding whether to participate in this research study titled: EFFECT OF HYOSCINE N-BUTYL BROMIDE IN THE DURATION OF LABOUR IN TERM PREGNANCIES IN NAUTH NNEWI.

We respectfully invite you to participate in a research study. You are not under any obligation to participate in this study: we assure you that your pregnancy, labour and puerperal care will not suffer in any manner in the event you refuse participation. It is your right to demand information about any procedure or process in respect of the study. You also reserve the right to withdraw from the study at any stage.

STUDY PURPOSE

The purpose of this study is to examine whether intramuscular administration of HBB would shorten the duration of the first stage of labour in women with term pregnancies that presented in established labour in Nnewi, South-east Nigeria.

STUDY PROCEDURE

The study will include pregnant women that present to the labour ward in established labour. If you decide to participate in this study, you will undergo the regular evaluation by your doctor. So the collection of the data will be from clinical folders and partographs. There will be no additional discomfort to you.

STUDY RISKS

There is no risk associated with participating in this study.
POTENTIAL BENEFITS

The immediate benefits include knowing whether HBB shortens the duration of the first stage of labour and thus helping in the formulation of labour ward protocols.

PARTICIPATION IS VOLUNTARY

Your participation in this study is completely voluntary. Whether or not you participate in this study, you will still get the standard medical treatment for your condition. You can withdraw from the study at any time, and such a decision will not affect your medical care.

CONFIDENTIALITY

Any information obtained during this study and discussed with you will remain confidential.

QUESTIONS

If you have any questions, please ask and we will do our best to answer them.

I, Mrs./Miss

-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------do hereby

give consent/permission to be included in the intended research as explained to me in English and or Igbo language and understood by me.

I have been made to understand that my participation in the study is voluntary and if I withdraw from the study, I will still enjoy the same standard of care given to other patients by the doctor without prejudice.
SIGNATURE OF PARTICIPANT _____________________________
DATE_________________WITNESSS__________________________
DATE ____________

NAME OF RESEARCHER; DR EJIKEME TOOCHUKWU BENJAMIN

PHONE NUMBER OF RESEARCHER—08036762142
APPENDIX 3

Nomogram for calculation of the sample size.
# APPENDIX 4: THE COMPREHENSIVE WORK PLAN

<table>
<thead>
<tr>
<th></th>
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<th></th>
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<td>6.</td>
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<td>X</td>
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<td></td>
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<td>7.</td>
<td>FINAL WRITE-UP</td>
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<td>X</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>SUBMISSION OF DESSERTATION TO COLLEGE</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL
P.M.B. 5025, NNEWI, ANAMBRA STATE, NIGERIA

Our Ref.: NAUTH/CS/66/VOL.8/29
Your Ref.:__________________________

Dr. Toochukwu Benjamin Ejikeme
Department of Obstetrics and Gynaecology,
Nnamdi Azikiwe University Teaching Hospital,
Nnewi

ETHICS COMMITTEE APPROVAL

RE: EFFECT OF HYOSINE N-BUTYLBROMIDE IN THE DURATION OF LABOUR IN TERM PREGNANCIES IN NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL
NNEWI SOUTH EAST, NIGERIA

We write to inform you that after due consideration of your research proposal, approval is hereby conveyed for you to commence the study.

The principal investigator is required to send a progress report to the Ethics Committee at the expiration of three (3) months after ethical clearance to enable the Committee carry out her oversight function.

Please note that this approval is subject to revocation if you fail to obtain proper authorization from your study site/unit.

Dr. Joy Ebenebe
Chairman, NAUTH Ethics Committee

Udemezue N.O (Mrs)
Sec., NAUTH Ethics Committee