RANDOMIZED DOUBLE-BLINDED STUDY OF EFFICACY OF HYOSCINE-N-BUTYL BROMIDE IN ACCELERATION OF LABOUR AMONG NULLIPAROUS WOMEN

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DECLARATION

I hereby declare that this work is original unless otherwise acknowledged. This has neither been presented to any college, faculty or school for the award of a degree, diploma or fellowship nor has it been submitted elsewhere for publication.

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CERTIFICATION

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ABSTRACT

BACKGROUND: Prolonged labour is still a common problem in our environment and its sequelae remain an important cause of maternal morbidity and mortality. With the introduction of active management of labour, the incidence of prolonged labour and its sequelae have been significantly reduced. Even at this, studies continue to explore ways to shorten labour and improve feto-maternal outcome. Some previous studies have confirmed Hyoscine Bromide in increasing cervical dilatation rate and shortening Active Phase Labour without untoward effects on the mother and baby. However Hyoscine Bromide is not commonly used for labour management in most supervised labour wards in spite of the published advantages. Hence, this study was designed to assess the effect of Hyoscine Bromide in the active phase in a randomised study to test the claims in previous studies.

OBJECTIVE: To determine the efficacy and safety of Hyoscine Butylbromide (in the form of Buscopan® from Boehringer Ingelheim Limited, Germany) in accelerating the active phase of labour in nulliparous women.

METHOD: A randomised double-blind study to be carried out on 128 nulliparas admitted in spontaneous active phase labour. The women were recruited based on inclusion and exclusion criteria and randomised into study and control groups. Either 40mg Buscopan or 2ml of injection water as placebo was given intravenously in two divided doses, given 30 minutes apart. Cervical dilatation rate and duration of active phase and second stage of labour was then recorded. Also to be determined were the rate of caesarean section, blood loss at delivery, and APGAR scores in the neonates in the two groups.

RESULTS: A total of 128 women yielded data for analysis. The mean time for the active phase of labour was 377.2±166.4 minutes in the study group and 412.7±160.6 minutes in the control group and this was not statistically significant (p=0.244; 95% CI 24.5 to 95.3). The cervical dilatation was 1.11±0.53 cm/hr in the study group and 0.94±0.36 cm/hr in the control group (p=0.056; 95% CI 0.003 to 0.33). In a subanalysis of the group without augmentation of labour, the duration of the first stage of labour was 230.56±72.01 minutes in the study group and 272.92±73.34 minutes in the control (p=0.04; 95% CI 1.41 to 83.31). The rate of cervical dilatation in the study group was 1.53±0.50 cm/hr and 1.24±0.34 cm/hr in the control group (p=0.02; 95% CI 0.04 to 0.53). There was no significant difference between the 2nd and 3rd stage of labour. The fetal heart rate, maternal pulse rate, blood pressure, and the APGAR score where not significantly different between the two groups.

CONCLUSION: The use of hyoscine-N-butyl bromide is effective in reducing the duration of active phase of labour amongst nulliparous women without contractile abnormalities. It’s use is not associated with any obvious adverse maternal or fetal outcome.
CHAPTER 1

INTRODUCTION

Prolonged labour is the most easily identifiable index of difficult labour. Over the years, the acceptable duration a parturient can safely stay in labour with minimal or no adverse effects to herself and her baby has gradually reduced. This is largely as a result of the advent of the concept of active management of labour.\(^1\) Short and possibly safe labour is desired by every woman and is the goal of every obstetrician. The aim of active management of labour, as enunciated by O’Driscoll in Dublin, was to prevent prolonged labour while achieving or maintaining a low rate of caesarean section.\(^2,3\) There is clear and documented evidence of the success of active management of labour in institutions where the protocol is practiced.\(^3-6\) The incidence of prolonged labour varies and depends on the accepted definition of prolonged labour, the protocol of labour management and the prevalence of fetopelvic disproportion.

Two major factors determine the duration of labour. These are uterine contractility and the rate of cervical dilatation. Cervical dilatation is the resultant effect of all the driving forces of uterine contraction acting against passive tissue resistance. Failure of the cervix to dilate in labour can result in prolonged labour. In addition to mechanical factors such as sweeping membranes, cervical stretching\(^7\) and amniotomy\(^8\), various pharmacological agents have been found to be effective in facilitating cervical dilatation. Sweeping and stretching of the cervix causes local release of prostaglandins. Amniotomy, especially when done
in early labour, augments and shortens the duration of labour by ensuring lug application of the presenting part to the cervix and thereby transmission of the forces of contraction down the cervix via the fetal spine leading to cervical stretching and Ferguson’s reflex\(^8,9\).

The role of oxytocin in the augmentation of labour has been established worldwide and also cervical application of hyaluronidase has been used with some success.\(^10\) Phloroglucinol, a hyaluronidase, results in a mean reduction of 23% in the second stage compared with placebo groups.\(^11\) Cervical application of relaxin and estradiol, has been used with some success.\(^12,13\) Prostaglandins in various formulations have been used for induction of labour especially prostaglandin E\(_2\) gel and misoprostol (E\(_1\) analogue) for cervical ripening. Unfortunately both prostaglandin and oxytocin can cause neonatal jaundice and even uterine rupture.\(^14\)

Various antispasmodics have been used over the years for shortening of labour duration. Valethamate bromide, a compound with neurotropic and musculotropic actions has been used to enhance relaxation of cervical musculature and faster cervical dilation with resultant shortened labour.\(^15\) Drotaverine hydrochloride, an isoquinolone, which selectively inhibit phosphodiesterase IV, has also been used to shorten the duration of the dilatation stage of labour with excellent results.\(^16\) It was found to be free from maternal and fetal side effects and also alleviated the distress inherent during labour.\(^17,18\) Hyoscine-N-butylbromide, a quarternary ammonium compound and a semisynthetic derivative of scopolamine, is a muscarinic antagonist and hence
could act as a cervical spasmolytic agent.\textsuperscript{19,20} It has an effective antispasmodic activity and is devoid of the side effect of atropine. It also does not cross the blood brain barrier and acts primarily by blocking the transmission of neural impulses in the parasympathetic ganglia of abdominal organs, apparently inhibiting the cholinergic transmission in the synapses.

Oxytocin has commonly been used worldwide for induction and augmentation of labour. It is fairly safe and effective, but has no pain relieving effect and its mode of action is mainly by stimulation of uterine contractions, which can become very strong, and in fact, the patient may feel more pain. Hyoscine N-butyl bromide acts by inhibiting cholinergic transmission in the abdominal and pelvic parasympathetic ganglia, relieving spasm in the smooth muscles of the genital organ, especially the cervico-uterine plexus and thus aiding cervical dilatation.\textsuperscript{21,22} Uterine contractions are not affected, rather due to better co-ordination between uterine contractions and cervical dilatation, the latter is said to increase.\textsuperscript{22} In addition, the pain relieving effects of parasympatholytics gives hyoscine N-butyl bromide an advantage.\textsuperscript{19}

Hyoscine N-butyl bromide in the form of Buscopan\textsuperscript{®} has been reportedly used to shorten the duration of labour in several hospitals especially in the West Indies, India and the Middle East countries.\textsuperscript{19,22-28} Several studies using different mode of administration and dosages of Buscopan\textsuperscript{®} have been carried out in these countries to assess its efficacy in shortening the duration of labour.\textsuperscript{19,22-28} Most of these studies seem to support its use. The mechanism by which it acts in the context of labour has not been fully elucidated, thus its routine use in
labour management is not widespread. This study was therefore designed to assess the effect of Hyoscine Bromide in the active phase in a randomised study to test the claims in previous studies and justify its utility, if any, in labour management.
CHAPTER 2

LITERATURE REVIEW

2.1 Background

Labour and delivery are active processes in which uterine contractions push a rigid object through a fixed aperture. The ability of the fetus to successfully negotiate the pelvis during labour is dependent on the complex interaction of three variables; uterine activity, the fetus and the maternal pelvis (powers, passenger and passage).

The power refers to the force generated by the uterine musculature. Uterine activity is characterized by the frequency, amplitude (intensity) and duration of contractions. If uterine contractions are "adequate" to effect vaginal delivery, one of two things will happen. Either the cervix will efface and dilate and the fetal head will descend progressively with intensity of the contractions till vaginal delivery when the pelvis is adequate. Or there will be worsening caput succedaneum (scalp oedema) and moulding of the fetal head (overlapping of the skull bones) with or without cervical affacement and dilatation when the pelvis is not adequate for the fetal head. The latter situation suggests the presence of cephalopelvic disproportion (CPD).

The passenger is the fetus. There are several fetal variables that influence the course and outcome of labour. These include the fetal size, lie, presentation, attitude, position and station. An abnormality of any of these variables may affect both the course and likelihood of vaginal delivery. The
passage consists of the bony pelvis (composed of the sacrum, ilium, ischium and pubis) and the resistance provided by the soft tissues. The shape of the female bony pelvis can be classified into four broad categories; gynecoid, anthropoid, android and platypelloid. This classification, based on the radiographic studies of Caldwell and Moloy, separates those with favourable characteristics (gynecoid and anthropoid) from those that are less favourable for vaginal delivery (android and platypelloid). In reality, however, many women fall into intermediate classes, and the distinctions become arbitrary. Although the assessment of fetal size along with pelvic shape and capacity is still of clinical value, it is a very inexact science. An adequate trial of labour is the only definitive method to determine whether a given foetus will be able to safely negotiate a given pelvis.

Pelvic soft tissues may provide resistance in both the first and second stages of labour. In the first stage, resistance is offered primarily by the cervix; whereas in the second stage, it is by the muscles of the pelvic flour. It has been proposed that rapid labour results from low pelvic resistance rather than from high myometrial activity. When cervical ripening is used before augmentation of labour, subsequent intrauterine pressures are lower compared with augmentation alone. However, this hypothesis has not received wide acceptance.
2.1.1 **Physiology of Labour**

Most guidelines for normal human labour progress are derived from Friedman’s clinical observation of women in labour.\(^{33,34}\) Friedman characterised a sigmoid pattern of labour course when graphing cervical dilatation against time.\(^{35}\) He divided labour into three functional divisions: the preparatory division, dilatational division and pelvic division. The preparatory division is better known as the latent phase. During this phase, little cervical dilatation occur but considerable changes take place in the connective tissue component of the cervix. The dilatation division or Active phase is the time period when dilatation proceeds at its most rapid rate to complete cervical dilatation. These two phases together make up the first stage of labour. The pelvic division or second stage of labour refers to the time of full cervical dilatation to the delivery of the infant.

Active labour demarcates a rapid change in cervical dilatation. The active phase begins once cervical dilatation progresses at a minimum rate of 1.2cm/hr for nulliparous women and 1.5cm/hr for multiparous women. This change to active phase usually occurs when the cervix is dilated between 3cm to 5cm. In the presence of regular uterine contractions accompanied by cervical dilatation of 3cm to 4cm, the threshold for active labour has likely been reached. Friedman observed that the mean duration of active phase labour in nulliparous women was 4.9 hours with a standard deviation of 3.4 hours.\(^{34}\) There was a large variation in his results, with the maximum duration of active phase reported to be 11.7 hours. Rates of cervical dilatation varied as much from 1.2 to 6.8cm/hour.
2.1.2 Disorders of the Active Phase of labour

Active phase of labour disorders may be divided into protracted (primary dysfunctional labour) and arrest (secondary arrest) disorders. Protraction is defined as a slow rate of cervical changes less than 1.2cm/hour for the nullipara and less than 1.5cm/hour for the multipara. These rates represent less than the 5th percentile for most gravida.

The most common cause of a protracted disorder is inadequate uterine activity. Another common cause is abnormal positioning of the fetal presenting part. Cephalopelvic disproportion (CPD) which refers to the disproportion between the size of the fetal head relative to the maternal pelvis, can be a cause of a protracted or arrest disorder. This is a diagnosis of exclusion, often made at the time a protracted labour course is observed. Most frequently, malposition of the fetal presenting part is the culprit rather than true CPD. Unfortunately there is no way to accurately predict CPD. It is estimated that thousands of unnecessary caesarean deliveries would need to be performed in low-risk pregnancies to prevent a diagnosis of true CPD.

An alternative classification system for disorders of active phase of labour is based on the electromechanical state of the uterus regarding uterine tone. Hypotonic dysfunction (hypotonic inertia) reflects an inefficient generation and propagation of action potentials through the myometrium or lack of contractile response of myometrial cells to the contractile signal. Hypotonic uterine contractions are infrequent, of low amplitude, and accompanied by low or normal baseline intrauterine pressure. Maternal discomfort is minimal. Hypertonic
dysfunction (hypertonic inertia) is primarily a condition of primigravidas and usually occurs in early labour. It is characterized by the presence of regular uterine contractions that fail to effect cervical affacement and dilatation. Frequent contractions of low amplitude are often associated with an elevated basal intrauterine pressure. Maternal discomfort is usually significant. There is also inco-ordinate uterine action. In this, uterine contractions shows remarkable variability as weak, relatively infrequent and short lasting at one time, and at another time, some minutes apart, contractions may be strong and of normal or even prolonged duration. This clinically, is associated with a cervical os dilatation rate of less than 1cm/hour in the absence of fetopelvic disproportion.\textsuperscript{41}

2.1.3 **Prolonged Labour**

Prolonged labour is defined as the spontaneous, first stage, active phase labour duration of over 12 hours for all parturients at term irrespective of age, parity and race.\textsuperscript{42} This is still a common problem in Nigeria and most parts of the underdeveloped world. Prolonged labour and its sequelae are important causes of maternal morbidity and contribute significantly to the half a million women worldwide who die annually as a result of childbirth.\textsuperscript{43,44}

Prolonged labour may be associated with serious complications for both the woman and the foetus. Infection, namely chorioamnionitis, is a consequence of prolonged labour, especially in the setting of ruptured membranes.\textsuperscript{45} In one report that analysed more than 500 women, labour was 4.7 hours longer on average when chorioamnionitis was diagnosed late in labour.\textsuperscript{46} Foetal infection
and bacteraemia, including pneumonia caused by aspiration of infected amniotic fluid, is linked to prolonged labour. In case of neglected, obstructed labour (more likely to be seen in developing countries), pressure necrosis may result in vesicovaginal, vesicocervical, or rectovaginal fistula. Obstructed labour accounts for about 8% of maternal mortality which occur mainly in developing countries.

2.2 Active Management of Labour

The concept of Active Management of Labour was introduced into labour management by O’Driscoll and associates from Dublin, Ireland in 1969. This expanded the existing knowledge and understanding of labour and its sequelae (prolonged labour) which was the dreaded scourge of obstetric practice at that time. Active management of labour (AML) was a package of principles upon which the conduct of labour was based. This dramatically reduced the duration of labour from the prevailing 24 – 48 hours to under 12 hours in the primigravidas who were often the victim of prolonged labour and its sequelae.

Prior to the advent of AML, it was common to find labour duration lasting 36 – 48 hours with its sequelae of high rate of feto-maternal morbidity and mortality. This was because labour was seen as a purely physiological process having a natural course which does not require any form of intervention especially in the first stage except for pain relief. Although the outcome of labour was known to be due to the interplay of uterine power, passenger and passage, the prevailing knowledge then, emphasised that any discrepancies between the
passenger and passage would automatically evoke a weak power (contractions) with consequent prolonged labour. Thus, any prolongation of labour was deemed to be due to cephalopelvic disproportion. It was also the belief then that abnormal uterine action manifested as hypo, hyper or in-coordinate uterine action. This if treated with oxytocin infusion was thought to result in uterine rupture.\textsuperscript{52,53} In addition, it was believed that fetal membranes in spontaneous labour should be maintained intact until late first stage or even till 2\textsuperscript{nd} stage of labour. Rupture of fetal membranes at an early stage of labour was thought to cause distressing titanic uterine contraction that could result in feto-maternal complications.\textsuperscript{54} Consequently, assistance in labour was commonly in the 2\textsuperscript{nd} stage of labour in which traction was believed to reduce the length of second stage, hence the design of several forms of traction forceps.

\subsection*{2.2.1 Principles of Active Management of Labour}

The practice of AML was founded on the following knowledge and principles:\textsuperscript{55}

i) Active phase labour is a definite clinical entity, which is the most important beginning of first stage of labour from when to assess labour duration.

ii) Cervical os dilatation is the most objective means of assessing labour progress and the normal rate is a minimum of 1cm/hr throughout first stage of labour and whatever contractions that ensures this rate is adequate.
iii) Forewater amniotomy in early active phase of labour facilitates cervical os dilatation at the minimum rate of 1cm/hr and does not cause any fetomaternal complications.

iv) Prolonged labour is preventable by early detection of slow rate of cervical dilatation of less than 1cm/hr using the partograph and immediate institution of corrective measures to restore dilatation rate back to 1cm/hr.

v) All varieties of abnormal uterine action are features of uterine inertia, which could be manifest in the first or second stage of labour. Uterine inertia responds well to oxytocin augmentation with improved cervical os dilatation in the first stage and head descent in the second stage.

vi) Uterine inertia is the commonest cause of failure of cervical os to dilate at the rate of 1cm/hr in active phase especially in primigravida. This is even so when uterine contractions are deemed adequate or CPD was clinically suspected.

vii) In the primigravida in whom there is poor progress, a diagnosis of CPD can only be entertained after oxytocin augmentation has been used to eliminate uterine inertia by inducing strong contractions. Oxytocin augmentation in such circumstances, will not cause uterine rupture provided there is no previous scar of any type.

viii) Second stage labour duration is not the simplistic 1 hour in the primigravida and 30 minutes in the multipara but that second stage of labour is composed of two phases, phase I and phase II.
ix) In the conduct of deliveries, assistance in the second stage can be reduced to only low forceps with the avoidance of midcavity or rotational forceps or vacuum extraction when care is taken to eliminate uterine inertia especially in phase I of the second stage.

x) Exposure of any parturient to over 12 hours of active phase labour contractions evoke spiralling feto-maternal complications, but close companionship for parturients in active phase improves performance in labour; raises moral and decreases the need for pain relief.

2.2.2 Issues about Active Management of Labour

Active management of labour brought the features of active phase labour into limelight. This signified the true beginning of labour which should be monitored based on the anticipation that progress, if normal, will be with cervical os dilatation rate at the minimum of 1cm/hr as the evidence that contractions are adequate irrespective of the quality of the uterine contraction. Artificial rupture of membranes was performed as soon as active phase was confirmed. This would aid the attainment of the cervical os dilatation rate at the minimum of 1cm/hr and also reveal the colour and consistency of the liquor. The distress of active phase labour pains was lightened by the consistent presence of a personal nurse and assurance that delivery will occur within 12 hours of the active phase of labour.

Poor or incomplete implementation of AML has ended up with contrary results with respect to prolonged labour and caesarean section rate. Several
randomised controlled trials have been carried out to assess the efficacy of AML.\textsuperscript{59-61} In most of these studies only the duration of labour was reduced but the caesarean section rate was not significantly reduced. In all of these studies, there were no strict adherence to the women establishing first in active phase of labour,\textsuperscript{62} vaginal examination in some were performed at 2 hour or 3 hourly intervals and augmentation regimen used a much lower dose of oxytocin.\textsuperscript{63} The protocol for AML in Dublin has remained the same over the years. Current data still confirms the caesarean section rate of 11 – 12 percent, a perinatal mortality rate of 7 per 1000, instrumental delivery rate of 3.7% and prolonged labour rate (labour duration over 12 hour) of 1.6%.\textsuperscript{64,65}

The excellent result was because AML easily identified uterine inertia (especially in the primigravida), which was more commonly mistaken for cephalopelvic disproportion. This was then effectively treated with oxytocin augmentation instead of caesarean delivery. Hence AML was recommended as a strategy to reduce the high caesarean section rate in the primigravida. With the excellent results and popularity of AML worldwide, serious criticism soon arose because of difficulty in reproducing same results elsewhere even from several randomised controlled studies. The major reason for failure to fully reproduce the Dublin result was poor diagnosis of the entry point into labour supervision with principle of AML and the cost constraint preventing hourly vaginal examination, prophylactic augmentation, the customised childbirth classes and one nurse per patient in most of the trials.
Phillpott and Castle were the first to present a protocol based on the partograph for management of labour based on the principle of AML. It was based on the anticipation of normal progress at 1cm/hr cervical dilatation rate with good results at an affordable cost at least for developing countries.\textsuperscript{66} With the composite partograph AML can be modified to suit the local needs and thus avoiding the full Dublin format. Such modification has been demonstrated by the experience at the University of Benin Teaching Hospital in Benin, Nigeria. Following an adapted AML protocol, prolonged labour rate and caesarean section rate was reduced from the prevailing 33% and 34% to 4.7% and 5.8% respectively and augmentation rate of 14.7% within 5 years of the approach.\textsuperscript{67,68} Yet the protocol did not involve hourly vaginal examination or customised childbirth classes but relied on confident diagnosis of active phase labour and appropriate use of oxytocin augmentation. This was commenced only in situations when cervical os dilatation rate was 2 hours less than 1cm/hr objectively defined as a cervical os dilatation graph crossing the individualised action line constructed at 2 hours to the right and parallel to the individualised alert line.

Though AML has reduced the rate of prolonged labour, many elements of its approach have remained controversial. The rising C/S rate worldwide is also a cause for worry,\textsuperscript{69,70} despite the various protocol of AML applied by different institutions. The ideal pattern of labour management and intervention has yet to be determined. With the continuing research to find the ideal management and intervention, several medications apart from oxytocin have been used as part of the protocol in a bid to reduce the incidence of prolonged labour while still
maintaining a reduced caesarean section rate and good neonatal outcome. One example of such medication is Hyoscine N-butyl bromide (Buscopan®).

2.3 **Hyoscine N-butyl bromide (HBB, Buscopan®)**

Hyoscine N-butyl bromide (HBB), also known as scopolamine butylbromide, is a peripherally acting antimuscarinic, anticholinergic agent used as an abdominal specific antispasmodic.\(^2\) It is a quaternary ammonium compound and a semi-synthetic derivative of scopolamine. Scopolamine (hyoscine) is a naturally occurring tertiary amine alkaloid esters of tropic acid, which occur in *hyoscyamus* or *henbane*, as the *(−)* stereoisomer.\(^7\) It is marketed under the trade name Buscopan by Boehringer Ingelheim Gmbh, Germany.

2.3.1 **Chemistry**

Its chemical name is \((1S, 3S, 5R, 6R, 7S)-8\text{-Butyl – 6, 7-epoxy-3-[(S) – tropoyloxy]}\) with molecular formula \(C_{21}H_{30}BrNO_4\) and molecular mass 440.4. In terms of physicochemical properties, it is a white or almost white odourless or almost odourless, powder, soluble 1 to 1 in water, 1 in 50 of alcohol, and 1 in 5 of chloroform. Ten percent solution in water has a pH of 5.5 to 6.5. Structurally, it exists as a quaternary ammonium compound and as a single positively charged cation throughout the entire pH range.\(^7\)

2.3.2 **Mechanisms of Action**

Hyoscine N-butyl bromide like atropine causes reversible blockage of cholinomimetic actions at muscarinic receptors. Mutation experiments suggest that aspartate in the receptors forms the characteristic bond with the nitrogen atom of acetylcholine; this amino acid is also required for binding of
antimuscarinic drugs. When it (hyoscine or HBB) binds to the muscarinic receptor, it prevent actions such as the release of inositol triphosphate (IP$_3$) and the inhibition of adenylyl cyclase that are caused by muscarinic agonist.

2.3.3 Pharmacodynamics

Muscarinic receptor antagonists prevent the effects of acetylcholine by binding to muscarinic cholinergic receptors at the neuroeffector sites on smooth muscle, cardiac muscle and gland cells; in peripheral ganglia; and in the central nervous system. In general, muscarinic receptor antagonist cause little blockage at nicotinic receptor sites. However, the quarternary ammonium antagonist like the HBB, generally exhibit a greater degree of nicotinic blocking activity, and consequently are more likely to interfere with ganglionic or neuromuscular transmission.

HBB, being a quarternary compound, penetrates the blood-brain barrier poorly and thus have little or no effect on the central nervous system. Therefore, anticholinergic side effects at the central nervous system do not occur. Peripheral anticholinergic effects result from a ganglion-blocking action within the visceral wall as well as from anti-muscarinic activity. HBB is believed to act predominantly at the abdominal and pelvic parasympathetic ganglia, thus relieving spasm in the smooth muscles of gastrointestinal, biliary, urinary and female genital organs.

2.3.4 Pharmacokinetics

As a quarternary ammonium compound, HBB is highly polar and therefore, only partially absorbed following oral administration (8%) and the systemic
availability has been reported as less than 1%.\textsuperscript{27} Despite low blood levels, HBB undergoes rapid tissue absorption after oral administration. After intravenous administration, HBB is rapidly distributed (\(t^{1/2}a = 4\) min, \(t^{1/2}b = 29\) min) into the tissues. The volume of distribution (Vss) is 128L.

Because of its high affinity for muscarinic receptors and nicotinic receptors, HBB is mainly distributed on muscle cells of the abdominal and pelvic areas as well as the intramural ganglia of the abdominal organs.\textsuperscript{74} The high tissue affinity of the substance is further reflected in the extremely short distribution half-life (\(t^{1/2}a\)) in plasma of approximately 2–3 minutes. Despite low systemic bioavailability, hyoscine butyl bromide remain available in high concentration at the site of action. The half-life of the terminal elimination phase (\(t^{1/2}g\)) is approximately 5 hours. Plasma protein binding (albumin) of HBB is approximately 4.4%. Like other cationic drugs, HBB interacts with the choline transport system of human placental epithelial cells in vitro. Transfer of hyoscine butyl bromide to the foetal compartment has not been proved.\textsuperscript{74}

A high portion that is absorbed undergoes elimination in an unchanged form within the first few hours of administration and later in the metabolised portion predominates. Clinical studies with radiolabelled HBB show that after intravenous injection, 42 to 61\% of the radioactive dose is excreted renally and 28.3\% to 37\% feacally. The portion of the unchanged active ingredient in the urine is approximately 50\%. The metabolite excreted via the renal route bind poorly to the muscarinic receptors and therefore not considered to contribute to the effect of HBB.\textsuperscript{74}
2.3.5 **Indications and Clinical Use**

Buscopan® (HBB) is primary indicated for the relief of acute genitourinary or gastrointestinal spasm (renal or biliary colic) or to produce smooth muscle relaxation prior to radiological procedures such as pyelography or other diagnostic procedures where spasm may be a problem (example; gastro-duodenal endoscopy, hysterosalpingography).

2.3.6 **Pregnancy Safety**

HBB is a pregnancy category (USA FDA) C drugs. Studies in animal have not revealed any adverse effects on the foetus (teratoenic or embryocidal) but there are no controlled studies in women or and animals are available. The drug should thus be given only if the potential benefit justifies the potential risk to the foetus. Previous studies done on the use of HBB in labour; have not demonstrated any significant adverse effect either on the mother or foetus.

2.3.7 **Interaction/Synergism with Oxytocin**

There is no known (or published) interaction or synergism of HBB with oxytocin. In most previous studies done, oxytocin was used for labour augmentation when indicated with no adverse effect credited to drug interaction or synergism of HBB and oxytocin.

2.3.8 **Side effects of HBB**

Many of the undesirable effects of Buscopan can be assigned to the anticholinergic properties of the drug. These side effects are generally mild and self-limiting. They include: xerostomia (dry mouth), dyshidrosis, visual
accommodation disorder, tachycardia, dyspnoea and urinary retention. There are also rare reports of dizziness, blood pressure decrease and flushing.\textsuperscript{74,77} Other undesirable effects though also rare include skin reactions, angioedema, fixed drug eruption, anaphylactic reaction and anaphylactic shock including fatal outcome. Adverse events reported during therapy include increased pulse rate, diarrhoea, nausea, retinal pigmentation and glaucoma. Thus Buscopan is contraindicated in patients with myastheniagravis, untreated narrow glaucoma, stenotic lesions of gastrointestinal tract, tachycardia, angina, cardiac failure and megacolon.

2.4 \textbf{Hyoscine Butyl Bromide: Use in Obstetrics}

Hyoscine butyl bromide has been used for many years in obstetrics as an analgesic and semi-hypnotic, either alone or in conjunction with various other drugs. Due to its smooth muscle relaxing effect, it was thought that the drug might aid relaxation of the cervix during labour. Early trials of Buscopan in labour were carried out as early as 1952.\textsuperscript{78-80} Both trials seem to show that the administration of Buscopan results in a considerable shortening of the 1\textsuperscript{st} stage of labour. It is thought that Buscopan by inhibiting cholinergic transmission, relieves spasm in the smooth muscles of the female genital organs, especially the cervico-uterine plexus and thus aids cervical dilatation.\textsuperscript{22} Though uterine contractions are not affected, there is a better co-ordination between uterine contractions and cervical dilatation, which results in increased cervical dilatation.\textsuperscript{22} Also since vagotonic states lead to increased tension at the lower
uterine segment and cervix, parasympatholytics are also useful in arrested or delayed cervical dilatation.26

Hyoscine butyl bromide is commonly used as part of the active management of labour aimed at reducing prolonged labour, labour duration and caesarean section rate without having any adverse effects on the mother or foetus. This practice is common in several hospitals in India, West Indies and Middle East.22-28 Many studies have been carried out in these countries to evaluate the effects of HBB in the active management of labour using different route of administration and different dose regimens. Although, the efficacy of the drug has been proven in various studies, there is still no clear evidence to recommend its routine use in labour.19

2.4.2 Previous Studies of HBB in Labour

Most of the previous work reported in the literature were done in India and some in West Indies and the Middle East. Bhattacharya et al.,19 studied the effect of 20mg of HBB given intramuscularly on 100 primigravidas. They found that the mean labour time was shortened by 3 hours 40 minutes and 81% delivered within 8 hours. Samal et al.,23 in a similar study showed a shortening of labour by 2 hours 42 minutes with 88% women delivering within 8 hours. Tewari et al using a dose of 40mg HBB for the 1st time given intravenously, though in two divided doses given 20 minutes apart, found labour to be shortened by 5 hours 12 minutes compared to control.81 Most of these earlier studies were
strictly not randomised controlled trials thus reducing the strength of their findings.

Sirohiwal et al working in India, studied 200 pregnant women (both nullipara and multipara) to evaluate the efficacy of 20mg HBB suppositories in shortening the first stage of labour.\textsuperscript{24} It was a prospective study dividing alternate women entering the study into study group and control group. The mean and standard deviation duration of the first stage of labour after 3cm cervical dilation was 123.9 $\pm$ 66.9 minutes in the study group and 368.1 $\pm$ 133.0 minutes in the control group. The difference was statistically significant. There was a highly significant reduction in the duration of the first stage of labour in both nullipara and multipara when compared with the control group. There were no statistical significant differences in the second and third stages of labour in both groups. The neonatal outcome was similar in both groups and the drug was well tolerated by all patients with no adverse effect seen. This study did not evaluate the impact on caesarean section rate.

Samuels et al working in the West Indies studied 129 women to evaluate the effect of HBB on the 1\textsuperscript{st} stage of labour.\textsuperscript{25} Both primigravidas and multigravidas were studied using 20mg of HBB given intravenously. It was a double-blinded, randomised controlled, clinical trial. The mean time for the first stage in the control group was 228 minutes (3.8 hours), compared with 156 minutes (2.6 hours) in the drug group. This represents a decrease of 31.7% which was statistically significant. There was no significant change in the duration of the second and third stage of labour and no difference in blood loss.
The Apgar scores were similar in both groups. There was however, a slightly (though not statistically significant) increase in the caesarean section rate in the study group. Though randomization was done using a computer program, both primigravidas and multigravida were grouped together. Thus the parity state may have influenced the outcome of the study.

Aggarwal et al working in India, while assessing the role of hyoscine butyl bromide as labour analgesia, evaluated its effect in shortening the duration of active phase of labour among 104 primigravidas. It was a prospective randomized control trial. However, randomization was by consecutive randomization, that is alternate women were allocated to test and control groups. Also the allocation of groups was known to the principal investigator. HBB (40mg) given intravenously as a single dose, was used for the study group and normal saline as placebo for the control group. The mean duration of labour was 3 hours 46 minutes in the study group compared to 8 hours 16 minutes in the control group. This represent a decrease of 54.44% which was statistically significant. Fifty women (96%) in the test group had duration of labour less than 8 hours as compared to 18 women (34%) in the control group and these results were statistically significant. The effect on the second and third stage of labour was not assessed. Unlike the finding of Samuels et al., there was a slight increase (though not statistically significant) in the caesarean section rate in the control group. The neonatal outcome was comparable in both groups. No adverse maternal outcome was noted during the study.
Gupta et al. also in India did a study to compare the efficacy of Drotaverine hydrochloride and HBB in the augmentation of labour. It was a prospective randomized study of 150 women (both primigravida and multigravida) in active phase of labour. In this study, active phase labour was defined as cervical dilatation of more than 3cm in the presence of moderate uterine contractions. Randomization to the study group was done using a simple randomization method. A group received 40mg of intramuscular drotaverine hydrochloride, the second group 20mg intravenous hyoscine (given every 30 minutes for a max of 3 doses) while the 3rd group were not given any medication (as the control group). All women with a single cephalic term pregnancy (irrespective of parity) and those with high risk with various medical disorders or bad obstetric history were included in the study. The mean duration of the active phase of labour was $4.48 \pm 2.26$ hours, $3.9 \pm 2.42$ hours and $3.6 \pm 2.07$ hours in group 1, 2 and 3 respectively. The differences were not statistically significant. There was no difference in the duration of the second and third stage of labour. The incidence of postpartum haemorrhage was similar among the 3 groups but they did not report on the effect on caesarean section rate, however, no adverse maternal or foetal outcomes were reported in this study.

Makvandi et al in a recent study on primigravidae reported on the outcome of HBB given per rectum. It was a randomized double-blind placebo-controlled clinical trial using 20mg of HBB rectal suppository. Random number were assigned to each package using a block randomization method (block size = 4). A total of 130 primigravid women admitted in active phase, defined as cervical
dilatation of 3 – 4cm in the presence of moderate uterine contractions, were studied. Those with medical and obstetric conditions were excluded from the study. The study also excluded those who had augmentation of labour using oxytocin. The mean duration of active phase of labour was 141.0 ± 81.7 minutes in the experimental group and 230.1 ± 169.6 minutes in the control group. This represented a decrease of 38.72% which was statistically significant. The mean duration of the second stage of labour was 38.8 ± 24.3 minutes in the experimental group and 51.7 ± 23.8 minutes in the control group. These were all statistically significant. There was no significant difference in the caesarean section rate between the groups. The fetal heart rate, maternal pulse rate, blood pressure and the neonatal APGAR score were similar between the two groups. The drug was well tolerated by all participants and no adverse effect was noted.

Over the years it has been a practice in our Labour Ward to occasionally use Buscopan ostensibly to aid cervical softening and dilatation. This is usually given slowly at a dose of 20mg intravenously in parturients already in established active phase labour. This dose is sometimes repeated after 1 – 2 hours to a maximum of three doses if the desired effect of cervical softening and dilatation is not achieved. From our own experience this seems to be effective in some cases, however, the evidence is mostly anectodal. No clinical trial has been done in our centre to evaluate the value of this practice. Also after a careful search of the literature, not much work have been done on the effect of HBB in the course and outcome of labour in our environment, where prolonged labour and its sequelae is still of concern.
CHAPTER 3

AIMS AND OBJECTIVES

3.1 Justification for the study

Studies from elsewhere have reported conflicting results of the effect of Buscopan® on labour course and outcome. We have occasionally employed Buscopan® given intravenously in our practice at the University of Benin Teaching Hospital, to aid cervical dilatation. The evidence for its efficacy in our practice is largely anectodal.

3.2 Aims and Objectives

a) Primary Objective:- To determine the efficacy of Hyoscine N-Butylbromide (Buscopan®) in reducing the duration of active phase of labour in nulliparous women.

b) Secondary Objective:- To determine the safety of Hyoscine N-Butylbromide (Buscopan®) use (both to the mother and foetus) in labour.

3.3 Working Hypothesis

Hyoscine N-Butylbromide (Buscopan®) is effective in reducing the duration of active phase of labour and its use in labour is safe for both the mother and foetus.
CHAPTER 4
METHODOLOGY

4.1 Patients and Methods

This study was designed as a double-blinded randomized controlled study conducted at the Labour Ward suite of the University of Benin Teaching Hospital (UBTH) Benin City.

4.1.1 Patient recruitment / allocation

Women for the study were recruited from the antenatal clinic of our institution. Informed consent was obtained in the antenatal clinic during the patient routine antenatal visits at 36 weeks gestation. This was after the purpose, procedure, benefits, discomfort, risks and precautions associated with the study has been fully explained to the them. Adequate opportunity was provided at that time for women to ask any question or concern regarding the study. It was fully explained to them that their participation is entirely voluntary. Also, if they were unwilling at any point to participate, they were completely at liberty to refuse to, and they were assured that it would not be held against them in any way, then or in future, in their management in UBTH.

4.1.2 Patient assessment

At presentation in labour, those who had provided written consent were then assessed for enrolment into the study. Those found to be in active phase labour, defined as cervical dilatation of \( \geq 4 \text{cm} \) in the presence of at least one palpable uterine contractions in 10 minutes, were then recruited based on the inclusion criteria listed below.
Inclusion criteria

- Nulliparity
- Aged ≥ 18 and <35 years
- Singleton foetus at a gestational age between 37 – 42 weeks (at term)
- Cephalic presentation
- Spontaneous active phase labour with cervical dilatation 4 or 5cm (Early active phase labour)

Exclusion Criteria

- Previous uterine scar
- Antepartum haemorrhage
- Cephalopelvic disproportion (from obvious pelvic deformity)
- Malpresentation
- Spontaneous active phase labour with cervical dilatation ≥6cm
- Twin gestation
- Prior prolonged rupture of membranes
- Pre-eclampsia and other hypertensive disease in pregnancy
- Other medical conditions
4.1.3 **Drug administration**

The syringes containing the drug (Hyoscine Butylbromide in the form of Buscopan® from Boehringer Ingelheim Limited, United Kingdom) and placebo (sterile injection water) were prepared under aseptic condition by a Pharmacist who was not included in the study. It was on a rolling basis (that is batches of five were prepared as additional participants are enrolled). Each syringe prepared in the morning by the pharmacist contained either 2mls of hyoscine butyl bromide (40mg) or 2mls of injection water. Both liquids are colourless, so the syringe containing the drugs was indistinguishable from those containing placebo (injection water). A computer program (SPSS version 15 Random number generator) was used to generate a random sequence of numbers. Sequentially numbered, sterile syringes were then prepared using the random numbers to determine their content; placebo or hyoscine butyl bromide. Only the Pharmacist knew the correlation between the label on the syringes and their content, and only revealed it after the study was completed. The participants (those recruited for the study) received the content of the syringe, given intravenously in 2 doses; 1ml given 30 minutes apart. This was given when they were assessed as being in active phase labour with cervical dilatation of 4 or 5cm as confirmed by the senior registrar (or by principle investigator) in the labour ward. The labour ward staff (midwives, residents and consultants) and the principle investigator were blinded as to whether the active drug or placebo was administered.
4.1.4 **Labour monitoring**

The progress of labour was closely documented, with the conduct of labour for both groups of patients in accordance with our normal Labour Ward protocol which is based on the principle of active management of labour. This entailed a strict diagnosis of active labour, early amniotomy, frequent vaginal assessment (2-4 hours), oxytocin for slow labour progress and one-to-one care. Routine amniotomy was performed at the vaginal examination which confirmed the women in established active phase labour if their foetal membrane had not spontaneously ruptured. According to our labour ward protocol, the second vaginal examination is performed 4 hours after the initial examination (vaginal examination) and then subsequently every 2 hours to assess the progress of labour and all findings were recorded on the partogram maintained throughout the labour. Analgesic in the form of pentazocine and tramadol was given as labour analgesia, as epidural analgesia is not a routine in our centre. Oxytocin augmentation was initiated if the progress of labour (as assessed from the partograph) was unsatisfactory as evidenced by a plotted cervical os dilatation crossing the action line (they also remained as part of the study). Intervention through instrumental or caesarean delivery was dictated by the usual obstetric indications. Intrapartum fetal surveillance (fetal monitoring) was done by intermittent auscultation using Doppler ultrasound (sonicaid) at least every 15 – 30 minutes in the first stage and every 5 minutes in the second stage, as well as the uterine contractions (assessed every 30 minutes). In the presence of high risks for fetal compromise such as abnormal auscultation (bradycardia,
tachycardia or irregular fetal heart rate) or vaginal bleeding, a continuous electronic fetal monitoring was used. Neonatal APGAR score was determined 1 and 5 minutes after birth.

All sheets (containing the raw data obtained during the study) were collected and kept in a filling drawer. At the end of the study, the data was disaggregated using the record of randomization sequence and the label on the syringe to sort the participants and their data into the appropriate groups (case and placebo).

4.1.5 **Assessment of adverse effects**

The women were educated on the symptoms of possible adverse drug reaction and were counselled to notify the labour ward nursing staff or the attending doctor if ever noticed. Their vital signs (pulse rate, blood pressure, respiratory rate and temperature) were checked regularly. An ophthalmologist was available to review those with visual symptoms or signs.

4.1.6 **Termination of Study**

If any of the conditions listed below was noticed in the course of the study, such patient was withdrawn from the study:

- Patients desire to withdraw from the study for whatever reason(s)
- Those wrongly recruited based on the inclusion and exclusion criteria.
- Those with adverse drug reaction noticed in the course of the study.
4.2 Sample Size

Sample sizes for the control and study group was determined using previous studies as a guide, with the formula:\(^8^2\)

\[
n = \frac{(u + v)^2 (\sigma_1^2 + \sigma_0^2)}{(\mu_1 - \mu_0)^2}
\]

Where

- \(n\) = required minimum sample size
- \(u\) = one–sided percentage point of the normal distribution corresponding to, 100% - the power.

Thus, since power for this study is 95%

100% -95% = 5%, therefore \(u = 1.64\)

- \(v\) = percentage of the normal distribution corresponding to the required two sided) significance level.

Thus, since the significance level for the study = 5%,

\(v = 1.96\)

\(\mu_1 - \mu_0\) = Difference between the means. For this study a duration of 60 minutes was considered as the smallest clinically significant difference.

\(\sigma_1\ \sigma_0\) = Standard deviation. The standard deviation of 80.7minutes (for the study group) and 96.0minutes (the control group) for nulliparous selected from the study performed by Sirohiwal et al in 2005 was used.
Therefore,

\[ n = (1.64 + 1.96)^2 \left( 80.7^2 + 96.0^2 \right) \]

\[ 60^2 \]

\[ = (12.96) \times (6512.49 + 9216) \]

\[ 3600 \]

\[ = 203841.2304 \]

\[ 3600 \]

\[ = 56.6 \]

A minimum of 60 women was required in both the study and control arm.

4.3 Data Management and Statistical Analysis

Data obtained were fed into a Personal Computer (PC) and analysed using the Statistical Package for Social Sciences (SPSS) software, version 15 (2006, SPSS Inc, Chicago IL, USA). Absolute and relative frequencies was determined for categorical variables while mean and standard deviation would be determined for continuous variables. Continuous variable was analysed by student t test and \( \chi^2 \) test (chi square test) was used for categorical variable. Were the \( \chi^2 \) test could not be applied for categorical variables, such as the 1\textsuperscript{st} and 5\textsuperscript{th} minutes APGAR score, the Mann-Whitney test was used to evaluate the level of significance. With a confidence interval of 95\%, a \( p \) value of < 0.05 was considered statistically significant.
4.4 Ethical Consideration

Ethical approval for the study was obtained from the Ethical Committee of the University of Benin Teaching Hospital, Benin City. In seeking the approval, it was clearly stated that patients confidentiality would be maintained. Patients were not identified by name on the data extraction sheet. The responsibility to do and maximise good and do no harm was assured. All patient received standard clinical care and none faced additional risk on account of this study. Also, fairness and equity in the care to all participants in the study was assured.

4.5 Limitations of the study

One obvious limitation of this study was the difficulty in making an exact evaluation of cervical os dilatation. This is due to inter- and intra-personal observer variation in making this assessment. However, the assessment was made by just two senior registrars (the main investigator and the labour ward senior registrar). Another limitation was the difficulty in knowing the exact time of full cervical dilation since hourly assessment was not done. This might have affected the calculation of the duration of the first stage of labour and consequently the cervical dilatation rate. However, the admission-delivery interval was not affected by this. Also blood loss evaluation was another limitation. This was done by visual evaluation in both groups.
4.6 **Work Plan**

The work was commenced in April 2012 though patient recruitment from the antenatal clinic commenced in March 2012. The study ran for a duration of 4 months. I was personally involved in counselling and recruitment of the women for the study. All questions and concerns raised were handled by me. I did over 40% of the 1st vaginal examination of the women recruited and was present at most of their delivery. I as well as other labour ward staff was blinded from the content of the syringes to remove any bias. History of neonatal admission into SCBU within 1 week of birth was retrieved from the babies case note or by direct information from the parturient by phone call. Data extracted was analysed by me. I am presenting the completed work for the May 2013 Part II examination of the National Postgraduate Medical College of Nigeria.
CHAPTER 5

RESULTS

A total of 128 nulliparous women who met the criteria for the study and gave consent were recruited. After the data were disaggregated using the record of randomization sequence, a total of 62 nulliparous women formed the buscopan group while 66 nulliparous women formed the control group.

Sociodemography

Table I showed the sociodemographic characteristic of the study population. The age in both the study group and control group were comparable with a p value of 0.91. The mean age of the study group was 28.4± 2.7 years while that of the control was 28.4± 2.9. The educational status, social class and previous history of pregnancy in both the study group and control were comparable with p. values of 0.41, 0.09 and 0.06 respectively. The mean body weight of the study group was 79.8± 11.6 kilogram while that of the control was 78.1± 9.5 kilogram. These were comparable with a p. value of 0.361. Also, the body mass index between the study group and the control were also comparable. The two groups were also comparable in terms of history of rupture of membrane before presentation, gestational age and cervical dilatation at presentation (Table I).
Duration of the Stages of Labour

The mean ± standard deviation duration of the active phase was 377.2±166.4 minutes in the study group and 412.7±160.6 minutes in the control group. This difference was not statistically significant (p = 0.24; 95% CI 24.5 to 95.3). There was no statistical difference in the duration of the second and the third stages of labour in the two groups (Table II). The rate of cervical dilatation was 1.11±0.53 cm/hr in the study group and 0.94±0.36 cm/hr in the control group (p = 0.05; 95% CI 0.003 to 0.33) and this was not statistically different. Since the exact time of full cervical dilation is difficult to ascertain, the admission (into active phase) delivery interval was compared in the two groups. The mean ± standard deviation duration in the study group was 414.9±169.9 minutes while in the control group it was 438.4±161.8 minutes (p = 0.445; 95% CI 37.2 to 84.3). This was not statistically significant. Thirty-six women (62.1%) in the study group had a duration of labour less than 8 hours as compared to 46 women (78%) in the control group, and this result was not statistically significant (OR = 2.16, p value = 0.06).
### Table I: Sociodemographic Characteristics of Study Population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study Group (Buscopan Group)</th>
<th>Control Group (Placebo Group)</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Age(yrs) (mean value ±SD)</td>
<td>28.4± 2.7</td>
<td>28.4± 2.9</td>
<td>0.913</td>
</tr>
<tr>
<td>2 Level of education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Nil</td>
<td>O (0%)</td>
<td>O (0%)</td>
<td>O.409</td>
</tr>
<tr>
<td>b) Primary</td>
<td>O (0%)</td>
<td>O (0%)</td>
<td></td>
</tr>
<tr>
<td>c) Secondary</td>
<td>11 (17.7%)</td>
<td>9 (13.6%)</td>
<td></td>
</tr>
<tr>
<td>d) Tertiary</td>
<td>51 (82.3%)</td>
<td>57 (86.4%)</td>
<td></td>
</tr>
<tr>
<td>3 Social class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>11 (17.7%)</td>
<td>23 (34.8%)</td>
<td>0.091</td>
</tr>
<tr>
<td>Class II</td>
<td>40 (64.5%)</td>
<td>34 (51.5%)</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>11 (17.7%)</td>
<td>9 (13.6%)</td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Class V</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>4 History of previous Pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Yes</td>
<td>30 (48.4%)</td>
<td>43 (65.2%)</td>
<td>0.056</td>
</tr>
<tr>
<td>b) No</td>
<td>32 (51.6%)</td>
<td>23 (34.8%)</td>
<td></td>
</tr>
<tr>
<td>5 Body weight (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean value ± SD</td>
<td>79.8±11.6</td>
<td>78.1±9.5</td>
<td>0.361</td>
</tr>
<tr>
<td>6 Body mass index (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean value ± SD</td>
<td>29.2±4.0</td>
<td>29.0±3.8</td>
<td>0.761</td>
</tr>
<tr>
<td>7 Gestational age (days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean value ± SD</td>
<td>277.1±7.9</td>
<td>279.2±6.6</td>
<td>0.098</td>
</tr>
<tr>
<td>8 Rupture of memb before presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Yes</td>
<td>1 (1.6%)</td>
<td>1 (1.5%)</td>
<td>0.964</td>
</tr>
<tr>
<td>b) No</td>
<td>61 (98.4%)</td>
<td>65 (98.5%)</td>
<td></td>
</tr>
<tr>
<td>9 Cervical dilation at presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) 4cm</td>
<td>44 (71.0%)</td>
<td>43 (65.2%)</td>
<td>0.481</td>
</tr>
<tr>
<td>b) 5cm</td>
<td>18 (29.0%)</td>
<td>23 (34.8%)</td>
<td></td>
</tr>
</tbody>
</table>
Table II: Duration of the Stages of labour

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Study Group (Buscopan Group)</th>
<th>Control Group (Placebo Group)</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 1st stage (Active phase) (minutes)</td>
<td>377.2± 166.4</td>
<td>412.7± 160.6</td>
<td>0.244</td>
</tr>
<tr>
<td>2 2nd stage (minutes)</td>
<td>27.3± 9.6</td>
<td>25.8± 8.4</td>
<td>0.351</td>
</tr>
<tr>
<td>3 Admission to delivery interval (minutes)</td>
<td>414.9± 169.9</td>
<td>438.4± 161.8</td>
<td>0.445</td>
</tr>
<tr>
<td>4 3rd stage</td>
<td>4.1± 1.1</td>
<td>4.1± 1.0</td>
<td>0.792</td>
</tr>
<tr>
<td>5 Cervical dilatation rate (cm/hr)</td>
<td>1.1± 0.53</td>
<td>0.94± 0.36</td>
<td>0.046</td>
</tr>
<tr>
<td>6 Delivery duration n(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before 8hours</td>
<td>36 (62.1%)</td>
<td>46 (78%)</td>
<td>0.060</td>
</tr>
<tr>
<td>After 8hrs</td>
<td>22 (37.9%)</td>
<td>13 (22 %)</td>
<td></td>
</tr>
</tbody>
</table>

*Values are given as mean± SD, unless otherwise indicated.

Augmentation of Labour

Progress of labour was adjudged unsatisfactory (slow) in 76 women based on their cervical dilation plotted on their partogram crossing the action during their intrapartum monitoring. Augmentation of labour was thus ordered; 34 representing 54.8% in the study group and 42 representing 63.6% in the control
group. When compared, this was not statically significant ($p$ value = 0.31).

Eighteen women in the study group (52.9%) had their augmentation of labour less than 4 hours as compared to 27 women (64.3%) in the control group. This was not statistically significant ($p$ value=0.32). Table III.

In a subanalysis of the group without augmentation of labour (Table IV), the duration of the first stage of labour was $230.56 \pm 72.01$ minutes in the study group and $272.92 \pm 73.34$ minutes in the control group ($p = 0.043$; 95% CI of 1.41 to 83.31). This was statistically significant. The rate of cervical dilation in the study group was $1.53 \pm 0.50$ cm/hr and $1.24 \pm 0.34$ cm/hr in the control group ($p = 0.02$; 95% CI 0.04 to 0.53). This was also statistically significant. There was no significant difference in the duration of the second and third stage of labour between the study and control groups.

For the group who had their labour augmented with oxytocin, the findings are different. The duration of the different stages of labour, the admission to delivery interval and the rate of cervical dilation were not statistically different between the study and control group. Table V.

**Mode of delivery and neonatal outcome**

Table VI showed the mode of delivery and outcome of the study population. There was no significant statistical difference in the mode of delivery between the two study group ($p$ value = 0.59). There was a slight increase in the caesarean section rate in the control group compared to the study group (10.6% versus 6.5%), but this failed to achieve statistical difference (OR= 1.72, $p$ value = 0.59). The indications for the caesarean section were cervical stasis (4),
cephalopelvic disproportion (4) and fetal distress (3). This was comparable in both study group (p value = 0.76). There were 3 cases of instrumental deliveries, 1 forceps delivery for intrapartum pre-eclampsia and 2 vacuum extractions for poor maternal effort in 2\textsuperscript{nd} stage. After excluding those with caesarean section, the mean ± standard deviation blood loss was 170.5 ± 25.2ml in the study group and 196.4 ± 94.4ml in the control group. The difference was statistically significant. (p value = 0.046), however there was no incidence of primary post partum haemorrhage in both groups.

There was no significant statistical difference in the APGAR scores noted in 1 and 5 minutes (p values = 0.58 and 0.26 respectively). There were 5 cases of moderate to severe birth asphyxia in the control compared to 1 case of moderate asphyxia in the study group. These babies were all discharged in good condition. One neonate in the study group was admitted into SCBU for asphyxia (moderate) with hypoglycaemia while in the control group 2 neonates were admitted into SCBU for asphyxia with hypoglycaemia and another 2 neonates admitted for neonatal sepsis. All the neonate did well and were discharged in good condition.
### Table III: Comparison of Augmentation of labour

<table>
<thead>
<tr>
<th></th>
<th>Study Group (Buscopan Group)</th>
<th>Control Group (Placebo Group)</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Labour augmented</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>34 (54.8%)</td>
<td>42 (63.6%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>28 (45.2%)</td>
<td>24 (36.4%)</td>
</tr>
<tr>
<td>2</td>
<td>Duration of augmentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;4hours</td>
<td>27 (64.3%)</td>
<td>18 (52.9%)</td>
</tr>
<tr>
<td></td>
<td>&gt;4hours</td>
<td>15 (35.7%)</td>
<td>16 (47.1%)</td>
</tr>
</tbody>
</table>

### Table IV: Duration of Labour in those without Augmentation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Group (Buscopan Group)</th>
<th>Control Group (Placebo Group)</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 1st stage (Active Phase)</td>
<td>230.56± 70.01</td>
<td>272.92± 73.35</td>
<td>0.043</td>
</tr>
<tr>
<td>2 2nd stage (minutes)</td>
<td>28.78± 9.07</td>
<td>26.12± 6.25</td>
<td>0.236</td>
</tr>
<tr>
<td>3 3rd stage (minutes)</td>
<td>4.74± 0.656</td>
<td>4.33± 0.816</td>
<td>0.054</td>
</tr>
<tr>
<td>4 Admission Delivery</td>
<td>259.33± 73.85</td>
<td>299.04± 77.74</td>
<td>0.067</td>
</tr>
<tr>
<td>5 Cervical dilatation rate cm/hr</td>
<td>1.53± 0.50</td>
<td>1.24± 0.34</td>
<td>0.02</td>
</tr>
</tbody>
</table>

a values are given as mean ± SD, unless otherwise indicated.
### Table V: Duration of Labour in those with Augmentation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Group (Buscopan Group)</th>
<th>Control Group (Placebo Group)</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st stage (Active Phase) (minutes)</td>
<td>505± 109.08</td>
<td>508.49± 130.93</td>
<td>0.908</td>
</tr>
<tr>
<td>2nd stage (minutes)</td>
<td>26.1± 10.12</td>
<td>25.54± 9.61</td>
<td>0.820</td>
</tr>
<tr>
<td>3rd stage (minutes)</td>
<td>3.45± 0.1</td>
<td>3.94± 1.06</td>
<td>0.057</td>
</tr>
<tr>
<td>Admission Delivery (minutes)</td>
<td>531.0± 113.15</td>
<td>534.03± 132.06</td>
<td>0.924</td>
</tr>
<tr>
<td>Cervical dilatation rate cm/hr</td>
<td>0.75± 0.18</td>
<td>0.74± 0.17</td>
<td>0.79</td>
</tr>
</tbody>
</table>

*a* values are given as mean ± SD, unless otherwise indicated.

### Table VI: Mode of Delivery and Outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Group (Buscopan Group)</th>
<th>Control Group (Placebo Group)</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode Of Delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I) SVD</td>
<td>56 (90.3%)</td>
<td>58 (87.9%)</td>
<td>0.588</td>
</tr>
<tr>
<td>II) Instrumental</td>
<td>2 (3.2%)</td>
<td>1 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>III) Caesarean</td>
<td>4 (6.5%)</td>
<td>7 (10.6%)</td>
<td></td>
</tr>
<tr>
<td>Blood lose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± s.d (excluding c/s)</td>
<td>170.5 ± 25.2</td>
<td>196.4 ± 94.4</td>
<td>0.046</td>
</tr>
<tr>
<td>Neonatal outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i) Apgar score @ 1 min. median (range)</td>
<td>8 (5 - 9)</td>
<td>8 (3-9)</td>
<td>0.578</td>
</tr>
<tr>
<td>ii) Apgar score at 5 min. median (range)</td>
<td>9 (7 - 9)</td>
<td>9 (6-9)</td>
<td>0.261</td>
</tr>
<tr>
<td>iii) SCBU admonition Yes</td>
<td>1 (1.6%)</td>
<td>4(6.1%)</td>
<td>0.194</td>
</tr>
<tr>
<td>No</td>
<td>61 (98.4%)</td>
<td>62(93.9%)</td>
<td></td>
</tr>
</tbody>
</table>
Response of Maternal and Fetal Vital Signs to Administration of Drug/Placebo

There was no significant difference in the fetal heart rate between the two groups within an hour of administration of the buscopen or placebo. There were only 3 reported cases of fetal heart rate irregularities (2 in the control group and 1 in the study group) for which caesarean delivery was done. All the babies did well and were discharged in good condition. There was no significant statistical difference between the groups in the maternal pulse rate, systolic blood pressure and diastolic blood pressure (Table V), within one hour of admission. Significant blood pressure elevation (BP ≥ 140/90mmHg) was recorded in 12.9% in the study and 18.2% in the control group. This was not statistically significant (p value = 0.41). There was however no history of eclampsia and only one needed forcep delivery to shorten her second stage due to the intrapartum pre-eclampsia. Though there was slight improvement in the contraction frequency of the control, 48 (72.7%) versus 38 (61.3%), this did not reach statistical significance (p value = 0.168) (Not shown in the table). The drug was well tolerated by all patient and the only adverse effect noted was dry mouth which occur in 4 (6.5%) women in the study group as against 6 (9.1%) in the control group. This was not statistically significant (p value = 0.578) and was only noted in patients whose labour lasted beyond eight hours. The effect of dehydration of the labour was not ruled out.
Effect of Previous Abortion on the Outcome

Table VI showed the effect of previous abortion (either induced or spontaneous) on the duration of the 1\textsuperscript{st} stage, admission-delivery interval and on the rate of cervical dilatation in the study population. There were no significant statistical differences in the outcome of the above mentioned variables.

### Table VII: Fetal and maternal response in vital signs within 1 hour after administration of buscopan or placebo \(^a\)

<table>
<thead>
<tr>
<th>Vital Signs</th>
<th>Study Group (Buscopan Group)</th>
<th>Control Group (Placebo Group)</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Fetal heart rate</td>
<td>142.1±4.0</td>
<td>142.1±4.0</td>
<td>0.933</td>
</tr>
<tr>
<td>2 Maternal pulse rate</td>
<td>84.4±4.9</td>
<td>83.9±5.8</td>
<td>0.642</td>
</tr>
<tr>
<td>3 Systolic bld pressure</td>
<td>120.5±7.8</td>
<td>121.2±12.7</td>
<td>0.699</td>
</tr>
<tr>
<td>4 Diastolic bld pressure</td>
<td>74.2±7.8</td>
<td>76.8±6.4</td>
<td>0.071</td>
</tr>
<tr>
<td>5 Blood pressure (BP≥140/90mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>8 (12.9%)</td>
<td>12 (18.2%)</td>
<td>0.411</td>
</tr>
<tr>
<td>No</td>
<td>54 (87.1%)</td>
<td>56 (81.8%)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) values are given as mean ± SD, unless otherwise indicated.
Table VIII: Effect of Previous Abortion on the Outcome a

<table>
<thead>
<tr>
<th></th>
<th>Outcome</th>
<th>Primigravidge</th>
<th>Hx of Previous Abortion</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1st stage (minutes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i) Buscopan group</td>
<td>402.9±183.2</td>
<td>347.8±142.6</td>
<td>0.211</td>
</tr>
<tr>
<td></td>
<td>ii) Control group</td>
<td>370.7±206</td>
<td>437.6±122.9</td>
<td>0.177</td>
</tr>
<tr>
<td></td>
<td>2 cervical dilation rate (cm/hr)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i) Buscopan group</td>
<td>1.1±0.5</td>
<td>1.0±0.4</td>
<td>0.331</td>
</tr>
<tr>
<td></td>
<td>ii) Control group</td>
<td>1.1±0.5</td>
<td>1.3±0.3</td>
<td>0.214</td>
</tr>
<tr>
<td></td>
<td>3 Admission–delivery interval (minutes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i) Buscopan group</td>
<td>448.8±187.4</td>
<td>376.8±140.8</td>
<td>0.104</td>
</tr>
<tr>
<td></td>
<td>ii) control group</td>
<td>397.6±209.8</td>
<td>462.8±122.0</td>
<td>0.193</td>
</tr>
</tbody>
</table>

a values are given as mean ± SD, unless otherwise indicated.
CHAPTER 6
DISCUSSION

Various drugs and nonpharmacological methods have been introduced to shorten the duration of labour and reduce the maternal and neonatal morbidity. Hyoscine-N-butyl bromide, a muscarinic antagonist that acts as a cervical spasmylytic agent, has been used to shorten the duration of labour. This practice which is common in several hospitals in the West Indies, India and the middle East, is also done in our centre at the university of Benin Teaching Hospital. This study which was carried out to validate this practice showed no significant shortening of the duration of the different stages of labour or improved rate of cervical dilatation when the entire study population was analysed. However on subanalysis of the group who had no augmentation of labour, there was a significant shortening of the duration of the first stage of labour and an improved rate of cervical dilatation.

The lack of statistical difference showed in duration of active phase labour between study and control group shown in this study are in constrast to the report by serohiwal et al.\textsuperscript{24} who found a shorter duration of the first stage of labour in nulliparas who had Buscopan in early labour. Similar observations of significant reduction in the duration of the first stage of labour with hyoscine N-butyl bromide were also reported by Bhattacharya et al.,\textsuperscript{19} Samuels et al.\textsuperscript{25} and Makvandi et al.\textsuperscript{28} These differences could be attributed to differences in methodologies. Sarohiwal, recruited all women who were in active labour with
cervical os dilatation of 3cm or more. There was no restriction on the extent of cervical os dilatation. Also, in the work by Samuels et al and Makvandi et al, there was no mention of a strict exclusion criteria of those whose cervical os dilatation was over 5cm. Recruiting parturients with advanced cervical os dilatation may have influenced their outcome. Our findings of no difference in labour duration between the study and control group is however similar to earlier report by Gupta et al, 27 and Al Dohams and Al Matar.83

In this study we noted a high rate of augmentation of labour with oxytocin both in the study and the control group. This is a sharp constrast to that noted by Samuels et al were the augmentation rate in the study group was 5% verses 11.6% in the control group.25 this differences in observation our study and the previous studies could be attributed to the strict diagnostic criteria of active phase labour adopted in our study. The assessment of cervical os dilatation at admission was done by a senior registrar thus reducing the chances of recruiting those whose cervical os dilatation were already greater than 5cm. Including those with cervical os dilatation greater than 5cm would mean enrolling those already in the rapid phase of cervical dilatation,24 and could therefore affect the outcome thus the observed difference between our study and theirs.19,24,25&28 This strict diagnosis of active phase of labour is one of the cardinal points in the active management of labour.55 This could also have accounted for the much higher duration of active phase labour noted in our study. It is noteworthy however, that
the duration of active phase is within the recommended average duration of 8 hours for the 1st stage of labour by NICE.\textsuperscript{84}

A subanalysis of patients (study and control group) who were not augmented was done to evaluate the effect of Buscopan on those without uterine contractile abnormality. We found that the cervical dilatation rate was significantly higher in the study group with consequent shorter duration of labour. This probably highlighted the effect of Buscopan more, than taking both augmented and non-augmented parturient together, as the expected site of activity of Buscopan is in the cervix. Contractile abnormality is a myometrial issue hence Buscopan did not affect duration of labour among augmented patient. This may have impacted on the statistics of this study when all the patients were considered together.

There was no significant difference in the duration of the second and third stages of labour between the study and control groups. This is similar to findings in previous studies\textsuperscript{24-27}. The rate of caesarean section in both the study group and the control group are comparable and this is similar to that reported by Makwandi et al. The caesarean section rate noted is also below the recommended WHO caesarean section rate of 10-15\%\textsuperscript{85}, a fact that could be attributed to the protocol of active management of labour used in our centre. The blood loss in both groups is comparable with no incidence of postpartum haemorrhage recorded. This rules out any adverse effect on the contractility of the uterus in the postpartum period. Interestingly also, the changes in the
contraction frequency following the administration of the buscopan or placebo were similar.

Apart from 3 parturients whose fetuses demonstrated fetal heart irregularities (1 in the study group and 2 in the control group), the fetal heart rate pattern (rate and variability) were normal. This is unlike that reported by Iravani and Bekhradinasab. Makvandi et al had suggested that the changes could be due to the intravenous route of administration used by Iravani and Bekhradinasab. However, this study used similar intravenous route and even a higher dose, but no such changes were noted. Although our study was not sufficiently powered to assess adverse neonatal outcome, the initial examination of each neonate, their Apgar score in 1 minute and 5 minutes after birth, showed no differences between the study and control groups. The maternal vital signs response in both groups was similar. This demonstrates the safety of the drugs to both the fetus and the parturient.
CHAPTER 7

CONCLUSION AND RECOMMENDATION

This study was able to demonstrate the efficacy of hyoscine-N-butylbromide in the form of buscopan in reducing the duration of the first stage (active phase) of labour among nulliparous women who had no contractile abnormalities. However, no efficacy was demonstrated when the entire study population was analysed. The study demonstrated the safety of the drugs to both the mother and their neonate.

Further multicentre study with large number of study and control group is recommended to confirm or refute the findings of this study. It may also be necessary to evaluate the benefit among multiparous women in labour.
REFERENCES


74. Drug Information: Buscopan®. Ingelheim, New Zealand: Boehringer Ingelheim Limited. Revised May 2010


APPENDICES

APPENDIX IA

INFORMED CONSENT FORM

TITLE OF STUDY: THE EFFICACY OF HYOSCINE-N-BUTYL BROMIDE IN ACCELERATION OF LABOUR AMONG NULLIPAROUS WOMEN: A RANDOMIZED DOUBLE-BLINDED PLACEBO-CONTROLLED CLINICAL TRIAL

PRINCIPAL INVESTIGATOR: Dr. Benedict Nyerovwo OGBIMI; Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital.

FINANCIAL SPONSORSHIP: This research project is self-sponsored.

PURPOSE OF THE RESEARCH

It is important you read and understand the following explanation of the proposed study procedures before agreeing to participate. This information describes the purpose, procedures, benefits, discomforts, risks and precautions associated with this study. It also describes your right to refuse to participate or withdraw from the study at any time. In order to decide whether you wish to participate in this research study, you should understand enough about its risks if any and benefits to be able to make an informed decision. This is known as the informed consent process. Please ask that any word(s) you do not understand be explained to you before signing this consent form. Make sure all your questions have been answered to your satisfaction before signing this document.

About the Study: Prolonged labour is still a common problem in our environment and most part of the underdeveloped world, and its sequelae, remains an important cause of maternal morbidity and mortality. With the introduction of active management of labour, which is also practiced at our labour ward, the incidence of prolonged labour and its sequelae has significantly reduced. However, the ideal pattern of labour management and intervention is yet to be determined. Several medications apart from oxytocin, has been used to accelerate labour progress. One of such is Buscopan.
PROCEDURES INVOLVED IN THE STUDY

**What is required?** Apart from this information sheet, you will be given a Consent Form in which you will formalize your willingness to participate. That is required to assure that your participation is entirely voluntary. Thereafter, you will be required to complete a questionnaire at admission into labour ward. This questionnaire has questions about your biodata. At admission into active phase labour you would be administered either 40mg buscopan or 2ml of injection water as placebo. The labour would be monitored in our usual protocol.

**COMPENSATION**
There shall be no financial compensation for participation in this study.

**VOLUNTARY PARTICIPATION**
Please note that your participation in this research is entirely voluntary. If you are unwilling at any point to participate, you are completely at liberty to refuse to, and this will not be held against you in any way, now or in future, in your management in the University of Benin Teaching hospital or any of its affiliated institutions.

**RISKS**
You face no additional risks participating in this study. Buscopan is routinely used in our labour ward to aid cervical dilation with no recorded adverse effect previously.

**BENEFITS**
You may not benefit directly from the study. However, you will receive standard clinical care and you are not facing any additional risks on account of this study.

**CONFIDENTIALITY**
All information obtained will be known only to the investigator. Data will be coded and put in a data bank. There will be no identification of the patient by name while the data is being analyzed. The study result may be published in scientific journal without identifying the subjects by name.
CONTACT INFORMATION

Dr. Ogbimi Benedict  
Department of Obstetrics and Gynaecology,  
University of Benin Teaching Hospital,  
Benin City,  
Phone Number: 08035773968  
Email: benedictogbimi@yahoo.com

Chairman, Ethics and Research Committee,  
University of Benin Teaching Hospital  
Benin City.  
Phone Number: 08181940459  
Telegram: UNITECHOS, BENIN  
Telex: 41120 NG

CERTIFICATE OF CONSENT

I have read the above information (or it has been read to me). I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction.

(A) I consent voluntarily to take part as a participant in this research.

(B) I do not consent to participate in this research

Name of Participant: ________________________________

Signature of Participant: ________________________________

Date: ________________________________
APPENDICES

APPENDIX IB

INFORMED CONSENT FORM

PIDGIN ENGLISH VERSION

NAME OF THE WORK: RANDOMIZED DOUBLE-BLINDED STUDY OF EFFICACY OF HYOSCINE-N-BUTYL BROMIDE IN ACCELERATION OF LABOUR AMONG NULLIPAROUS WOMEN.

The main person who get the work: Dr. Ogbimi Benedict; Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital.

WHO DE PAY FOR THE WORK: Na the main person who get the work na go pay for the work.

THE REASON FOR THE WORK

Before you go join do the work, e dey good make you read and know watin the work dey about. The things wen you go read so go show watin won make us do the work, as we go take do the work, the things wen we go gain, some small things wen you no like wen go fit happen as the work dey go on, wahala wen fit shele and also the things we go do to avoid am. E go still tell you say you get the power not to join the work and also the power to comot from the work any time you want to. For you to agree to join the work, e good make you sabi well, well, the wahala wen fit shele and the better wen you go fit gain. Na this one we dey call 'informed consent process'. Before you put your hand ‘for paper’ say you won do the work, ask anything wen no clear for your mind. I beg, make sure say every thing clear for your mind before you put your hand for paper.

De Work: the condition wen woman wen e one born go de labour past the time wen she suppose to don born e dey well well for our area and many other area wen never open. The wahala wen go fit follow go fit make the woman get many many sickness and go fit still kill the woman. With de way wen oyibo people dey take care of woman wen e dey labour, de same thing wen we de do for here, the problem of women wen de stay tay for labour and the wahala wen dey follow don come down well well. As e come dey na, the real way wen dem suppose take
care of women wen e wen born, dem never know’em. Many medicine apart from the one wen oyibo dey call ‘oxytocin’ wen e dey make women dey quick dey born dey. One of this medicine na’em oyibo dey call Buscopan.

**Wetin dey?**. No be only this paper go tell you watin you suppose know and do for this work, another one still dey wen you go write say you ready to do the work from your mind no be say na by force. After you don put hand for paper, e get the questions wen you go answer the time wen you don dey labour. Wen dem don check you say you don dey labour, dem go come give that injection wen dey de call Buscopan or ordinary water injection. Na the way wen we dey tay take care of women wen e won born, na so we go still take care of you.

**COMPENSATION**

Dey no go give you any money for this work when you wen do so.

**VOLUNTARY PARTICIPATION**

I beg, make you know say, this work wen you won join so, na your mind em come from and no be force dey force you. If you don gree say you won do de work but come say you no go fit do de work again, you go fit comot, wahala no dey. Say because you change you mind, e no go affect the wen dey go take care of you for UBTH or any other hospital when UBTH get.

**RISKS**

Fear no dey say because you dey for this work. De injesjon wen dem dey call Buscopan, na injesjon wen we dey use for here for women wen won born to make dem born quick. Since we de use this injesjon wahala never dey.

**BENEFITS**

Even say you no gain for the work, dem go take care of you and the belle well well. No fear say because you dey for this work.

**CONFIDENTIALITY**

Na only de main person wen dey do de work go know de things wen come out of the work. We go do am the way wen nobody go fit know and wen result don com
out, nobody go know who and who get which result. Even wen we decide to put wetin we see for the work for book, we no go write any body name for the book

CONTACT INFORMATION

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CERTIFICATE OF CONSENT

I don read wetin dem write about the work (or dey don read am to me). Dem give me chance take ask questions about de work and for all de questions I get better answer.

(C) I agree to take part for this work from my own mind

(D) I no agree to take part for this work.

Name of Participant:______________________________

Signature of Participant:____________________________

Date:______________________________
APPENDIX II

DATA EXTRACTION SHEET

A.  i) Hospital No: ________________  ii) Tel No: ________________________
    iii) Age: ________________  iv) Education: ________________________
    v) Occupation: __________  vi) Spouse Occupation: ________________

B.  i) Weight: ________________  ii) Height: _____  iii) BMI: ________________
    iv) Gravidity: ________________  v) Gestational Age ________________

C.  i) SROM before admission: Yes or No
    ii) Cervical dilatation at admission: ________________________________
    iii) FHR at Admission: ________________  iv) 1 hr later: ________________
    v) Pulse Rate at Admission: _______  vi) 1 hr later: ________________
    vii) Bp at Admission: ________________  viii) 1 hr later: ________________

D.  i) Labour Augmentation with oxytocin: Yes or No
    ii) Cervical dilatation at AOL: _________________________________
    iii) Highest dose of oxytocin: _________________________________
    iv) Duration of AOL: _________________________________

E.  i) Mode of Delivery: SVD/Forceps/Vacuum/C-section
    ii) If not SVD, indicate: ________________________________

F.  i) Duration of Active phase (1st stage) ______________________________
    ii) Duration of 2nd stage: ________________________________
    iii) Problems in 2nd stage Yes or No  iv) Nature: ________________

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v) Duration of 3rd stage: ________________________________

vi) Problems in 3rd stage Yes or No vii) Nature: ________

viii) Admission to Delivery Interval: ________________________________

ix) Total blood loss: ________________________________

xiii) Immediate medical problem: HBP/Eclampsia

G. i) Birth Weight: ________________________________

ii) APGAR score: ________________________________

iii) Admission into SCBU: ________________________________

iv) History of NNJ: Yes or No

vi) History of NNS: Yes or No

H. Side Effects/Adverse Effect of Buscopan (Tick)
   i) Xerostomia (Dry mouth)

   ii) Dyshidrosis

   iii) Visual disorder

   iv) Flushing

   v) Skin reaction

   vi) Angioedema

   vii) Anaphylactic reaction/shock

   viii) Dyspnoea
APPENDIX III

SCORING SYSTEM FOR SOCIAL CLASS

A. Husband's occupation

Score: 1. Professionals, top civil servants, politicians and businessmen.

2. Middle-level bureaucrats, technicians, skilled artisans and well-to-do traders

3. Unskilled workers and those in general whose income would be at or below the national minimum wage.

B. Level of education attainment

Score: 0. Education up to university level

1. Secondary or tertiary level below the university (e.g. college of education, school of nursing etc).

2. No schooling or up to primary level only.

SOCIAL CLASS = Score A + Score B.

APPENDIX V

ETHICS AND RESEARCH COMMITTEE APPROVAL

UNIVERSITY OF BENIN TEACHING HOSPITAL
P.M.B. 1111 BENIN CITY NIGERIA

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CHAIRMAN:
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ETHICS AND RESEARCH COMMITTEE CLEARANCE CERTIFICATE

PROTOCOL NUMBER: ADM/E 22/A/VOL. VII/764

PROJECT TITLE: “THE EFFICACY OF HYOSCINE-N-BUTYL BROMIDE IN ACCELERATION OF LABOUR AMONG NULLIPAROUS WOMEN: A RANDOMIZED DOUBLE-BLINDED PLACEBO-CONTROLLED CLINICAL TRIAL”

PRINCIPAL INVESTIGATOR(S): DR. BENEDICT NYEROVWO OGBIMI

DEPARTMENT/INSTITUTION: DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY, UNIVERSITY OF BENIN TEACHING HOSPITAL, BENIN CITY

DATE CONSIDERED: NOVEMBER 10, 2011

DECISION OF THE COMMITTEE: APPROVED

REMARK:
CHAIRMAN: PROF. M.N. OKOBIA
SIGNATURE & DATE: 10/11/2011
SUPERVISORS: PROF. A.E. ORHUE, PROF. A.B.A. ANDE, DR. M.E. AZIKEN

DECLARATION BY INVESTIGATOR(S)
PROTOCOL NUMBER (please quote in all enquiries)

To be completed in four and three copies returned to the secretary, Ethics and Research committee, Clinical services and Training Division. University of Benin Teaching Hospital Benin City.

I/We fully understand the conditions under which I am/we are authorized to conduct the above mentioned research and I/We undertake to resubmit the protocol to the Ethics and Research Committee.

Signature: ____________________________ Date: 16/11/2011