

(RESEARCH ARTICLE)



Prevention of prolonged labour in term nulliparas with oxytocin alone versus with oxytocin and an antispasmodic

Awopola Ibiebelem Jumbo ^{1,*}, Esther Ijeoma Nonye-Enyidah ¹, Rose Sitonma Iwo-Amah ¹, Nonyenim Solomon Enyidah ², Bapakaye Ngeri ¹, Chinweowa Ohaka ¹, Roseline Beauty Iheagwam ¹ and Peacebe Sunday Abere ¹

¹ Department of Obstetrics and Gynaecology, Rivers State University Teaching Hospital, Port-Harcourt, Nigeria.

² Department of Internal Medicine, Rivers State University, Port-Harcourt, Nigeria.

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Abstract

Background: Poor progress of labour is a common problem with nulliparous deliveries. It occurs when the cervical dilatation rate in the active phase of the first stage of labour is <1cm/hr, and is mainly due to poor uterine contractions or slow cervical dilatation. Without interventions, poor progress could degenerate into prolonged labour which is associated with increased maternal and perinatal morbidity and mortality.

Augmentation of labour with oxytocin is the traditional management for poor progress as it enhances uterine contractions. At times, despite adequate uterine contractions poor progress will persist due to cervical smooth muscle spasms. Antispasmodics can relieve smooth muscle spasms.

Aim/objective: This study compared the duration of labour in term nulliparous parturients with poor progress following augmentation with oxytocin alone versus with oxytocin and an antispasmodic (drotaverine).

Methods: The study was a single-blinded randomized controlled trial involving 156 term nulliparous parturients with poor progress of labour, that were randomized into two groups in eight months. Each group had 78 parturients which were augmented with either oxytocin with placebo or oxytocin with drotaverine. They were monitored until delivery and the duration of labour in both groups after the intervention was compared. Data obtained were analysed using SPSS version 23 software. The level of significance was set at 0.05.

Results: The two groups were similar in their sociodemographic characteristics, and the mean pre-intervention duration of labour was also similar (6.02 ±2.04 vs. 6.09± 2.07hr p=0.23). In this study 135(86.5%) parturients had vaginal delivery while 21(13.5%) had emergency caesarean section. Among those who had a vaginal delivery, the mean duration of labour following augmentation was significantly shorter in the oxytocin-drotaverine group than in the oxytocin-placebo group (6.20 ±0.40hrs vs. 6.64±0.34hrs, MD- 26.4minutes, p<0.01). There was no difference in the duration of the second stage of labour in both groups.

Conclusion: The use of drotaverine with oxytocin in managing poor progress of labour in term nulliparous women leads to a significantly shorter duration of the first stage of labour than oxytocin alone.

Keywords: Poor progress; Prolonged labour; Augmentation; Drotaverine; Oxytocin

* Corresponding author: Jumbo Awopola Ibiebelem

1. Introduction

Labour is a natural process of childbirth occurring after foetal viability. It is characterised by regular painful palpable uterine contractions, effacement and dilatation of the cervix, the descent of the presenting part and delivery of the baby and placenta per vaginam [1]. The time of onset of labour is a critical determinant of perinatal outcome. Normal labour occurs at term which is a period between 37-42 weeks during which neonatal outcome is optimal [2].

Labour is divided into the first, second and third stages [1,3]. The first stage begins from the onset of labour to full cervical dilatation (10cm) and is subdivided into the latent and active phases [1,3]. The latent phase is characterised by progressive effacement and slow cervical dilatation up to 3cm, while the active phase begins from 4cm cervical dilation and has a rapid cervical dilatation rate of at least 1cm/hr [3-5].

Poor progress of labour occurs when the cervical dilatation rate in the active phase is slower than 1cm/hour [4,6]. If no intervention, poor progress may degenerate into an arrest in cervical dilatation or progress to prolonged labour [4,6]. Prolonged labour occurs when the active phase of the first stage of labour last more than 12 hours, and is associated with significant maternal and perinatal morbidity and mortality [2,7]. Prolonged labour occurs mainly due to problems with uterine contractions or cervical dilatation [8,9]. The total duration of labour is largely determined by the duration of the active phase of labour [2].

Active management of labour (AML) was introduced to reduce the incidence of prolonged labour [10]. Amniotomy and oxytocin augmentation are essential components of the AML and are the traditional modality of preventing prolonged labour in women with poor progress as they improve uterine contractions [2,9]. In some cases, in spite of adequate uterine contractions slow progress of labour persists due to cervical smooth muscle spasms [8,9]. Cervical smooth muscle spasms are a major contributor to prolonged labour [9,11].

Antispasmodics are agents used to relieve smooth muscle spasms. They may be effective in relieving cervical smooth muscle spasms that occur in labour but are hardly used with oxytocin for the prevention of prolonged labour [12,13]. Antispasmodics can be neurotropic or musculotropic [12,13].

Neurotropic antispasmodics relieve smooth muscle spasms by antagonising acetylcholine on the muscarinic receptors of the nerve endings supplying the muscle, while musculotropic antispasmodics act directly on the smooth muscle to inhibit phosphodiesterase type IV enzymes [12,13].

An antispasmodic agent that is suitable for labour should have a quick onset of action, a long duration of action, and no adverse effect on the mother and foetus [14]. In search of an ideal antispasmodics for labour, drotaverine a superior musculotropic antispasmodic agent has excellent pharmacokinetics [14,15]. The onset of action is 30 minutes, the duration of action is 4 hours, and it has no harmful effect on the mother or foetus. Compared with other antispasmodics drotaverine has minimal side effect profile [14,15]. Since drotaverine has the potential of relieving cervical smooth muscle spasms, its use with oxytocin may lead to faster cervical dilatation with uterine contraction and thus reduce the incidence of prolonged labour. However, this combination has hardly been tried in preventing prolonged labour.

Aim/objective

The study compared the mean duration of labour in term nulliparas with poor progress of labour augmented with oxytocin alone versus with oxytocin and drotaverine.

1.1. Study hypothesis

H₀1: There is no difference in the mean duration of the active phase of labour in term nulliparas with poor progress of labour augmented with oxytocin alone versus with oxytocin and drotaverine.

H_A1: There is a difference in the mean duration of the active phase of labour in term nulliparas with poor progress of labour augmented with oxytocin alone versus with oxytocin and drotaverine.

2. Methodology

2.1. Study Area

The study was carried out at the labour ward of the Rivers State University Teaching Hospital (RSUTH). The RSUTH is a tertiary health facility located in Port Harcourt, the capital and largest city in Rivers State, Nigeria. It is the largest state-owned hospital and serves the health needs of residents of the state and neighbouring states. It is also a training centre for resident doctors and medical students of Rivers State University. The average delivery in the RSUTH is 2294 deliveries per year [8,16].

Rivers State is a state in Nigeria located in the south-south region. It has a large reserve of natural gas and crude oil that makes it a hub of the oil and gas industry. The population of Rivers State is about 7,303,924 persons [17].

2.2. Study Population

The study was carried out amongst nulliparas in labour at the labour ward of the RSUTH between 7th January 2021 and 23rd August 2021.

2.2.1. Inclusion criteria

All booked nulliparous parturients at term with normal lie and presentation who had spontaneous labour and gave consent

2.2.2. Exclusion criteria

Contraindications to vaginal delivery

Parturients with previous laparotomy, multiple pregnancies, or medical/obstetric co-morbidity

Parturients who presented in advanced labour (cervical dilatation ≥ 7 cm) and

Women with known allergies to either drug.

2.3. Sample size determination

The sample size was calculated with the formula for comparing two groups in a clinical trial [18].

$$\text{Sample size per group (n)} = \frac{2(Z_{\alpha/2} + Z_{\beta})^2 P(1-P)}{(P_1 - P_2)^2}$$

Where:

$Z_{\alpha/2}$ = standard normal deviation (usually set at 1.96 for a 95% confidence limit)

Z_{β} = power of the study (usually set at 80% = 0.84)

$$P = \frac{P_1 + P_2}{2}$$

P_1 = proportion of the women on drotaverine who had vaginal delivery was 93% in a previous study = 0.93 [17]

P_2 = proportion of the women on placebo who had vaginal delivery was 76% in a previous study = 0.76 [17]

$$P = \frac{0.93 + 0.76}{2} = 0.845$$

$$n = \frac{2(1.96 + 0.84)^2 0.845(1 - 0.845)}{(0.93 - 0.76)^2} = 71$$

Assuming a 10% attrition rate (AR) = 7.1

Sample size per group = 71 + 7.1 = 78.1

A minimum sample size of 78 each was required in each study group.

Therefore, a total of 156 women participated in the study.

2.4. Study design

The study was a single-blinded randomized controlled trial.

2.5. Sampling Method

A multiphase random sampling was employed. In the first phase, parturients were screened with routine history and examination, those who met the inclusion criteria were informed of the study and written informed consent was obtained from those that indicated interest to participate. In the second phase, all consenting parturients had an amniotomy in the early active phase of labour (4 to 5cm cervical dilatation) and were re-assessed in four hours. Those with slow progress in labour (<1cm/hour) were identified and randomized into two groups that were augmented with either oxytocin and a placebo or oxytocin and drotaverine.

2.6. Study Procedure

All booked antenatal women who were potentially eligible for the study were identified in the antenatal clinic from the 35th week of gestation and were informed about the study. When they presented in labour, routine history clinical examination and investigations were done for them as for women in labour. Those who were eligible for the study were identified and given detailed information about the study. Informed written consent was obtained from those who showed interest to participate.

The participants were assessed as routine for women in labour, and the findings were documented. An artificial rupture of membranes (ARM) was done for them in the early active phase (4 to 5cm cervical os dilatation) and the labour progress was monitored on a partograph.

A digital vaginal examination was repeated in 4 hours, parturients with normal labour progress (≥ 1 cm/hour) were excluded from the study and continued with routine care, while those with cervical dilatation rate of less than 1cm/hour were considered to have poor progress of labour. They were randomized into two groups for the augmentation of labour. Group A received 10IU oxytocin in saline with 2ml of diluted vitamin B complex (which serves as a placebo) while Group B received 10IU oxytocin in saline with 2ml of drotaverine.

The randomization was by balloting. The parturients balloted from 156 folded pieces of paper in a box (in which either code A or B was written) until a sample size of 78 parturients per group was reached. Code A represented 2ml of normal saline mixed with vitamin B-complex. This was constituted by adding 5ml of injection vitamin B-complex into 1 litre of normal saline, from this 2ml was withdrawn in a 2ml syringe. Code B represented 2ml (40mg) of drotaverine, which was also withdrawn in a 2ml syringe. Both A and B have the same colour, the participants were blinded to what each code represented.

Three drug packs were provided and stored in the department's refrigerator. Two of the packs were labelled either A or B. Pack A contained several 2ml syringes, containing 2mls of normal saline-vitamin B complex mixture which served as a placebo. Pack B contained several 2ml syringes containing 2mls (40mg) of drotaverine. The third pack was not labelled and contained several ampoules of oxytocin. These packs were provided in batches of ten per day.

Injection drotaverine hydrochloride (40mg/2ml) manufactured by Sanofi-Aventis Zrt Hungary and Injection oxytocin (10IU/ml) manufactured by Novartis Pharmaceutical Switzerland were used for the study.

Following randomization, the parturients received an intramuscular dose of either a placebo or drotaverine with synchronous titration of 10IU oxytocin in 1 litre of normal saline (10mU/ml). The oxytocin titration was started at 15drops per minute (7.5mU/minute) and was increased every thirty minutes by 15drops/minute (7.5mU/minute) until adequate uterine contractions of 3-5 contractions lasting between 45-60seconds is achieved or maximum of 60 drops per minute (30mU/minute) was reached. This was based on the departmental protocol. Labour monitoring with a partograph was continued until delivery, and the third stage of labour was managed actively.

The biodata of each parturient, the intervention group, the time and cervical dilatation at the diagnosis of the active phase, and full cervical dilatation were recorded. The time of delivery of the baby was also recorded. The study lasted between 7th January 2021 and 23rd August 2021.

2.7. Data Analysis

The data obtained were entered into an Excel spreadsheet and analysed using IBM SPSS version 23.0 for Windows® statistical software. Results of categorical variables were presented in tables as frequencies and percentages, while numerical variables were summarized with means and standard deviation.

Descriptive analysis was done for socio-demographic characteristics. The student t-test was used to compare the mean duration of the first and the second stages of labour in both groups. The level of significance (α) was set at 0.05.

CONSORT FLOW DIAGRAM FOR THE STUDY

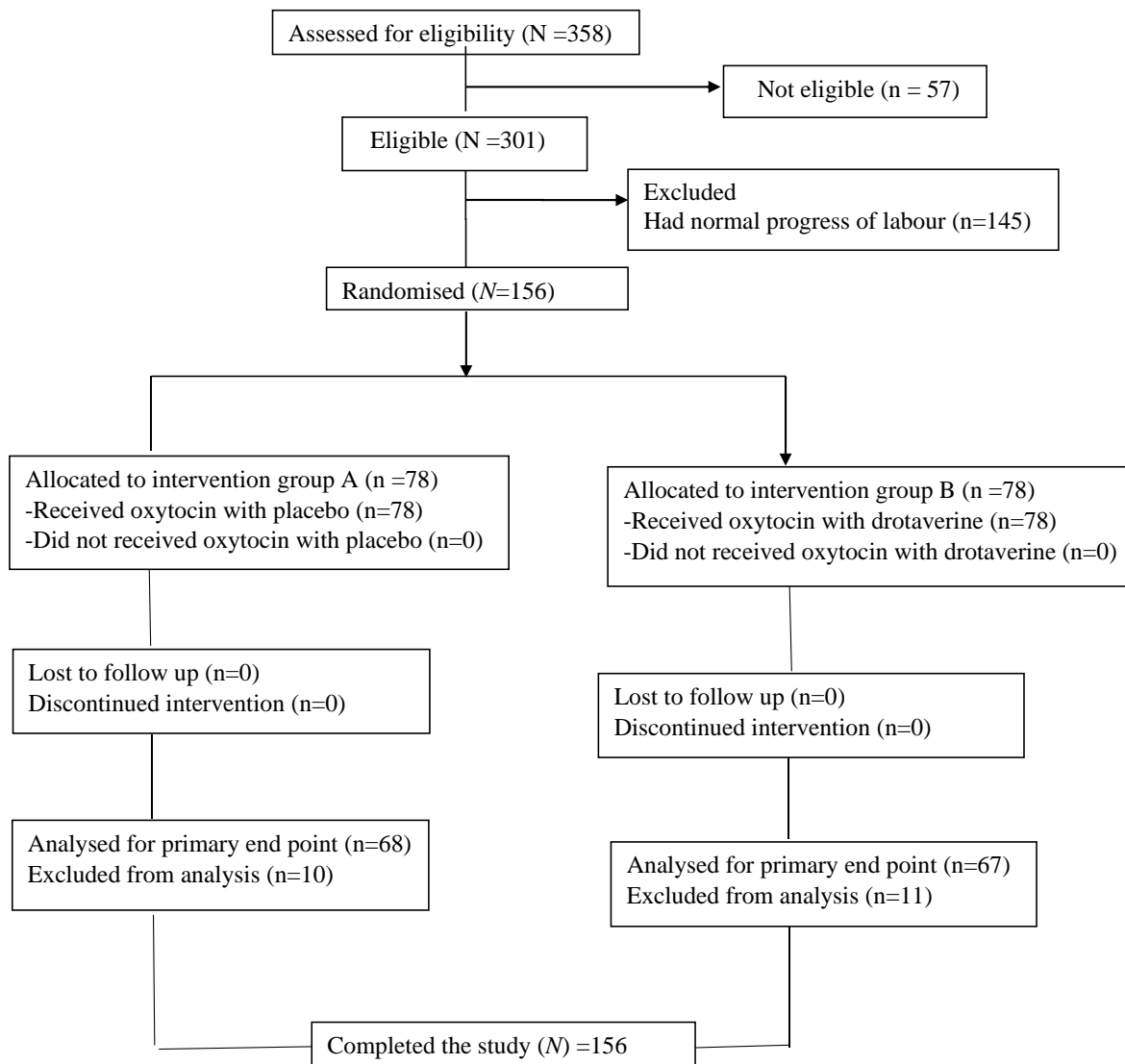


Figure 1 Consort flow diagram for the study

3. Results

A total of 301 parturients were eligible for the study and 156 of them had poor progress in labour giving an incidence of 51.8%. They were randomized into two groups of 78 each. Group A received oxytocin with a placebo while Group B received oxytocin with drotaverine.

Table 1 showed the socio-demographic characteristics of the study participants and their pre-intervention duration of labour. The participants were between 20 and 40 years and were all at term. The mean maternal ages of Group A and

Group B were similar (28.78 ±6.23 vs. 28.23±6.09years, $p = 0.58$). The gestational ages in both groups were also similar (38.92 ± 1.48 vs.38.74±1.45weeks, $p = 0.45$). In Group A, the majority 41 (52.6%) had secondary education and in Group B, the majority 45 (57.7%) had secondary education. There was no difference in the educational level of both groups $p=0.79$. In group A, 74(94.9%) of the parturients were married and in group B 72(92.3%) were married. There was also no difference in the marital status of both groups ($p= 0.51$). The mean pre-intervention duration of labour in Group A and B were similar (6.02 ±2.04 vs 6.09± 2.07hr, $p=0.82$) Therefore, both groups were similar in all their baseline characteristics.

In this study, 135 (86.5%) had vaginal deliveries while 21(13.5%) had emergency caesarean section. Of the vaginal deliveries, 68 (87.2%) were in Group A while 67 (85.9%) were in Group B shown in Table 1, there is no difference in the mode of delivery in both groups.

Table 1 Pre-intervention Characteristics of the Study Participants

Characteristics		Study groups (N) = 156		Test statistics	p-value
		GROUP A (Oxytocin with Placebo) n= 78	GROUP B (Oxytocin with Drotaverine) n=78		
Mean Maternal Age		28.78 ±6.23years	28.23 ±6.09years	t (154) = 0.56	0.58
Maternal Age Range		21-40years	20-39years		
Mean Gestational age		38.92±1.48weeks	38.74±1.45weeks	t (154) = 0.76	0.45
Gestational Age Range		37-41weeks	37-41weeks		
Level of education	Primary	10 (12.8%)	8 (10.3%)	$\chi^2(1,156) = 0.49$	0.79
	Secondary	41 (52.6%)	45 (57.7%)		
	Tertiary	27 (34.6%)	25 (32.0%)		
Marital status	married	74(94.9%)	72(92.3%)	$\chi^2(1,156) = 0.43$	0.51
	Single	4(5.1%)	6(7.7%)		
Mean pre-intervention duration of labour		6.02 ±2.04hr	6.09± 2.07hr	t(154) = 0.23	0.82
Mode of delivery	Vaginal delivery n=135 (86.5%)	68 (87.2%)	67 (85.9%)	$\chi^2(1,156) = 0.06$	0.82
	Caesarean section n=21(13.5%)	10 (12.8%)	11 (14.1%)		

$\chi^2(a,b)$ = chi-square test (degree of freedom, sample size), t(a) = t-test (degree of freedom)

Following augmentation, the mean duration of labour among those who had vaginal deliveries in both groups was compared as shown in Table 2.

Table 2 Assessment of duration of active labour in both groups

Variables	GROUP A Oxytocin with placebo n=68	GROUP B Oxytocin with drotaverine n=67	Test statistics	p-value
Mean duration of labour	6.64±0.34hrs	6.20 ±0.40hrs	t(133) = 6.8	< 0.01*
Mean duration of the second stage	38.04 ± 18.01hrs	35.83±16.60hrs	t(133) = 0.74	0.46

*= statistically significant ($p < 0.05$)

3.1. Hypotheses testing

3.1.1. The mean duration of labour

H₀1: There is no difference in the mean duration of labour in both groups.

H₀1: $\mu_{1A} = \mu_{1B}$

H_{A1}: There is a difference in the mean duration of labour between the two groups.

H_{A1}: $\mu_{1A} \neq \mu_{1B}$

Level of significance (α) = 0.05

Mean duration of labour ($\pm SD$) in group A (x_{2A}) = 6.93 ± 0.65 hr

Mean duration of labour ($\pm SD$) in group B (x_{2B}) = 6.27 ± 0.37 hr

$t(154) = 4.23, p < 0.01$

The null hypothesis was rejected at a 5% level of significance as $p < 0.05$. Therefore, there is convincing evidence that parturients in Group B had a shorter duration of labour than those in Group A.

4. Discussion

Poor progress is a common complication of nulliparous labour and could lead to prolonged labour if no intervention. In this study, 156 out of 301 eligible nulliparous parturients had poor progress in labour which gives an incidence of 51.8% which is consistent with 50-55% in the general population [6,8]. The socio-demographic characteristics and pre-intervention duration of labour in the study groups were similar, hence the groups were homogeneous and the differences noted can be attributed to the effect of augmentation.

The duration of the first stage of labour is an important determinant of the total duration of labour and perinatal outcome [2]. In this study, the mean duration of labour in the oxytocin drotaverine group was much shorter than the oxytocin placebo group (6.20 ± 0.40 hrs vs 6.64 ± 0.34 hrs MD-26.4minutes $p < 0.01$), perhaps drotaverine ability to relieve cervical spasm could have led to faster cervical dilatation with uterine contractions in the oxytocin drotaverine group. This finding was consistent with earlier studies that showed that drotaverine contributes to a shorter duration of labour by enhancing cervical dilatation [19-24]. It, however, differed from the findings of Correa et al which showed no difference in the duration of labour when oxytocin was used with the antispasmodic-hyoscine compared with oxytocin alone [25]. This variation may be due to differences in the mechanism of action between hyoscine and drotaverine, as hyoscine is a neurotropic antispasmodic while drotaverine is a musculotropic antispasmodic.

The duration of the second stage of labour has a significant impact on maternal morbidity as well as perinatal morbidity and mortality. In this study, the mean duration of the second stage of labour in the oxytocin drotaverine group was similar to that in the oxytocin placebo group (35.83 ± 16.60 hrs vs 38.04 ± 18.01 hrs $p = 0.46$). This may be because the duration of the second stage is determined by the strength of uterine contractions and maternal pushing efforts both of which are affected by oxytocin [26]. Drotaverine is believed to act on the lower segment and therefore does not affect uterine contractions [19]. This finding was consistent with earlier studies that showed that drotaverine does not affect the duration of the second stage of labour.

This study was limited to nulliparous women at term with poor progress of labour in RSUTH where all labour is managed according to protocol. In addition, this study did not assess the caesarean section rate, maternal satisfaction and side effects of combining both drugs. Further, multi-centre studies may be needed in this regard to improve the generalizability.

5. Conclusion

The study showed that the addition of drotaverine to the standard management of poor progress of labour with oxytocin augmentation in term nulliparas leads to a significantly shorter duration of the active phase of the first stage of labour.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

Ethical approval was obtained from the Rivers State Health Research Ethics Committee.

Statement of informed consent

Written informed consent was obtained from all individual participants included in the study.

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