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Original article

Metoclopramide Versus Hyosine Butyl-Bromide in Shortening Duration of First Stage of Labour Among Nulliparous Women in Abakaliki, Ebonyi State

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Abstract

Background: Administering antispasmodics during labour could lead to faster and more effective dilatation of the cervix preventing prolonged labour. However, due to scarce information on it, with no generally agreed protocol for its use in labour. This study is aimed to see if we can have more positive findings to support the existing literature for probable consideration as a protocol in labour management. ***Methodology:*** This was equivalence, open label; placebo controlled randomized trial among nulliparous women over a six months period. Eligible participants were randomized to receive a slow intravenous medication of one of these three medications-Metoclopramide (10mg), Hyoscine Bromide (20mg) or placebo. They were managed according to the institutional intrapartum protocol. Primary outcome was the duration of first stage of labour. Secondary outcome includes the rate of cervical dilatation, total duration of labour, route of delivery and Apgar score at 5th minute. Data was analysed with SPSS, version 25.0 (2017, SPSS Inc., Chicago IL, USA) and by the concept of intention to treat protocol. P-value of less than 0.05 was taken as significant. ***Results:*** Sixty women were included in the metoclopramide group, 59 women in the hyoscine bromide group and 61 women in the placebo group. There was statistically significant difference in the mean reduction of the first stage of labour (263.84±139.44mins=Metoclopramide), (Hyoscine Bromide=241.33±121.56mins) and (placebo = 318.43±203.44mins). The total mean duration of labour was significantly significant different among the groups (P<0.05), (295.86±138.7 = Metoclopramide, (271.69±122.35 = hyoscine butyl bromide) and (350.24±201.48 = placebo). There are no statistically significant differences among other variables studied. ***Conclusion:*** Metoclopramide is as effective as hyoscine butyl bromide in shortening duration of first stage of labour in nulliparous women with no recorded adverse effect. I recommend that they should be introduced as part of the protocol in active management of labour. ***Clinical Trial.gov*:** NCT05222646

Keywords: ***Prolonged labour, Metoclopramide, Hyoscine Bromide, active phase of labour.***

Introduction

Labour is a sequence of uterine contractions that results in effacement and dilatation of the cervix leading to the expulsion of the fetus and the products of conception [1]. Prolonged labour contributes to increased perinatal and maternal morbidity and mortality [2,3]. Active management of labour reduces the incidence of prolonged labour without having significant adverse effects on the mother and the fetus [4].

Reducing the length of labour is a highly desirable goal of intrapartum care [5]. The safety of active management of labour has been demonstrated by several prospective randomized control trial [6]. A shorter duration of labour from admission to delivery has been consistently reported in numerous studies of women treated with active management protocol [5-7]. However, prolonged labour still occurs [2,3].

Efforts have been made in studies to shorten the duration of active labour by enhancing the progress of labour [8]. These interventions includes: the use of analgesics, oxytocics, prostaglandins derivatives and smooth muscle relaxants [8]. Smooth muscle relaxants are well accepted in enhancing the progress of

labour. Smooth muscle relaxants inhibit impulses in the form of spasm that impairs effective cervical dilataion [9].

Hyoscine butyl bromide is an anticholinergic and antispasmodic9, analgesic and sedative drug [9,10]. Hyoscine has also be found to be effective in improving cervical spasm and facilitating cervical dilatation during the course of labour [10,11]. There are evidence of its safety in labour [9-11]. Metoclopramide is frequently employed in delivery rooms as analgesic and antiemetic, however a study at Saudi Arabia noted that it enhances cervical dilatation during active phase of labour [12]. There is limited evidence to support universal acceptability of metoclopramide as an agent for enhancing cervical dilatation hence, we evaluated its role in shortening duration of first stage of labour in sub-Saharan Africa.

Methodology

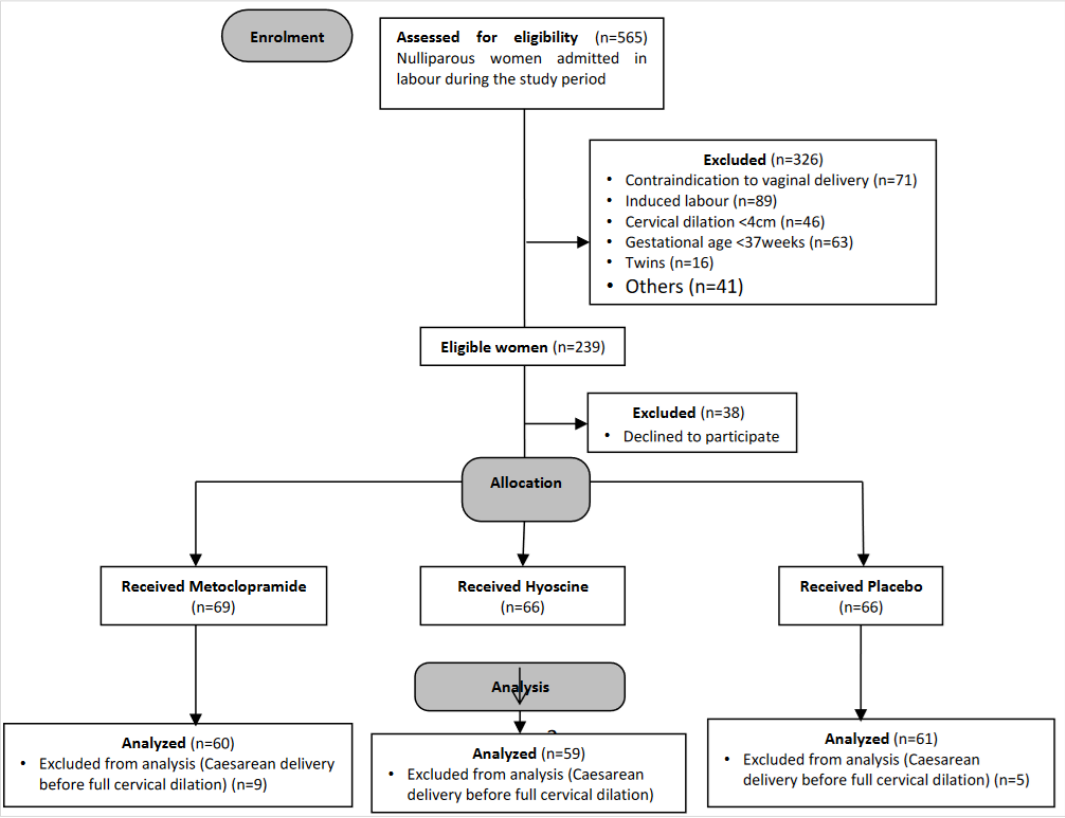
This was an equivalence open label placebo controlled randomized control trial on the efficacy of metoclopramide versus hyosine N butyl bromide in shortening the duration of first stage of labour in the Department of Obstetrics and Gynaecology of Alex Ekwueme University Teaching Hospital Abakaliki and Mile Four Hospital Abakaliki, all in Ebonyi State Nigeria. The study lasted for duration of six months from 4th of March 2021 to 1st of August 2021. Both facilities used share similar intrapartum protocol based on active management of labour and patients at both facilities share similar socio-demographic characteristics.

The sample size was calculated using the formula for a clinical equivalence randomized controlled trial (continuous variables) as stated by Zhong [13]. Nulliparae who met the inclusion criteria were recruited from the antenatal clinic and antenatal ward. Consent obtained was subsequently reinforced when they presented in labour. The participants were randomized by means of computer-generated random numbers using the software research randomizer®. Thus a total of 186 participants were to recruited giving a total number of participants per group as 62. Allocation was done in the ratio of 1:1:1.

Group A: Received 1ml (20mg) of Hyoscine Butyl Bromide intravenously in active phase of labour.
Group B: Received 1 ml (10mg) of Metoclopramide intravenously in active phase of labour.
Group C: Received 1ml of sterile water intravenously in active phase of labour.

On admission into the labour ward, the antenatal record was retrieved and reviewed, history was taken, a full physical examination performed and diagnosis of labour made. The patient is then admitted into the labour ward if in active phase of labour and artificial rupture of membrane done. Participants received a single dose given intravenously, when they were assessed to have cervical dilatation between 4-6 centimetres in labour. Oxytocin was used to augment labour when uterine contractions were inadequate. Vaginal examination was done at presentation and another is performed 4 hours later if patient is in active of labour. Thereafter, it is repeated 2 hourly in the first stage and as indicated in the second stage. Labour was monitored with the partograph.

Consort Diagram



The primary outcome measure was the duration of first stage of labour. The secondary outcome measures included the rate of cervical dilatation, total duration of labour, mode of delivery, APGAR score, NICU admission, and maternal adverse effect, these were recorded in a proforma. For patients who experienced severe nausea and vomiting, Promethazine was given intramuscularly (10 mg stat). No patients showed extrapyramidal symptom(s) due to Metoclopramide. However, Chlorpromazine was made available as an antidote. The participants and their babies were followed up till 24 hours after delivery for any adverse effect as the half-life of the drug is 7-16 hours.

Data Collection and Statistical Analysis

At the end of the study, the profoma sheets were separated using the record of randomization sequence and the data in the appropriate groups were transferred into Microsoft excel. Data was analysed with SPSS, version 25.0 (2017, SPSS Inc., Chicago IL, USA) and by the concept of intention to treat protocol. Absolute and relative frequencies of categorical variables mean and standard deviation of continuous variables was calculated. Continuous variables were analysed by Z-test. Person Chi Square test was use for comparing categorical variables. Analysis of variance (F-ratio) was used amongst comparison groups, and a post hoc analysis was done where necessary. P-value of less than 0.05 was taken as significant.

Results

A total of 201 pregnant women who met the inclusion criteria consented to this study. Thus, the data of 180 pregnant women were used for the analysis. Of these, 60 clients received Metoclopramide, 59 clients received Hyoscine butyl bromide while 61 clients received sterile water for injection (placebo).

Table 1: Maternal and gestational ages of participants

Demographic Variables	Metoclopramide (n=60)	Hyocine (n=59)	Placebo (n=61)	χ^2	P-value
Maternal age (years)					
<20	4 (6.7%)	7 (11.8%)	4 (6.6%)	1.43	0.488
20-29	33(55.0%)	27(45.8%)	31(50.8%)	1.02	0.601
30-39	18(30.0%)	21(35.6%)	22(36.1%)	0.61	0.737
≥40	5 (8.0%)	4 (6.8%)	4 (6.6%)	0.17*	0.919
Mean maternal age	27.86 ± 7.19	27.96 ± 7.11	28.29 ± 6.42	0.06**	0.938
Mean gestational age	39.15± 1.42	38.68 ± 1.44	39.09 ± 1.31	2.01**	0.137

**Fisher's exact test used* ***ANOVA test used*

This table shows no statistical significant difference in the demographic variables studied.

Table 2a: Mean duration of first stage of labour amongst the groups

Duration of Labour	Metoclopramide (n=60)	Hyoscine Bromate (n=59)	Placebo (n=61)	F-ratio	P-value
Mean first stage (mins)	263.84±139.44[a]	241.33±121.56[a]	318.43±203.44[b]	3.736	**0.026**

Same alphabet not significant (P>0.05) *Different alphabet significant (P<0.05)*

This table shows that the first stage of labour duration was prolonged statistically in the placebo group when compared to the metoclopramide and Hyoscine groups.

Table 2b: Post-hoc test of the comparison of duration of first stage of labour using Least Square Difference

Drug 1	Drug 2	Mean Difference	95% C.I of Difference	P-value
Metoclopramide	Hyoscine Bromate	22.51	-25.01-70.03	0.350
	Placebo	64.59	1.71-127.47	**0.044**
Hyoscine Bromate	Placebo	77.10	16.26-137.94	**0.013**

This shows no statistical significant difference between metoclopramide and Hyoscine group when compared in shortening the duration of labour. However, active labour duration was prolonged statistically in the placebo group when compared to the metoclopramide and Hyoscine groups.

Table 3a: Comparison of Labour Characteristics among the Groups

Variables	Metoclopramide (n=60)	Hyocine (n=59)	Placebo (n=61)	F-ratio	P-value
Cervical dilation on admission (cm)					
Range	4-6	4-6	4-6		
Mean	4.9 ±0.76	4.9±0.67	5.03±0.93	0.538	0.585
Rate of cervical dilation (cm/hr)					
Range	1-3	1-3	1-3		
Mean	1.64±0.85[a]	1.84±0.76[a]	1.11±0.83[b]	10.194	**<0.001**
Duration of second stage (mins)					
Range	21-65	20-61	22-64		
Mean	26.61±13.58	25.42±11.63	27.44±12.77	0.383	0.682
Duration of third stage (mins)					
Range	5-21	6-23	5-24		
Mean	12.47 ± 4.66	13.24±4.73	12.41±5.08	0.547	0.580
Overall duration of labour (min)					
Range	179-362	181-373	177-367		
Mean	302.92±118.71[a]	279.99±122.35[a]	358.28±161.48[b]	3.892	**0.022**
Estimated postpartum blood loss (ml)					
Range	250-400	250-450	250-450		
Mean	238.44±100.85	246.89±101.77	249.03±99.56	0.186	0.830

a - Same alphabet not significant (P>0.05) *b - Different alphabet significant (P<0.05)*

This table showed statistical significant difference in the rate of cervical dilation and overall duration of labour when metoclopramide and Hyoscine groups were compared with the placebo group.

Table 3b: Post-hoc test of the comparison of labour characteristics using Least Square Difference

Labour Characteristics	Drug 1	Drug 2	Mean Difference	95% C.I of Difference	P-value
Rate of cervical dilation (cm/hr)	Metoclopramide	Hyoscine Bromate	0.20	-0.09-0.49	0.179
		Placebo	0.53	0.23-0.83	**0.001**
	Hyoscine Bromate	Placebo	0.73	0.44-1.02	**<0.001**
Overall duration of labour (min)	Metoclopramide	Hyoscine Bromate	22.93	-24.58-70.44	0.341
		Placebo	55.36	2.74-107.98	**0.039**
	Hyoscine Bromate	Placebo	111.39	62.41-160.37	**<0.001**

This table showed statistical significant difference in the rate of cervical dilation and overall duration of labour when metoclopramide and Hyoscine groups were compared with the placebo group. However, when both metoclopramide and Hyoscine groups were compared, there was no statistical difference between them.

Table 4: Mode of Delivery among the groups

Mode of Delivery	Metoclopramide (n=60)	Hyocine (n=59)	Placebo (n=61)	χ^2	P-value
Vaginal delivery	51(85.1%)	50(84.7%)	48(78.7%)	1.832*	0.856
Forceps delivery	2 (3.3%)	2 (3.4%)	2 (3.3%)		
Vacuum delivery	2 (3.3%)	3 (5.1%)	3 (4.9%)		
Caesarean section	5 (8.3%)	4 (6.8%)	8(13.1%)		

** Fisher's exact test used*

The table did not show any statistical significant difference on the mode of delivery.

Table 5: Maternal Outcome

Variables	Metoclopramide (n=4)	Hyocine (n=3)	Placebo (n=5)	χ^2	P-value
Postpartum haemorrhage	2(50.0%)	1(33.3%)	1(20.0%)	0.49*	0.784
Retained placenta	2(50.0%)	2(66.7%)	4(80.0%)	1.00*	0.608
ICU admission	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Maternal death	0 (0.0%)	0 (0.0%)	0 (0.0%)		

**Fisher's exact test used*

There was no statistical significant difference on the maternal outcome measures.

Table 6: Neonatal outcome

Variables	Metoclopramide (n=60)	Hyocine (n=59)	Placebo (n=61)	Test Statistic	P-value
Mean APGAR score at 1min	8.52±1.66	8.67±1.74	8.23±2.24	0.834*	0.436
Mean APGAR score at 5min	9.22±0.91	9.36±0.90	9.17±0.96	0.678*	0.509
NICU admission					
Yes	4(6.7%)	4 (6.8%)	9 (14.4%)	3.041**	0.218
No	56(93.3%)	55(93.2%)	52(85.2%)		
Mean Birth weight (kg)	3.16±0.41	3.19±0.44	3.12±0.45	0.394*	0.675

**ANOVA test used **Chi-square test used*

There was no statistical significant difference on the neonatal outcome measures.

Table 7: Comparison of side effect profile of research drugs

Variables**	Metoclopramide (n=60)	Hyocine (n=59)	Placebo (n=61)	χ^2	P-value
Nausea	8(13.3%)	7(11.9%)	2 (3.3%)	4.18	0.124
Vomiting	5 (8.3%)	6(10.2%)	4 (6.6%)	0.51	0.774
Dry mouth	5 (8.3%)	7(11.9%)	3 (4.9%)	1.89	0.388
Constipation	6(10.0%)	5 (8.5%)	2 (3.3%)	2.24*	0.326
Diarrhoea	1 (1.7%)	2 (3.4%)	3 (4.9%)	0.99*	0.609
Dizziness	2 (3.3%)	3 (5.1%)	2 (3.3%)	0.34*	0.845
Headache	4 (6.7%)	4 (6.8%)	3 (4.9%)	0.23*	0.892

**Fisher's exact test used ** Multiple responses applied*

Table showed that the drugs used were statistically safe in pregnancy.

Discussion

This study was set out to determine if Metoclopramide was as effective as Hyoscine Butyl Bromide in shortening duration of first stage of labour in nulliparous women. The mean age of participants and the gestational age at presentation in this study was 28±7.2yrs and 39±1.41wks respectively. There was no statistical significant difference when groups were compared, which showed homogeneity

of the demography of the studied participant and so, the outcome of the study can be generalised within the study population. This was similar to what was obtained by Barau et al in Abuja and Ellaithy et al in Saudi Arabia [12,14].

The result obtained in this study indicated that both Metoclopramide and Hyoscine butyl Bromide significantly reduced the duration of first stage of labour in nulliparous women. The participants who received hyoscine butyl bromide had a shorter duration of first stage of labour than those who received metoclopramide but was not statistically significant. The participants who received placebo had the longest duration of first stage labour when compared to the other groups. This finding concurs with those of Seckharat L et al, Ellaithy et al and Mahmoud E et al [12,15]. The similarity in the result may be due to adoption of similar methodology which includes similarity in patient selection, randomization and route of drug administration [11,16]. This differed from study by Barau et al, were they noted that the use of hyoscine butyl bromide did not shorten the duration of first stage of labour [14]. This finding may be due to the route of drug administration which was intramuscular and also there study was not parity dependent as they had participants across all parities while our study had only nulliparous women.

Study showed statistical significant difference in the rate of cervical dilation and overall duration of labour when metoclopramide and Hyoscine groups were compared with the placebo group. However, when both metoclopramide and Hyoscine groups were compared, there was no statistical difference between them. This result is similar to findings from similar studies [6,12,15,17]. This similarity may be due to similar methodology. There was no statistical significant difference in the mean duration of the 2nd and the 3rd stages of labour in the three groups when compared. This finding concurred with those of Sekhavat L et al, Qahtani N et al and Samuel et al which also did not demonstrate any difference in the mean duration of 2nd and 3rd stages of labour [12,18]. This is because the actions of antispasmodics in labour are mainly on the cervix with little effect in promotion of uterine contractility [19]. This finding in 2nd and 3rd stage of labour obtained in this study did not agree with the finding obtained by Barau and colleagues in Abuja [14] who noted a reduction in second stage of labour amongst the parturient that received hyoscine butyl bromide, this was because they aggregated both the nulliparous and multiparous women in labour together and did not consider the impact of parity on the progress of labour.

There was no maternal adverse effect observed in the study. This concurs with similar studies on maternal side effects [12,15,20]. This may be due to the fact that these antispasmodics does not affect the uterine musculature as such the contractility of the uterus is not affected. Also, it has not been demonstrated to affect the blood coagulability. The mode of delivery was not statistically significant. This finding is similar to what was obtained by previous studies [6,12,14,16]. There was no neonatal and fetal adverse effect observed in the study. This is similar to finding of Mahmoud et al [15] and Ellaithy [12] who also noted that use of antispasmodic did not affect the APGAR Scores of the babies following delivery. Therefore these drugs are safe to the pregnant women.

Conclusion

This study generally showed that Metoclopramide is as effective as Hyoscine butyl Bromide in shortening the duration of first stage of labour in nulliparous women. It also showed that these drugs are safe to both the pregnant women and their babies.

Recommendations

1. Any of the two drugs (metoclopramide or hyoscine butyl bromide) can be used as an antispasmodic for active management of labour to shorten duration of first stage of labour.
2. A larger multicentre study is necessary to fully evaluate this finding

Area of Further Research

There may be need to compare the rate of shortening duration of labour of first stage of labour in nulliparous when a single dose of these drugs were administered with another arm having repeat doses of these drugs are administered at 2-4 hour interval apart.

Strength of Study

This was a randomized controlled trial as such confounding variables are inherently eliminated. This study was limited to only nulliparous women with term pregnancies in labour alone as such the effect of increasing parity in shortening the duration of labour is eliminated. Also use of an independent assessor during the labour process increased the external validity of this work.

Informed Consent

A signed consent was obtained by the researcher and research assistants before recruitment of the participants into the study after appropriate counselling.

Ethical Approval

Ethical approval was obtained for the study from the research and ethics committee of both Alex Ekwueme Federal University Teaching Hospital, Abakaliki and Mile 4 Hospital Abakaliki. Patients signed written and informed consent forms after carefully explaining the objectives, procedure, and full implications of participation in the study. This study was conducted in compliance with the ethical standards of our institution on human subjects and with the Helsinki Declaration.

Clinical Trial Registration

The work was registered with the ClinicalTrials.gov with clinical trial number; - NCT05222646

Funding

All the financial implications of this study were borne by the researchers.

Conflict of Interest

No conflict of interest was declared. The entire drug was obtained from a private pharmacy without any company incentives or inducement.

Authors Contribution

Emmanuel C UWAKWE conceptualised the topic. All the authors were involved in data collection and literature review. Emmanuel C UWAKWE and Darlington-Peter C UGOJI supervised the work. All the authors wrote the final draft and approved the final manuscript.

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Data Availability

Data would be available upon reasonable request.

List of Abbreviations

Mg: Milligram
SPSS: Statistical package for social science
Mins: Minutes
4th: Fourth
1st: First
Ml: Milliliter
NICU: New born intensive care unit
N: Number
>: Greater than
<: Less than
*: Asterics
%: Percentage
Cm: Centimeter
Hr: Hour
ANOVA: Analysis of variance
/: Per
A: Not significant
B: Significant

References

[1] Carol LA, Ashley SR. Labour and Delivery. In: Current Diagnosis and Treatment in Obstetrics and Gynaecology. Decherney AH, Nathan L(eds). McGraw Hills Medical Publishing Company 2013:125

[2] Bohra U, Donnelly J, O'Connell MP, Geary MP, Mac Q K, Keane OP. Active management of labour revisited: The first 1000 Primiparous labour in 2000.J Obstet Gynecol 2003;23:118-120.

[3] Horsager R, Roberts SW, Rogers VL, Santiago-Muñoz PC, Worley KC, Hoffman BL. eds.; Physiology of Labour: Williams Obstetrics Study Guide, 24e. McGraw Hill; 2014. Accessed January 29, 2022. https://accessmedicine.mhmedical.com/content.aspx?bookid=1131&sectionid=68979936

[4] Word R.A, Li X, Hina. Dynamics of cervical remodelling during pregnancy and parturition: Mechanism and Concepts. Semin Reprod.Med.2007;25(1)69-79

[5] O'Driscoll K, Meagher D, Boylan P Active management oflabour.3rd ed. London: Mosby-Year Book 1993.

[6] Ibrahim R, Nwobodo E I, Tunau K A, Burodo A T, Suleiman B,Garba J A et al. The effect of hyoscine butyl bromide in shortening the duration of first stage of labour: A single-blind randomized control study. Tropical Journal of Obstetrics and Gynaecology 2019;36,28-32.

[7] Cromi A, Ghezzi F, Agosti M,Uccela S,Pia N, Serati M,et al. Use of an antispasmodic(rociverine) to shorten the length of labour: a randomized, placebo-control trial. AOGS. 2011; 90:12,1371-1378.

[8] Sadler LC, Davison T, Mac Cowan LM. A randomized control trial and meta-analysis of active management of labour. BJOG 2000; 107,909-915.

[9] Lope- Zeno JA, Peaceman AM, Adashek JA, Socol ML.A control trial program for active management of Labour. N. Engl. Jbn Med.1992:326:450-454.

[10] Frigoletto F D, Jr, Lieberman E, Lang JM et al A clinical trial of active Management of labour N. Eng. J.Med.1995;333:745 -750

[11] Thapa M, Saha Pradhan A, Shrestha S. Effectiveness of drotaverine Hydrochloride in progression of labour. Nepal Journal of Obstetrics and Gynaecology.2007;2(2)9-11

[12] Sekhavat L, karbasi SA, Fallah R, Mirowliai M. Effect of hyoscine butyl bromide first stage of labour in multiparous women. African Health Sciences 2012;12(4):404-411.

[13] Zhong B. How to calculate sample size in Randomized Controlled Trial? Journal of Thoracic Dis 2009; 1(1): 51-54.

[14] Barau D, Agidi E, Onafowokan O, Adebayo F. Effect of hyoscine butyl bromide on the course of Labour. Open Journal of Obstetrics Gynaecol.2018;8,1102-1108

[15] Mahmoud E. et al. Different Modalities of First Stage Enhancement of labour. Gen Health and Med.Sci 2015;2:1-4

[16] Rohwer AC, Khondowe O, Young T. Antispasmodics for labour. Cochrane Database of Systemic Reviews 2013,6

[17] Changede PR, Tank P.The effect of Hyoscine butyl bromide on the duration and course of labour. Indian Journal of Obstetrics and Gynaecology Research 2016;3(3),148-152.

[18] Qahtani N H A, Hajeri F A. The effect of Hyoscine butyl Bromide in shortening the first stage of labour; a double blind randomized controlled clinical trial. Therapeutics and Clinical risk management 2011;7,495-500.

[19] Fardiazar Z, Nikanami F, Mashayekhi S, Ghojazadeh M. Hyoscine N-butyl bromide v versus atropine as labour accelerant and analgesic;a randomized clinical trial .Pak .J boil Sci.2013;16(9),443-445

[20] Samuel L, Christie L, Roberts GB, Fletcher H, Fredrick J. The effect of Hyoscine butyl bromide on the first stage of labour in term pregnancies. BJOG 2007;114(2),1542-1546