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EFFECT OF HYOSCINE-N-BUTYL BROMIDE ON CERVICAL EFFACEMENT AND DILATION DURING NORMAL LABOR

By

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ABSTRACT

Background: Labor is a multifactorial and dynamic process which involves myometrial contraction, cervical ripening and dilation and the expulsion of the fetus and placenta in an orderly manner.

Objective: To study the efficacy and safety of Hyoscine-N-butyl bromide (HNBB) on enhancement of cervical effacement and dilation during normal labor, duration of labor and mode of delivery compared to the control group.

Patients and methods: This was a randomized un blinded controlled trial was conducted on pregnant women in active phase of first stage of labor from those attendant labor ward of Obstetrics and Gynecology Department at Sohag General Hospital. 200 pregnant women were recruited to this study and divided into 2 equal groups. Study group received Buscopan 20 mg diluted in 9 ml saline slowly intravenously and control group received 10 mL normal saline.

Results: The mean duration of active phase of labor in the study group and control group was found to be 186 and 338 minutes respectively (p value = 0.0001). No significant difference was observed in the duration of second and third stage of labor, mode of delivery, birth weight, Apgar score and color of the liquor in both the groups.

Conclusion: Administration of HNBB i.v. significantly reduced the duration time of cervical dilation in the active phase of first stage of labor, thereby reducing the total duration of labor. Hyoscine –N- butyl bromide is a new aid in the management of uncomplicated labor for a convenient shorter and safer physiological delivery making it more tolerable for the mother.

Keywords: Hyoscine-N-butyl bromide, Cervical Effacement, Dilatation, Normal Labor.

INTRODUCTION

Labor is the last few hours of human pregnancy. It is characterized by forceful and painful uterine contractions that effect cervical dilation and cause the fetus to descend through the birth canal. During the first 36 to 38 weeks of normal gestation, the myometrium is in a preparatory yet unresponsive state. Concurrently, the cervix begins an early stage of remodeling yet maintains structural integrity. Following this prolonged uterine quiescence, a transitional phase follows during which myometrial unresponsiveness is suspended and the cervix undergoes ripening, effacement, and loss of

structural cohesion *(Cunningham et al., 2018)*.

Prolonged labor is a significant contributor to increase in cesarean section rate and has shown to raise the risk four to six times and contributes to high rate of chorioamnionitis, postpartum hemorrhage, excessive cranial moulding leading to increase perinatal, infant morbidity and mortality. It also made way for certain remote complications like genital prolapse, disability of bladder sphincter mechanisms, and certain late psychological sequelae which affected the mother in her attitude towards further child bearing *(Tadevosyan et al., 2019)*.

The two major factors that determine duration of labor are uterine contractility and rate of cervical dilation. In addition to mechanical factors such as sweeping of membranes, cervical stretching and amniotomy, various pharmacological agents have been found to facilitate cervical dilation. The role of oxytocin and prostaglandins has been established worldwide in augmentation of labor and the cervical application of hyaluronidase has also been used with some success *(Sekhavat et al., 2012)*.

Hyoscine-N- butylbromide (HNBB) belongs to the parasympatholytic group of drugs and is a semisynthetic derivative of scopolamine. It is an effective antispasmodic drug without the untoward side effects of atropine. HNBB acts primarily by blocking the transmission of neural impulses in the intraneural parasympathetic ganglia of abdominal organs, apparently inhibiting cholinergic transmission in the synapses of the abdominal and pelvic parasympathetic ganglia, thus relieving spasms in the smooth muscles of gastrointestinal, biliary, urinary tract, and female genital organs, especially the cervicouterine plexus, thus aiding cervical dilatation and thus reducing the duration of labor *(Rohwer et al., 2012)*.

Obstetricians from various parts of the world have studied the efficacy of Hyoscine-N-butyl bromide on cervical dilation and found that its efficacy is comparable to other drugs for cervical dilatation. The results are conflicting some of the studies demonstrated the efficacy in augmenting labor, while others showed no effect *(Aldahhan et al., 2011)*.

The aim of the present study was to study the efficacy and safety of Hyoscine-N-butyl bromide (HNBB) on enhancement of cervical effacement and dilation during normal labor, duration of labor and mode of delivery compared to the control group.

PATIENTS AND METHODS

This was a randomized un blinded controlled trial was conducted on pregnant women in active phase of first stage of labor from those attendant labor ward of Obstetrics and Gynecology Department at Sohag General Hospital from February to July 2019. Two hundred pregnant women were recruited to this study. All patients were primigravidae and in active phase of labor 3-4 cm dilation of internal os with bulging of membranes.

Inclusion criteria: Women with:

1. Primigravidae from 20 to 35 years old.
2. Normal singleton pregnancies, longitudinal lie, with Vertex presentation and average size with

normal situated placenta and average amniotic fluid.

3. Pregnancy at 37-41 weeks.
4. Active phase of labor at 3-4 cm cervical dilation with true labor contractions and bulging of membranes.
5. Spontaneous onset of labor and intact fetal membrane.

Exclusion criteria: Women with:

1. History of medical disorders.
2. Scarred uterus.
3. Multiple pregnancy.
4. Malpresentations.
5. Cephalo-pelvic disproportion.
6. Induced labor.
7. Premature rupture of membranes.
8. Poor CTG prognosis.

Patients who met the inclusion criteria were asked to participate in the study and a verbal consent was obtained from each patient after explaining thoroughly the nature and the scope of the study.

The patients were divided into two equal groups:

- **Group I (study group)** received 20 mg of HNBB diluted in 9 ml of saline solution) slowly intravenously.
- **Group II (control group)** received 10 ml placebo.

Every patient was subjected to:

- Complete history taking: The patients were subjected to careful general, abdominal and local examinations.
- General examination including: Vital signs, cardiac and chest, head and neck examinations, lower limb and lastly abdominal examinations.
- Obstetric abdominal examination including: Fetal lie, presentation, head station, estimated fetal weight, fetal heart rate, uterine contractions and amount of liquor by using U.S.
- Local examination: Inspection of external genitalia and a septic per vaginal examination done to note the dilation, effacement and position of cervix, status of membranes and assessment of adequacy of pelvis.
- Obstetric Ultrasound was applied for fetal biometry estimation, confirmation of fetal lie and position, assessment of amniotic fluid volume and turbidity, localization of placenta and exclusion of any fetal anomalies.
- Cardiotocography (CTG) was applied to detect early fetal distress.
- In both groups, active management of labor was carried out in the form of rupture of membrane (fore water) once patient entered active phase of labor.
- Laboratory investigations: Complete blood count, blood grouping and Rh, liver and kidney functions.

The following parameters were monitored in both groups:

1. Progress of labor with partogram: Frequency and duration of uterine contractions were recorded every 30 minutes based on per abdominal examination. Cervical dilatation and effacement were recorded second hourly per vaginal examination. Station and position of the presenting part were recorded second hourly per vaginal examination.

2. Maternal parameters: Pulse and respiratory rates were being recorded 30 hourly intervals. Blood pressure was recorded at hourly intervals. Anticholinergic side effects: restlessness, flushing of face etc if any recorded.
3. Fetal parameters: Fetal heart rate was recorded every 15 minutes by auscultation. Color of amniotic fluid was noted. Apgar score of the newborn was recorded at one and five minutes after birth. Newborn baby requiring NICU was recorded if any.

Intervention:

- When active phase of labor has started, a single dose of HNBB 20 mg and 10 ml of saline by direct slow IV injection as formal explained for patients' groups.
- When dilation had not increased by at least 1-1.5 cm per hour amniotomy was performed progress was again assessed at two hours.
- When dilation had not increased, a low dose protocol of oxytocin infusion was started. Oxytocin was diluted in the form of IU in 500 ml glucose 5% making a concentration of nearly MU oxytocin to one ml glucose solution. Infusion was instituted at the rate of one to two milliunit (15-30 drops) per minute and increased gradually in increment of 1-2 milliunit interval, until 3 uterine contractions were noted in a 10 minutes' period.

Ethical considerations:

The study was approved by the Scientific Ethical Committee of Faculty of Medicine, Al-Azhar University (Assuit). An informed written consent was taken from every participant in the study.

Statistical analysis:

The data in this study were analyzed using the statistical package for the social science (SPSS software version 25.0). The analysis was performed using the following procedures. Student's test (t-test): was used to check the significance between continuous data (quantitative items between two different groups). Chi-square test (X^2) was used to check the significance between categorical data (qualitative items between two different groups). The probability (P value < 0.05) was taken as the limit of statistical significance.

RESULTS

Majority of the patients in study group and in control group were in the 20-27 years' age group. There was uniformity of cases with regard to mean age, maternal body mass index and period of gestation **(Table 1)**.

Table (1): Patient's characteristics

Patient's Groups / Characteristics	Study Group (n=100)		Control group (n=100)		P-value
	No	%	No	%	
Age (years)					
20-27 years old	71	71%	69	69%	>0.05
28-35 years old	29	29%	31	31%	
Mean ± SD	25.76 ± 7.71		25.69 ± 4.13		
Range	(20 – 35)		(20 – 35)		
Maternal body mass index (BMI)					
19 – 24	45	45%	42	42%	>0.05
25 – 29	53	53%	54	54%	
> 30	2	2%	4	4%	
Mean ± SD	24.42 ± 3.40		24.72 ± 3.50		
Period of gestation at recruitment (weeks)					
37-39 weeks	62	62%	64	64%	>0.05
40-41 weeks	38	38%	36	36%	
Mean ± SD	38.95 ± 1.18		38.99 ± 1.19		

The difference between the two groups was not statistically significant as regarding cervical effacement and dilatation at the time of injection of patients in the 2 groups **(Table 2)**.

Table (2): Cervical effacement at the time of injection

Patient's Groups / Cervical condition	Study Group		Control Group		P value
	NO.	%	NO.	%	
Cervical effacement at the time of injection					
50%	48	48%	50	50%	>0.05
60%	52	52%	50	50%	
Cervical dilation at the time of injection					
3 cm	70	70%	72	72%	>0.05
4 cm	30	30%	28	28%	
Total	100	100%	100	100%	
Mean ± SD	4.30 ± 0.46		4.27 ± 0.45		

In study group 100 % of the patients had active phase of 1st stage < 6 hours and none of the patients had active phase of 1st stage > 6 hours. In control group 61 % of the patients had active phase of 1st stage < 6 hours and 39% of the patients had active phase of 1st stage > 6 hours.

The mean duration of 1st stage (active phase) of labor in study group was 186.53 minutes (3 hours 6 minutes), and in control group was 338.10 minutes (5 hours 38 minutes), The mean duration of 1st stage (active phase) of labor in study group was shortened significantly as compared to control group **(Table 3)**.

Table (3): Duration of 1st stage (active phase) of labor

Groups / Time	Study Group		Control Group		P value
	NO.	%	NO.	%	
< 2 hours	15	15%	0	0%	0.0001
2-4 hours	71	71%	21	21%	
4-6 hours	14	14%	40	40%	
> 6 hours	0	0%	39	39%	
Total	100	100%	100	100%	
Mean ± SD	186.53± 54.53		338.10± 92.90		

The mean duration of 2nd stage of labor in study group was 47.35 minutes and in control group was 53.22 minutes. The mean duration of 3rd stage of labor in study group was 8.34 minutes and in control group was 8.62 minutes. The mean difference between the two groups was not statistically significant **(Table 4)**.

Table (4): Duration of 2nd and 3rd stage of labor

Groups / Time	Study Group (n=95)		Control Group (n=92)		P value
	NO.	%	NO.	%	
Duration of 2nd stage of labor					>0.05
< 30 mins	40	42.1%	20	21.8%	
30 mins -1hour	52	54.8%	53	57.6%	
> 1 hour	3	3.1%	19	20.6%	
Mean ± SD	47.35± 20.79		53.22± 35.80		
Duration of 3rd stage of labor					>0.05
0-10 mins	90	94.8%	85	92.3%	
10-20 mins	5	5.2%	7	7.7%	
Mean ± SD	8.34± 1.87		8.62± 2.28		

In study group 96.8 % of the patients had total duration of labor < 8 hours and 3.2% of the patients had total duration of labor > 8 hours. In control group 36.9 % of the patients had total duration of labor < 8 hours and 63.1 % of the patients had total duration of labor > 8 hours.

The mean duration of total duration of labor in study group was 236.98 minutes (3 hours 57 minutes), and in control group was 407.08 minutes (6 hours 47 minutes), The mean duration of total duration of labor in study group was reduced by (2 hours 7 minutes) as compared to control group. The difference between the groups was statistically significant **(Table 5)**.

Table (5): Total duration of labor (drug to delivery interval)

Groups / Time	Study Group		Control Group		P value
	NO.	%	NO.	%	
< 4 hours	20	21.1%	7	7.6%	0.0001
4-8 hours	72	75.7%	27	29.3%	
> 8 hours	3	3.2%	58	63.1%	
Mean ± SD	236.98 ± 66.41		407.08 ± 109.86		

The mean rate of cervical dilation in study group was 2.41 cm/hr. and in control group was 1.37 cm/hr. The mean difference between the two groups was statistically significant **(Table 6)**.

Table (6): Rate of cervical dilation.

Groups / Rate of Cervical dilation	Study Group		Control Group		P value
	NO.	%	NO.	%	
Up to 2 cm/hour	46	46%	94	94%	0.0001
2.1 – 3 cm/hour	35	35%	6	6%	
3.1 – 4 cm/hour	12	12%	0	0%	
4.1 – 5 cm/hour	7	7%	0	0%	
Mean ± SD	2.41 ± 0.85		1.37 ± 0.57		

There was no significant statistical difference between the two groups as regards the adverse effect of HNBB **(Table 7)**.

Table (7): Maternal adverse effects of Hyoscine-N-butyl bromide

Groups / Maternal adverse effects of Hyoscine-N-butyl bromide	Study Group		Control Group		P value
	NO.	%	NO.	%	
Dryness of mouth	2	2%	1	1%	>0.05
Tachycardia	2	2%	1	1%	
Flushing of face	1	1%	0	0%	
Headache	3	3%	2	2%	
Extra pyramidal	0	0%	0	0%	

There was no significant statistical difference between the two groups as regards Apgar score at 1 and 5 min, neonatal intensive care unit admission, and neonatal weight **(Table 8)**.

Table (8): Fetal and neonatal outcomes

Groups / Outcomes	Study Group (n=100)		Control Group (n=100)		P value
Apgar score at one minute (Mean ± SD)	8.50 ± 0.75		8.46 ± 0.82		>0.05
Apgar score at five minutes (Mean ± SD)	8.51 ± 0.70		8.53 ± 0.66		>0.05
Neonatal weight	3113.33 ± 249.83		3114.73 ± 255.98		>0.05
NICU admission	No	%	>0.05	%	>0.05
Yes	1	1%	2	2%	
No	99	99%	98	98%	

DISCUSSION

Our study found that administration of HNBB in 20 mg has significantly decreased the duration of first stage of labor without exerting such effect on the second and third stages of labor. On one hand, the physiological explanation of that is the primary site of action of HBB which is the cervix without effect on uterine contractility. That is very important as enhancement of uterine contractions that shorten the second stage is exposing both the parturient women and her fetus to risks especially injuries. On the other hand, if it exerted an inhibitory action on uterine activity, it can expose the woman to hazards of atonic postpartum hemorrhage and retained placenta *(Sekhavat et al., 2012).*

The study was done on age group ranging from 20 to 35 years old, patients aging < 18 years or > 35 years were excluded as pregnancy in this age group consider high risk pregnancy *(Samiya et al., 2010).* The mean duration of active stage of labor showing a decrease hence statistically significant. The mean duration of active phase of labor reduced by HNBB compared to control group. The reduction in the mean duration of first stage of labor with the use of HNBB has been found consistently in all these studies *(Gupta et al., 2011).* The mean duration of first stage of labor in our study was least compared to the other studies as regard to the sample size. The difference in the mean duration of active phase of labor between study and control group in our study was statistically significant *(Mohamed et al., 2017).*

In contrast to our study, *Gupta et al. (2011)* found that the active phase duration and rate of cervical dilation in the group that received HBB were not significantly different from the control group. Similar observations were made by *Aldahhan et al. (2011)* who demonstrated duration of active phase in cases (246 min.) to be significantly longer compared to that in controls (204 min.) which is in contrast to the present study.

In the present study the mean rate of cervical dilatation was 2.41 cm/h in the study group and 1.37 cm/h in the control group. However, in the study by *Shwetha et al. (2016),* the mean cervical dilation rate was 2.78 cm/h in the study group and 1.97 cm/h in the control group.

In the study by *Edessy et al. (2015),* the mean cervical dilation rate was 1.8 cm/h in the study group and 0.98 cm/h in the control group. In study by *Makvandi et al. (2011),* the cervical dilation rate was found to be 2.6 cm/hour in primi study group & 1.5 cm/hour in primi control group.

In the present study, the mean duration of second stage of labor in the present study was 47 min. and 52 min. in study group and control group respectively. This difference was not statistically significant. In another study by *Sekhavat et al. (2012),* mean duration of second stage labor in Buscopan group was 20 min. vs. 25.8 min. in control group with no significant decrease.

Aldahhan et al. (2011), in their study, found the mean duration of second stage labor to be 15.6 min. and 12.7 min. in Buscopan and control group respectively, thus showing no decrease of duration.

In the present study, the number of cases delivered by cesarean section was

5% in study group and 8% in control group. There were no significant differences in terms of Apgar scores noted at 1 and 5min, and birth weight. No adverse maternal and fetal effects were observed in both HNBB and placebo groups.

Our study was an important randomized un blinded controlled trial. Its sample size was the largest among the studies reported to date. It was limited to primigravida women who were more suspected to abnormal progress of labor and subjected to more hazards of prolonged labor. Our intervention led to shortening of the duration of first stage of labor.

The shortening of the 1st stage of labor was associated with lower risk of postpartum hemorrhage, chorioamnionitis, puerperal, and neonatal sepsis. It also raised maternal tolerability to vaginal delivery decreasing the risk of cesarean section resulted from maternal exhaustion or psychological troubles associated with labor pain especially in developing areas without high availability of epidural analgesia *(Kirim et al., 2015)*.

There was no effect on the second and third stages of labor. That was also beneficial as the hastened second stage was associated with increased risk of maternal and fetal birth injuries.

CONCLUSION

Administration of HNBB i.v significantly reduced the duration time of cervical dilation in the active phase of first stage of labor, thereby reducing the total duration of labor. Hyoscine –N- butyl bromide i.v. did not have any unfavorable side effects on the uterine contractions (It did not alter the second and third stage of labor). It is cheap, easy to be used and safe without any significant maternal or fetal side effects.

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تأثير عقار هيوسين -ن- بيوتيل بروميد على ترقيق عنق الرحم وتوسيعه أثناء الولادة الطبيعية

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خلفية البحث: الولادة هى عملية طبيعية تتميز بزيادة عدد وقوة ومدة إنقباضات الرحم من ناحية ومن الناحية الأخرى زيادة إتساع وقابلية عنق الرحم للاتساع بالتزامن مع نزول وخروج الجنين خلال قناة الولادة.

الهدف من البحث: دراسة مدى فاعلية وأمان عقار هيوسين –ن- بيوتيل بروميد على ترقيق عنق الرحم وتوسيعه أثناء الولادة الطبيعية.

المريضات وطرق البحث: تم إجراء هذه الدراسة على مائتين من السيدات اللاتي كن فى مرحلة المخاض الأولى لهن في قسم التوليد وأمراض النساء في مستشفى سوهاج العام خلال الفترة من فبراير إلى يوليو 2019, وقد تم إختبار السيدات المشاركات في هذه الدراسه عشوائياً وتم تقسيمهن في مجموعتين متساويتين خلال فترة الدراسة.

نتائج البحث: يقلل عقار الهيوسين بشكل كبير من مدة توسع عنق الرحم في المرحلة النشطة من المرحلة الأولى من الولادة الطبيعية، وبالتالي تقليل المدة الإجمالية للولادة. كما أن عقار الهيوسين ليس له أي آثار جانبية سلبية على تقلصات الرحم, وهو لا يغير المرحلة الثانية والثالثة من المخاض.

الاستنتاج: عقار الهيوسين هو وسيلة فعالة وآمنة لتقصير مدة المرحلة الأولى من المخاض دون أي آثار ضارة على الجنين أو الأم ويتميز بتكلفته المنخفضة للغاية.

الكلمات الدالة : هيوسين – ن بيوتيل بروميد– ترقيق عنق الرحم – توسيع الرحم.