Rectal Hyoscine-N-Butylbromide Safely Accelerates Progress of Labor in Primipara: A Placebo-Controlled Study

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Abstract: **Objectives**: To evaluate the applicability of the administration of Hyoscine-N-butylbromide (HBB) as a therapeutic modality for acceleration of progress of labor in primipara. **Patients & Methods**: The study included 150 primiparae having normal-sized singleton fetus with cephalic presentation. At time of pregnancy diagnosis, patients' demographic and body constitutional data were determined. Parturient were randomly allocated into two equal groups: Control group received paracetamol 800 mg rectal suppository as placebo and Study group received buscopan compositum adult supp containing HBB 10 mg and paracetamol 800 mg. Both groups received nalbuphine, 10 mg intramuscular injection. All medications were administered during the active phase of the first stage of labor when cervical dilatation was 4 cm with 80% cervical effacement and regular uterine contraction at frequency of 3-4 contractions every 10 minutes. The durations of the first and second stages of labor were determined. **Results**: Mean duration of both first and second stages and total durations of active labor were significantly shorter in study group compared to control group. Fifty parturient had spontaneous rupture of membranes and 33 parturient required oxytocin augmentation with significantly higher frequency of spontaneous membrane rupture and the need for oxytocin in control group compared to study group. As regards mode of delivery, 40 parturient required instrumental aid with significantly higher frequency of need for instrumental delivery in control group compared to study group. Twenty-two neonates had Apgar score of <9; 13 in control and 9 in study group with non-significant difference between both groups. **Conclusion**: Rectal administration of HBB for primipara allows significant reduction of duration of first and second stages of labor without inducing significant maternal or fetal complications. Meticulous observation of the progress of pregnancy spared the possibilities for hastened delivery with its subsequent complications, so it is mandatory for such cases.

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1. Introduction

Hyoscine-N-butylbromide (HBB) is a quaternary ammonium compound belongs to the para-sympatholytic group of drugs. It is a semisynthetic derivative of scopolamine. It has peripheral anticholinergic action, but no central action as it does not cross the blood–brain barrier. HBB 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 without the untoward side effects of atropine **(Litta-Modignani *et al.*, 1977; Chang *et al.*, 1995; Ciccaglione *et al.*, 2001)**.

Normal labor, despite dating since presence of human being on the earth, still a matter of research and its management still a wide field for development. One of the important points for research is how to control the progress of labor, hasten its stages, minimize or abolish concomitant pain and minimize complications **(Zhang *et al.*, 2010; Caruselli *et al.*, 2011; Skrablin *et al.*, 2011)**. The use of nerve blocks for management of labor pain was beneficial but had concomitant side effects; mostly affecting progress of labor and increased frequency of instrumental or operative delivery. These effects could be attributed to abolishment of uterine contraction-cervical dilatation reflex leading to prolongation of duration of labor, despite disappearance of pain. Opioids had deleterious effects on fetal respiration and outcome **(Ullman *et al.*, 2010; Li *et al.*, 2010; Caruselli *et al.*, 2011; Mori *et al.*, 2011)**.

The use of antispasmodics for relieve of cervical dilatation pain was tried using multiple drugs with antispasmodic and/or analgesic actions either alone of in combinations **(Guerresi *et al.*, 1981; Mahon *et al.*, 1994; Jha *et al.*, 2003)**. The current comparative study aimed to evaluate the applicability of the administration of HBB as antispasmodic as a therapeutic modality for acceleration of progress of labor in primipara.

2. Patients and Methods

The current study was conducted at Obstetrics & Gynecology department, Faculty of Medicine, Benha

University Hospital since Jan 2010 till June 2011. After approval of the study protocol by the Local Ethical Committee and obtaining written fully informed patients' consents, 150 primiparae having normal-sized singleton fetus with cephalic presentation, were enrolled in the study. All parturient were selected from those attending the outpatient clinic for chemical and clinical diagnosis of pregnancy. Patients' demographic and body constitutional data were determined at time of diagnosis of pregnancy and were considered as baseline data. To exclude the impact of body weight on dosage of study drugs only women with body mass index ≤30 kg/m^2 were enrolled in the study.

Parturient were randomly, using sealed envelops, allocated into two groups: Control group (n=75) assigned to receive 2 paracetamol rectal suppositories (Tylenol, 350 mg/supp, Cilag, Egypt) as placebo and Study group (n=75) assigned to receive buscopan compositum adult supp (Cid Boehringer, Egypt) containing hyoscine-N-butyl bromide 10 mg and paracetamol 800 mg. Both groups received nalbuphine, 10 mg intramuscular injection. All medications were administered during active phase of first stage of labor when cervical dilatation was 4 cm with 80% cervical effacement and regular uterine contraction at frequency of 3-4 contractions/10 min.

The durations of the first and second stages of labor were determined. The duration of the first stage was calculated from the time of cervical dilatation of 3–4 cm in active labor (Time of administration of study drugs) until a fully dilated cervix was observed upon vaginal examination conducted every half an hour. Oxytocin augmentation was initiated if the initial progress of labor was unsatisfactory. The frequency of ruptured membrane, prolonged third stage and frequency of postpartum hemorrhage were recorded. The mode of delivery, maternal complications, and neonatal conditions at birth (Apgar score and weight) were also determined.

Statistical analysis

Results were expressed as mean±SD, range, numbers and percentages. Inter-group data was statistically analyzed using Wilcoxone Ranked test for related data (Z test) and Chi-square (X^2 test) test. Statistical analysis was conducted using SPSS statistical program, (Version 15, 2006). *P* value <0.05 was considered statistically significant.

3. Results

The study included 150 women fulfilled the inclusion criteria. Mean age of included women was 24.2±1.7; range: 20-27 years. There was non-significant difference (p>0.05) between women enrolled in both groups as regards age, weight, height and BMI. At time of admission, mean cervical dilatation was 3.5±0.5; range: 3-4 cm with non-significant difference between studied groups.

Mean duration of both first and second stages were significantly shorter in study compared to control group with significantly shorter mean total duration of active labor in study group compared to control group, (Table 2, Figs. 1 & 2).

All enrolled women passed their labor safely without complications or side effects of studied drugs. Fifty parturient (33.3%) had spontaneous rupture of membranes; 17 (22.3%) in control group and 33 (44%) in study group with significantly higher (X^2=5.173, p<0.05) frequency of spontaneous rupture of membrane in study group. Thirty-three parturient (22%) required oxytocin augmentation; 21 (28%) in control group and 12 in study group (16%) with significantly higher (X^2=3.290, p <0.05) frequency of the need for oxytocin in control group compared to study group. As regards mode of delivery, 40 parturient (26.7%) required instrumental aid; 35 parturient (23.4%) required suction and 5 (3.3%) had forceps delivery. There was significantly higher (X^2=5.173, p<0.05) need for instrumental delivery in control group compared to study group. However, 19 parturient (12.7%) had cesarean section; 12 in control group (16%) and 7 in study group (9.3%) with non-significantly (X^2=1.219, p >0.05) lower frequency in favor of study group. Twenty-two neonates had Apgar score of <9; 13 in control and 9 in study group with non-significant difference between both groups, (Table 3).

Table (1): Parturient' demographic data recorded at time of enrollment

			Control group	Study group	Total
Age (years)	Total		24.4±1.6 (21-27)	24±1.8 (20-27)	24.2±1.7 (20-27)
	Strata	≤23	22 (29.3%)	21 (28%)	43 (28.7%)
		>23-26	44 (58.7%)	47 (62.7%)	91 (60.7%)
		>26	9 (12%)	7 (9.3%)	16 (10.6%)
Weight (kg)			81.9±6.2 (69-96)	84.1±5.1 (71-94)	83±5.8 (69-96)
Height (cm)			165.6±4.8 (156-176)	168.5±4.7 (156-178)	167±5 (156-178)
BMI (kg/m^2)			29.9±2.1 (24.2-29.7)	29.6±1.3 (25.3-29.6)	29.8±1.7 (24.2-29.6)

Data are presented as mean±SD & numbers; ranges & percentages are in parenthesis

Table (2): Duration of first and second stages of labor reported for both groups of parturient

	Control	Study	Statistical analysis
Duration of first stage (hr)	7.8±1 (6-10.7)	6.4±1.3 (4.5-8.9)	Z=5.529, p<0.001
Duration of second stage (min)	1.5±0.4 (1-2.3)	1.3±2.1 (0.8-2.1)	Z=2.484, p=0.013
Total duration till delivery (min)	9.2±1.1 (7.8-12.1)	7.7±1.3 (5.4-10.4)	Z=6.093, p<0.001

Data are presented as mean±SD; ranges are in parenthesis

Table (3): Delivery data reported for both groups of parturient

		Control	Study	Statistical analysis
Spontaneous rupture of membrane	Yes	17 (22.3%)	33 (44%)	X^2=5.173, p <0.05
	No	58 (77.7%)	42 (56%)	
Oxytocin augmentation	Yes	21 (28%)	12 (16%)	X^2=3.290, p <0.05
	No	54 (72%)	63 (84%)	
Operative delivery	Yes	12 (16%)	7 (9.3%)	X^2=1.219, p >0.05
	No	63 (84%)	68 (90.7%)	
Vaginal delivery	Forceps	3 (4%)	2 (2.7%)	X^2=2.133, p>0.05
	Suction	22 (29.3%)	13 (17.3%)	
	Normal	38 (50.7%)	53 (70.7%)	
Prolonged 3rd stage	Yes	6 (9.5%)	4 (5.9%)	X^2=1.666, p >0.05
	No	57 (90.5%)	64 (94.1%)	
Postpartum hemorrhage	Yes	3 (4.8%)	2 (3%)	X^2=0.281, p >0.05
	No	60 (95.2%)	66 (97%)	
Apgar score	<9	13 (17.3%)	9 (12%)	X^2=1.415, p >0.05
	9-10	62 (82.7%)	66 (88%)	

Data are presented as numbers; percentages are in parenthesis

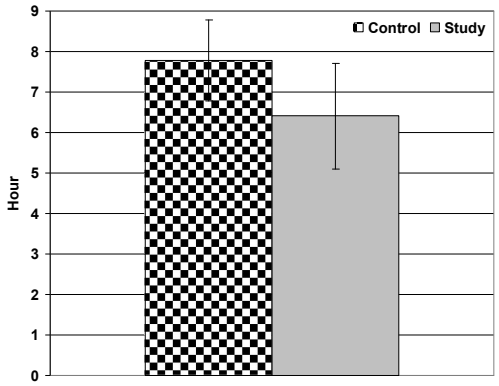

Fig. (1): Mean (±SD) duration of first stage recorded in both groups

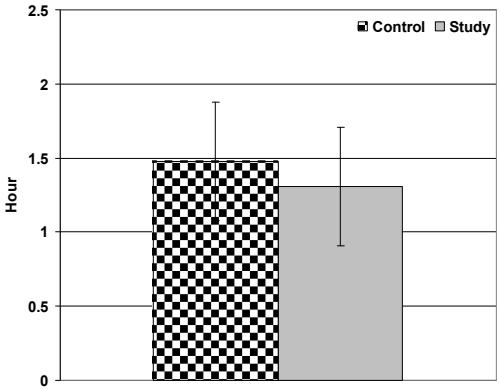

Fig. (2): Mean (±SD) duration of second stage recorded in both groups

4. Discussion

The current comparative study aimed to evaluate the applicability of rectal administration of HBB as a therapeutic modality for acceleration of progress of labor in primipara. Unfortunately, pure HBB rectal preparation was not available in Egypt, the commercial preparation available is a combination of HBB and paracetamol; so, control group was administered paracetamol of similar dose to equalize the effect of paracetamol in both groups so that the difference in results could be attributed to HBB alone.

Parturient received HBB showed significantly shorter duration of first and second stages of labor compared to those who did not receive HBB. These results manifest the beneficial effects of antispasmodics as modality for reduction of duration of active stages of labor. In line with these beneficial effects of HBB, there was significant reduction of the frequency of need for oxytocin augmentation and instrumental delivery in study group compared to control group. However, the safety of HBB was manifested as non-significant difference in the frequency of parturient had operative delivery, prolonged 3rd stage of labor or developed postpartum hemorrhage.

These data supported that previously reported in literature; **Sirohiwal *et al.* (2005)** reported a significant difference in the duration of active phase of labor between the control and study groups received HBB suppository. **Samuels *et al.* (2007)** found intravenous HBB is effective in significantly reducing

the duration of the first stage of labor by 31.7%, and it is not associated with any obvious adverse outcomes in mother or neonate. **Aggarwal *et al.* (2008)** evaluated the effects of 40 mg intravenous HBB as a labor analgesic and labor accelerant and reported pain relief of 35.6% on visual analog score and mean duration of labor was significantly reduced. **Qahtani & Hajeri (2011)** documented that HBB is effective in significantly reducing the duration of the first stage of labor, representing a decrease of 23.3% and is not associated with any apparent adverse maternal or neonatal outcomes. **Makvandi *et al.* (2011)** reported that the active phase and the second stage of labor were significantly shorter in the patients received HBB compared to control group with no significant difference between the two groups in the fetal heart rate, maternal pulse rate, blood pressure, and the APGAR score 1 and 5 minutes after birth.

On contrary to the obtained results; **Gupta *et al.* (2008)** found that the active phase duration and rate of cervical dilatation in the group that received HBB were not significantly different from the control group. Moreover, the results concerning the duration of the second stage are also discrepant, in contrary to the results of the current study, **Samuels *et al.* (2007)** and **Qahtani & Hajeri (2011)** reported non-significant reduction of the duration of the second stage.

These differences could be attributed to pharmacodynamics of the used forms of HBB. Rectal HBB may provide longer duration of action that may expand to overlap the second stage than injectable forms. Moreover, the outcome of rectal HBB may be influenced by the local effect of the rectal medication on the cervical region. Although the exact mechanism of action of HBB is not established, it is possible that induced relaxation enables more effective myometrical contractions. In support of this assumption, **Fujimoto *et al.* (2010)** using sagittal T2WI of the pelvis before and after administration of HBB with interval of 10 minutes in 22 healthy volunteers reported that areas of outer myometrium were significantly increased and mean relative signal intensity of junctional zone and outer myometrium were significantly increased after administration of HBB and considered these changes to be caused by an increase in interstitial fluid and vascular dilatation, while endometrium did not show significant changes.

The achieved results of shortening of the first stage of labor is of utmost importance for reduction of duration of severe pain concomitant with cervical dilatation especially in the inexperienced primipara who lack knowledge about pain of labor. Also, shortening of first stage reduces the frequency of risk of chorioamnionitis, neonatal sepsis, and puerperal sepsis, all of which increase in women with prolonged labor. As another advantage, short first stage with minimization of associated pain reduce the consumption of analgesia especially opiates which is associated with neonatal respiratory depression. Furthermore, the reduction in first stage duration may also prove to be of particular importance for women with a borderline placental reserve, oligohydramnios, or risk of prolonged variable deceleration during labor, as may be encountered in women with hypertension (both chronic and gestational) and in women with sickle cell anemia which may result in depletion of the fetoplacental reserves with consequent signs of fetal distress and an increased rate of cesarean section **(Maharjan & Karki, 2003; Capogna *et al.*, 2010; Zhang *et al.*, 2010)**.

Rodie *et al.* (2002) and **Myles & Santolaya (2003)** alleged that the significant shortening of the second stage may be accused as a cause for perineal tear and could be considered as one of pitfall of use of HBB; however, the current study reported significant shortening of the second stage but no parturient developed perineal tears in either group, this could be attributed to the meticulous observation for the progress of the first stage every 30 minutes so no case was allowed to proceed spontaneously. Secondly, the current study included only primipara in whom the progress from the first to the second stage require some time not as the multipara who may progress rapidly **(Cheng *et al.*, 2007)** and these studies tried HBB for mixed patients' population so the presence or high frequency of perineal tears mostly affected multipara. In line with shortening of the first and second stages; **Christianson *et al.*(2003)** documented that the increased duration of both the first and second stages of labor increased perineal injury risk and delivery with forceps was associated with a 10-fold increased risk of perineal injury. Also, **Pirro *et al.* (2007)** documented that the risk factors for sphincter injury and pudendal neuropathy include forceps delivery, large neonatal size, and prolonged second stage of labor and routine episiotomy does not prevent sphincter injury and may even predispose to it. As another support for advantages of shortening of the second stage, **Matsuo *et al.* (2009)** reported that wearing a dental support device may shorten the second stage of labor, and may decrease the number of failures to descend requiring operative intervention. **Allen *et al.*(2009)** indicted that risk of both maternal and perinatal adverse outcomes rise with increased duration of the second stage.

It could be concluded that rectal administration of HBB for primipara allows significant reduction duration of first and second stages of labor without inducing significant maternal or fetal complications. Meticulous observation of the progress of pregnancy spared the possibilities for hastened delivery with its subsequent complications, so it is mandatory for such cases.

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