

Hyoscine-N-Butylbromide and Progression of Labor at Different Stages

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Received 2016 October 29; Accepted 2016 December 06.

Abstract

Background: Given the importance of natural childbirth and emphasis on the normal vaginal delivery, and since important causes of having a C-section are lack of response to induction of labor with Syntocinon® injection and the fact that the cervix is unfavorable for labor.

Objective: The present study aims at achieving the best method of cervical ripening for pregnancy termination to reduce the C-section rate, labor duration, economic burden, and labor pain.

Methods: In this regard, the current study examined the effect of hyoscine-N-butylbromide (HBB) on the progression of cervical ripening in normal vaginal delivery. In the current prospective double-blind controlled clinical trial, 60 pregnant females referred to Valiasr hospital (with the mean age of 27.2 years) were randomly divided into 2 groups of experimental and control; HBB and normal saline (placebo) were intravenously administered in the active phase of labor.

Results: The pain reduction in the patients, the duration of drug action until the cervical dilatation, the number of drug use for the full cervical dilatation, the time of the onset of the first, second, and third stages of labor, the length of hospitalization until the delivery, the drug effect on the fetus and mother, and the delivery method were evaluated in both groups. HBB significantly reduced the duration of the first stage of labor; however, it did not affect the second and third stages. Moreover, no negative effects were observed on the mother and fetus health.

Conclusion: According to the obtained results, it can be concluded that the intravenous injection of HBB can be applied as an effective drug for labor progress; however, further clinical studies with larger sample sizes are required to confirm these findings.

Keywords: Hyoscine, Pregnancy, Intravenous Injection, Duration of Labor, Maternal and Neonatal Morbidity, Maternal and Fetal Heart Rate

1. Introduction

Labor is a physiological process that results in wide variations in a mother and enables the natural delivery of a fetus. This process is determined with a progressive cervical effacement, dilatation, or both occurring as a result of uterine contractions. These contractions can be repeated at least every 5 minutes and last for 30 to 60 seconds. A number of physiological events usually occur before the onset of the actual labor (1).

Given the importance of natural childbirth and emphasis on the normal vaginal delivery, and since important causes of having a C-section are lack of response to induction of labor with Syntocinon® injection and the fact that sometimes the cervix is unfavorable for labor (1-3), moreover due to contradictory results about the effect of hyoscine-N-butylbromide (HBB) on labor progress (3-5),

the current study aims at evaluating the effect of HBB on, C-section rate, labor duration, economic burden and labor pain. Besides, the current study examined the effect of HBB on the progression of cervical ripening in normal vaginal delivery in mothers referred to Valiasr hospital, Tehran, Iran.

2. Methods

It was a prospective double-blind controlled clinical trial. After taking their history and conducting general and vaginal examinations and considering the exclusion criteria including abnormal fetal heart rate, vaginal bleeding, placenta previa and placental abruption, multi-gestational pregnancy, advanced medical conditions such as a mother's heart disease, non-cephalic presentation, fetal macrosomia, history of infertility or fetal abnormalities

or death, grand multiparity (gravida greater than or equal to 5), rupturing of the amniotic sac, intrauterine growth restriction, fetal weight higher than 4000 grams, history of uterine surgery, maternal medical disease (especially heart disease), maternal tachycardia, history of preeclampsia, prescription of narcotic drugs and analgesics, oxytocin infusion in the first and second stages of labor, and also contraindications to prescribe HBB such as glaucoma and paralytic ileus, the pregnant females with the inclusion criteria including the term pregnant females with an indication of termination of pregnancy (37 - 42 weeks) and the conditions required for a normal delivery, females above 18 years old, having at least 3 spontaneous contractions (40 seconds) in 10 minutes, and experiencing amniotic sac rupture in the last 6 hours with spontaneously contractions participated in this study (1-5). Before carrying out any interventions, informed consent was obtained from the patients and their families and the advantages and disadvantages of this method were explained to them and the Helsinki protocols were considered. Rejection of the conditions by a patient did not make any changes in the treatment process.

The experimental group received 40 mg or 2 mL of HBB (hyoscine 1 mL by Caspian Tamin Pharmaceutical Company, Rasht, Iran) and the control group received 2 mL serum in the active phase of labor. By performing vaginal examinations at fixed intervals, the cervical dilatation and effacement were examined in the first and second stages of labor. Moreover, the rate of fetal descent, rate of C-section, amount of blood loss during labor through checking the hematocrit before and after childbirth, and APGAR (acronym for appearance, pulse, grimace, activity, and respiration) scores were also evaluated. In the absence of dilatation, the next dose of HBB was injected 4 - 6 hours later. It should be noted that the duration of drug action is 4 - 6 hours, it acts within 30 minutes to 1 hour, and its half-life is 4.8 hours (1-3). In the current study, the newborn's APGAR score was examined in the first and the fifth minutes and the mother's blood pressure was checked 30 - 60 minutes after the injection and thereafter, up to 4 hours, it was measured every hour. Fetal heart rate (FHR) was also evaluated immediately after the injection and every 15 to 30 minutes in the active phase of labor depending on the patient's condition. Patients with a good labor progress including dilatation, effacement, and descent (the dilatation was considered 1.2 cm and 1.5 cm per hour for nulliparous and multiparous females, respectively) had normal vaginal deliveries. In cases when lack of progress in labor, FHR drop, thick meconium passage by the fetus, significant vaginal bleeding, and umbilical cord prolapse occurred, C-sections were performed.

Vacuum extractor was used for females with sponta-

neous contractions, a suitable pelvis for a normal vaginal delivery, without fetal macrosomia and cooperative to deliver the fetus. Under such circumstances, the fetus head should be at a +3 station.

The fetal heart rate was examined before, immediately, and 1 hours after taking the drug. Maternal heart rate was checked before, immediately, 1 and 2 hours after taking the drug.

The potential side effects of this drug including dry mouth, tachycardia, nausea, and urinary retention were assessed through observation and examination. The patient was hydrated in the case of dry mouth. In case of nausea, metoclopramide was taken and in case of urinary retention, Nelaton catheters were used (Table 1).

Table 1. Characteristics of Natural Childbirth

Features	Nulliparous	Multiparous
Duration of the first stage	6 - 8 hours	2 - 10 h
Cervical dilatation during the active phase	1.2 cm/h	1.5 cm/h
Duration of the second stage	30 min to 3 h	5 to 30 min
Duration of the third stage	0 to 30 min	0 to 30 min

2.1. Data Analysis

The obtained data were analyzed using SPSS software, version 19 (IBM SPSS, Armonk, NY, USA). To determine the frequency, the central statistical indicators (mean) and dispersion indices (standard deviation) were applied. To indicate the relationship of quantitative and qualitative variables, student t test and Chi-square test were used, respectively. In addition, to investigate the relationship between 2 quantitative variables, the correlation coefficient was employed.

3. Results

A sample of 60 term pregnant females participated in the current study. They were divided into an HBB (experimental) and a placebo group (control). The mean age of the experimental group was 27 years with a standard deviation of 4.56 years and the mean age of the control group was 27.4 years with a standard deviation of 3.94 years. The youngest and oldest people in the study were respectively 20 and 42 years old. In Table 2, the duration of drug use for the full cervical dilatation, the duration of labor, the duration of the first and second stages of labor, length of hospitalization, and fetal heart rate traces were compared in the 2 groups that respectively received HBB and placebo. There was only a significant difference between the 2 groups in

the fetal heart rate before, immediately and 1 hour after taking the drug.

Table 2. Comparing Hyoscine-N-Butylbromide (HBB) and Placebo Groups in Various Stages of Labor^a

	Hyoscine	Placebo	P-Value
Duration of taking the drug till the full dilatation, h	3.57 ± 3.06	6.32 ± 3.16	0.000
Duration of labor, h	9.33 ± 5.15	12.25 ± 4.84	0.001
Duration of the first stage of labor, h	7.1 ± 4.65	10.65 ± 3.96	≤ 0.05
Duration of the second stage of labor, h	0.96 ± 0.43	0.77 ± 0.51	≥ 0.05
Length of hospitalization	1.16 ± 0.379	1.16 ± 0.379	≥ 0.05
Reassuring fetal heart rate	27 (45)	28 (46.7)	≥ 0.05
Non reassuring fetal heart rate	3 (5)	2 (3.3)	

^aValues are expressed as mean ± SD or No. (%).

In terms of maternal heart rate, before, immediately, 1 and 2 hours after taking the drug, there was a significant difference between the 2 groups considering the heart rate checked immediately and an hour after taking the drug. However, with regard to the fetal heart rate examined immediately after taking the drug, there was a significant difference between the 2 groups.

Tachycardia occurred after taking the drug in 1 subject in the control group (5.6%) and 17 subjects in the experimental group (94.4%). There was a significant difference between the 2 groups regarding tachycardia ($P = 0.000$).

Dry mouth occurred after taking the drug in 2 subjects in the control and 18 subjects in the experimental groups. In this regard, there was a significant difference between the 2 groups in terms of dry mouth ($P = 0.000$) (Table 3).

4. Discussion

In a study conducted in Ahvaz, the effect of HBB, rectal suppository on labor progress was examined in primigravida females. The rate of cervical dilatation was 2.6 cm/hour in the experimental group, and 1.5 cm/hour in the control (placebo) group. The active phase and the second stage of labor were significantly shorter in both groups. Additionally, there was no significant difference between the 2 groups in the fetal and maternal heart rate and maternal blood pressure (1).

Table 3. Comparing Hyoscine-N-Butylbromide (HBB) and Placebo Groups in Fetal and Maternal Heart Rate^a

	Hyoscine-N-Butylbromide	Placebo	P-Value
Fetal heart rate before taking the drug	137.43 ± 5.73	136.77 ± 14.55	> 0.05
Fetal heart rate immediately after taking the drug	147.67 ± 10.83	137.27 ± 13.53	0.002
Fetal heart rate an hour after taking the drug	139.5 ± 6.98	138.26 ± 11.66	> 0.05
Maternal heart rate before taking the drug	85.83 ± 9.37	85.93 ± 7.28	> 0.05
Maternal heart rate immediately after taking the drug	97.6 ± 10.37	86.2 ± 7.69	0.000
Maternal heart rate an hour after taking the drug	91.83 ± 8.18	86.2 ± 7.69	0.008
Maternal heart rate 2 hours after taking the drug	85.5 ± 8.27	86.2 ± 7.69	> 0.05

^aValues are expressed as mean ± SD or No. (%).

A study conducted on 97 primigravida females, compared the effect of HBB and placebo intramuscular injections on the active phase and the results indicated that the mean duration of the first stage in the control group was 216 minutes, compared to 165 minutes in the experimental group. However, there were no significant changes in the duration of the second and third stages of labor, blood loss and APGAR scores (2). Furthermore, lack of effectiveness of HBB and drotaverine hydrochloride in augmentation of labor was reported among Indian patients (3).

In another study, 52 patients placed in the experimental group received a slow intravenous injection of 40 mg HBB (as labor analgesic) in the active phase of labor, while the control group received 2 mL normal saline. The degree of pain reached its lowest level 2 hours later. The mean duration of labor was 3 hours 46 minutes in the experimental group compared to 8 hours 16 minutes in the control group. The pain relief of 36.7% was noted on visual analog score with the use of HBB (4).

In the same line, the effects of valethamate bromide and HBB on the first stage of labor in term pregnancies were evaluated. Fifty pregnant females received HBB, 50 pregnant females received valethamate bromide, and 50 pregnant females, considered as the control group, received no such injections. Valethamate bromide with vagolytic features affected the cervical dilatation and HBB

with spasmolytic features affected the duration of labor. The mean duration of the first stage was 11.19 hours in the control group, 7.73 hours in the valethamate bromide group, and 7.03 hours in the HBB group. No significant effects, except mild adverse effects such as tachycardia, dry mouth, and vomiting, were noted (5).

In another study, the mean time for the first stage in the control group was 228 minutes, compared with 156 minutes in the experimental group, which received HBB intravenously, representing a decrease of 31.7%. However, no significant changes were observed in the duration of the second and third stages of labor and in blood loss or APGAR scores (6). Moreover, several studies reported the effectiveness of HBB in the progress of dilatation and effacement and in shortening the first stage of labor (7, 8).

According to the obtained results, it can be inferred that the intravenous injection of HBB had positive effects on labor progress. This drug is a kind of anticholinergic/antispasmodic drugs which lessens the spasms of smooth muscles, such as those of the gastrointestinal and genitourinary systems (9). On the other hand, HBB crosses the placenta and its intravenous injection, especially near-term injections, may increase the fetal heart rate. According to some researchers, in some cases, the intravenous injection of this drug may reduce the variability of fetal heart beats and may even decrease the heart rate (1, 10, 11). Decrease in blood pressure, dry oral mucosa, nausea, vomiting, blurred vision, constipation, and urinary retention are some of the side effects of the anticholinergic HBB (12). Dizziness, restlessness, shivering, delusion, insanity, and behavioral disorders are other side effects of this drug (12). In the current study, applying HBB significantly increased the effacement and dilatation of the cervix. This finding was in line with the results of studies by Samuels et al. (6) and Sirohiwal et al. (8); however, it was not consistent with the results of a study in Sabzevar by Mortazavi and Rakhshani (13).

The onset of action of HBB on muscles is nearly an hour after taking the drug and the level of bioavailability of this drug is approximately 50% (14, 15). The current study compared the duration of the first stage of labor in the 2 groups and it was observed that the duration was significantly shorter in the experimental group, which received HBB, compared to the control group. However, no significant difference was observed between the 2 groups considering the duration of the second stage of labor. Similar results were obtained from studies conducted by Qahtani and Hajeri in Saudi Arabia (2) and Raghavan (5). A study by Makvandi et al. (1) in Ahvaz administered 20 mg of HBB rectal suppository in the experimental group and the placebo rectal suppository in the control group and indicated that the active phase and the second stage of labor were signif-

icantly shorter in both groups.

Gupta et al. (3) in India divided 150 pregnant females to 3 groups; injected HBB to 50 females, drotaverine hydrochloride to another 50, and no drugs to the third 50 females. After recording their observations, they reported lack of effectiveness of HBB and drotaverine hydrochloride. Samuels et al. (6) conducted a study in Jamaica and found that HBB decreased the duration of the first stage of labor; however, it had no significant effects on the second and third stages of labor. Furthermore, the results of a study in West Indies University, in Jamaica, indicated the effectiveness of HBB in the progress of dilatation and effacement and in shortening the duration of the first stage of labor (7). In the same line, a study in India demonstrated the effect of HBB in shortening the active phase of labor; however, it had no significant effects on the second and third stages of labor (8). Moreover, Aggarwal et al. (4) conducted a study on 104 primigravida females and indicated that a slow intravenous injection of 40 mg HBB relieved 25% to 75% of pain (with a mean of 35.6%) in the experimental group and 25% of pain (with a mean of 12.5%) in the control group ($P < 0.001$). This finding was not in line with the results of the current study. This difference may be due to the drug administration methods and its dosage.

In the current study, compared to the experimental group, the C-section rate was lower in the control group; however, this difference was not statistically significant. Probably in larger sample sizes, the type of delivery may be affected by the intravenous injection of HBB. Aggarwal et al. (4) examined a sample of 52 pregnant females and found no significant difference in terms of the type of delivery. HBB crosses the placenta and its intravenous injection, especially near-term injections, may lead to fetal tachycardia. According to some researchers, in some cases, the intravenous injection of this drug may reduce the variability of fetal heart beats and even fetal bradycardia (16). In the present study, there was no significant difference between these 2 groups considering the fetal heart rate before and an hour after taking the drug; however, compared to the control group, the fetal heart rate checked immediately after taking the drug was significantly higher in the experimental group. These findings were consistent with those of Sirohiwal et al. (8) and Makvandi et al. (1) indicating no significant difference between the groups. The results of a study by Iravani and Bekhradi Nasab demonstrated that 30 minutes after the intravenous injection of HBB, the fetal tachycardia and bradycardia occurred in 24% of the experimental group and 10% of the control group (17). The intravenous HBB quickly crosses the placenta and can cause fetal tachycardia and bradycardia (16, 17). Additionally, the present study observed no significant difference between the 2 groups considering the maternal

heart rate before and 2 hours after taking the drug; however, compared to the control group, the maternal heart rate, checked immediately and an hour after taking the drug, was significantly higher in the experimental group. These findings were consistent with those of Raghavan (5); however, these findings were not in line with the results of studies by Sirohiwal et al. (8) and Makvandi et al. (1) indicating no significant difference between the 2 groups. In addition, there was a significant difference between the 2 groups considering the maternal systolic and diastolic blood pressure before and an hour after taking the drug; however, no significant difference was found between the 2 groups regarding the maternal systolic and diastolic blood pressure checked immediately after taking the drug. In the current study, no significant differences were found between the 2 groups considering the newborns' APGAR scores examined in the first and fifth minutes. Similar results were reported in studies conducted by Samuels et al. in Jamaica (6), Qahtani and Hajeri in Saudi Arabia (2) and Iravani and Bekhradi Nasab in Iran (17).

Moreover, there were significant differences between these 2 groups regarding tachycardia and dry mouth. Both tachycardia and dry mouth were observed more in the experimental group compared to the control group. However, considering nausea and urinary retention, no significant difference was found between the groups. Raghavan (5) indicated that tachycardia, dry mouth, and vomiting were mildly higher in the experimental group compared to the control group. This is while the adverse maternal and fetal outcomes were not reported in the study by Sirohiwal et al. (8). In the current study, the duration of taking drug until full dilatation and the duration of labor were lower in the experimental group compared to those of the control group. This result was in line with the results of Aggarwal et al. (4). Examining the length of hospitalization and the normality of fetal heart rate monitored during labor indicated no significant differences between the 2 groups.

4.1. Conclusions

According to the obtained results, it can be concluded that the intravenous injection of hyoscine-N-butylbromide can be applied as an effective drug for the progress of labor; however, further clinical studies with larger sample sizes are required to confirm the safety of this drug and also to compare its efficacy with those of other similar drugs.

Acknowledgments

This article is part of the medical doctor's thesis entitled "Examine the Effect of Hyoscine-N-Butylbromide on

the First, Second, and Third Stages of Labor Progress in 2011 in Vali-e-Asr Hospital" with code 21807 that is sponsored by Tehran University of Medical Sciences has been implemented. There is no conflict of interest in the current study.

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