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The Effect of Intramuscular Administration of Atropine and Hyoscine Combination on Labor Progress and Maternal and Neonatal Outcomes in Primigravid Women

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ABSTRACT

***Background*:** Previous studies reported that neonatal and maternal complications as well as duration of labor could be diminished through labor management. Therefore, we aimed to evaluate the effect of intramuscular (IM) administration of atropine and hyoscine combination on labor progress and maternal and neonatal outcomes in primigravid women admitted to Taleghani Hospital of Arak, Iran.

***Methods*:** In this double-blind, placebo-controlled clinical trial, 216 primigravid women were randomly allocated to four groups (54 cases in each group) as follows: atropine group received 0.01-0.5 mg (1cc) of IM atropine; hyoscine group received 20 mg of IM hyoscine in a single dose; atropine and hyoscine combination group received 0.01-0.5 mg of atropine and 20 mg of IM hyoscine in a single dose; and control group only received IM injection of 1cc distilled water in a single dose. Thereafter, Bishop score, duration of the active phase and the second stage of labor, type of delivery, and Apgar scores at one and five minutes were recorded. Chi-square/Fisher's exact tests and One-way ANOVA were run, using SPSS version 20.

***Results*:** The Bishop scores were significantly higher in the atropine and hyoscine groups, compared to the other groups ($P<0.05$). Duration of the active phase in the atropine and hyoscine combination group was significantly shorter than the other groups ($P=0.001$). However, there was not a significant difference between the four groups in terms of duration of the second stage and Apgar scores at one and five minutes ($P>0.05$).

Conclusion: The atropine and hyoscine combination reduced the duration of active phase in the primigravid women without serious maternal or neonatal adverse effects.

Keywords: Active phase, Atropine, Hyoscine, Maternal and neonatal outcomes, Primigravid

Introduction

Duration and pain of labor are two important factors that can affect maternal and neonatal outcomes (1). Previous studies indicated the effect of atropine and hyoscine on assuaging pain, shortening the duration of delivery, effacement, dilatation, and shortening the duration of the first stage of labor (2).

Hyoscine butyl bromide (HBB) is a parasympatholytic agent derived from scopolamine. It is an anti-spasmodic agent blocking cholinergic transmission in the abdominal and pelvic parasympathetic ganglia and relieving spasms of smooth muscles in genitalia, exclusively the cervico-uterine plexus, which lead to cervical dilatation and reducing the duration of labor. Moreover, this drug affects other abdominal organs such as gastrointestinal, biliary, and urinary tracts (3).

Atropine is an anti-muscarinic agent that binds to muscarinic acetylcholine receptors, and in spite of hyoscine, it can pass the blood-brain barrier and affect the central nervous system (4). From a clinical point of view, atropine and hyoscine relax the lower segment of the uterus, diminish the uterine spasms, and reduce its contractions (5, 6). A study by Tabarraei et al. indicated that administration of hyoscine and atropine in primiparous women increased dilation and shortened the duration of labor (7).

However, results of the previous studies were not consistent and some of them did not demonstrate positive effect of HBB on shortening the duration of delivery (8-11). To shed light on

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the effects of these drugs on the delivery process, in this trial, we evaluated the effect of IM administration of atropine and hyoscine combination on labor progress and outcome in primigravid women. Moreover, we evaluated the possible adverse effects of these agents on preterm premature rupture of membranes (PPROM), the frequency of cesarean section, and Apgar scores.

Methods

In this double-blind, randomized, clinical trial, we recruited 216 primigravid singleton women, admitted to Taleghani Hospital of Arak, Iran, since March 2013 for one year. The Ethics Committee of Arak University of Medical Sciences approved the study protocol. Moreover, the patients were informed of the study objectives and written consent was obtained.

The inclusion criteria were as follows: 1) primigravida, 2) singleton pregnancy, 3) cephalic presentation, and 4) intact membrane. On the other hand, the patients with history of pregnancy complications, diabetes mellitus, renal problems, cardiovascular disorders, hypertension, and hyperthyroidism were excluded. The enrolled patients were randomly allocated into four groups (54 cases for each group) based on their admission date and file number.

The atropine group received 0.01-0.5 mg (1cc) of intramuscular (IM) atropine; the hyoscine group received 20 mg of IM hyoscine in a single dose; the atropine and hyoscine combination group received 0.01-0.5 mg of atropine and 20 mg of IM hyoscine in a single dose; and the control group only received IM injection of 1cc distilled water in a single dose.

A trained nurse, who was masked to study, performed the injections at the beginning of the active phase (at 3-4 cm dilatation). Duration of the active phase and the second and third labor stages were recorded; additionally, Apgar scores at one and five minutes as well as maternal and neonatal outcomes were recorded and compared.

Statistical analysis

Categorical data were presented as number (%), and the continuous data were reported as mean±standard deviation. Chi-square/Fisher's exact tests and One-way ANOVA were run, using SPSS version 20. *P*-value less than 0.05 was considered statistically significant.

Results

A total of 216 pregnant women with the mean age of 23.6±3.9 years, mean gestational age of 40.05±2.51 weeks, and mean birth weight of 3077.5±487.5 g were evaluated (Table 1). The Bishop score in the hyoscine group was higher than the other groups, and the difference between the four groups was significant (P=0.001). Duration of the active phase in the distilled water (DW) group was longer than the other groups, and the difference between the four groups was significant (P=0.001).

Duration of the second stage in the DW group was more prolonged than the other groups, but the difference between the four groups was not significant (P=0.09). Apgar scores at one and five minutes did not indicate any significant differences between the four groups (P=0.1 for both; Tables 2, 3). PPROM occurred in four patients and cesarean section was performed in five cases (Table 1).

Discussion

Active labor management leads to safe childbirth (12, 13), and for this purpose, a variety of agents such as anti-spasmodics, relaxants, and analgesics were trialed in previous studies (4, 7). To assess the effect of IM administration of atropine and hyoscine combination on labor progress and outcome, we evaluated 216 primigravid women in four groups. We found that Bishop score in the hyoscine group was higher than the other groups, and the difference between the four groups was significant.

Table 1. Maternal and neonatal characteristics

	Atropine	Hyoscine	Atropine and hyoscine	Distilled water
Age	23.2±4.1	23.6±4.3	23.9±3.7	23.7±4.1
Gestational age	40.8±5.6	38.9±1.06	39.3±1.02	39.5±3.10
Birth weight	3066.8±482.5	3066.8±482.5	3065.7±455.2	3089.2±495.10
Preterm premature rupture of membranes	1(1.9%)	0	3(5.6%)	4(7.4%)
Induction	53(98.1%)	45(83.3%)	52(96.3%)	51(94.4%)

Cesarean section	1(1.9%)	4(7.4%)	0	1(1.9%)

Table 2. The difference between the four groups in terms of maternal and neonatal outcomes

		N	Mean ± standard deviation	Min	Max	P-value (ANOVA)
Bishop score	Atropine	54	6.5±2.08	5.9	7.1	0.001
	Atropine and hyoscine	54	5.10±2.80	4.3	5.9	
	Hyoscine	53	7.7±1.8	7.2	8.2	
	Distilled water (DW)	54	2.7±1.4	2.3	1.3	
	Total	215	5.5±2.8	5.1	5.9	
Active phase	Atropine	54	195.5±99.8	20	535	0.001
	Atropine and hyoscine	54	242.4±102.08	30	480	
	Hyoscine	54	160.5±42.1	20	250	
	DW	54	378.8±90.1	90	620	
	Total	216	242.6±119.4	20	620	
The second stage	Atropine	54	39.5±23.09	10	155	0.09
	Atropine and hyoscine	54	45.1±21.8	10	125	
	Hyoscine	54	39.3±15.3	15	90	
	DW	54	48.3±20.9	25	150	
	Total	216	42.9±20.7	10	155	
Apgar score at one minute	Atropine	54	8.8±0.3	8	9	0.1
	Atropine and hyoscine	54	8.7±0.4	8	9	
	Hyoscine	54	8.6±0.5	7	9	
	DW	54	8.6±0.4	8	9	
	Total	216	8.7±0.4	7	9	
Apgar score at five minutes	Atropine	54	9.8±0.3	9	10	0.1
	Atropine and hyoscine	54	9.7±0.4	9	10	
	Hyoscine	54	9.7±0.5	8	10	
	DW	54	9.6±0.4	9	10	
	Total	216	9.7±0.4	8	10	

Moreover, the duration of active phase in the DW group was longer than the other groups, and the difference between the four groups was significant. The duration of the second stage in the DW group was more prolonged than the other groups, but the difference between the four groups was not significant. In addition, there was not a significant difference between the four groups in terms of one- and five-minute Apgar scores. Additionally, the four groups were not significantly different with respect to PPROM and cesarean section frequencies.

Consistent with our results, Samuels et al. indicated that hyoscine could significantly reduce the duration of active phase; however, hyoscine did not have any significant effect on blood loss, Apgar scores, the length of the second and third stages of labor, and the frequency of caesarean section (4).

A similar study was conducted by Tabarraei et al., which showed that the combination of hyoscine and atropine shortened the duration of active phase; nonetheless, the length of the second and third stages, Apgar scores, and cesarean section frequency were not affected by the administration of hyoscine and atropine combination (7).

Another study by Mortazavi et al. confirmed our results and showed that the duration of labor in the atropine group was less than the

combination of hyoscine and promethazine. Moreover, in line with Tabarraei et al., Mortazavi indicated that atropine increased cervical dilation (14).

Table 3. Comparison of maternal and neonatal outcomes (difference indicated between the two groups)

			P-value
Bishop score	Atropine	Hyoscine	0.001
		Atropine and hyoscine	0.004
		Distilled water (DW)	0.001
	Hyoscine	Atropine	0.001
		Atropine and hyoscine	0.001
		DW	0.001
	Atropine and hyoscine	Atropine	0.004
		hyoscine	0.001
		DW	0.001
	DW	Atropine	0.001
		hyoscine	0.001
		Atropine& hyoscine	0.001
Active phase	Atropine	Hyoscine	0.009
		Atropine and hyoscine	0.04
		DW	0.001
	Hyoscine	Atropine	0.009
		Atropine and hyoscine	0.001
		DW	0.001
	Atropine and hyoscine	Atropine	0.04
		hyoscine	0.001
		DW	0.001
	DW	Atropine	0.001
		hyoscine	0.001
		Atropine and hyoscine	0.001
The second stage	Atropine	Hyoscine	0.1
		Atropine and hyoscine	0.9
		DW	0.03
	Hyoscine	Atropine	0.1
		Atropine and hyoscine	0.1
		DW	0.4
	Atropine and hyoscine	Atropine	0.9
		hyoscine	0.1
		DW	0.03
	DW	Atropine	0.03
		hyoscine	0.4
		Atropine and hyoscine	0.03

A study by Qahtani et al. exhibited that hyoscine decreased the duration of the active phase without any remarkable adverse effects on mothers and neonates (15), which was in

Continuation of table 3.

			P-value
Apgar score at one minute	Atropine	Hyoscine	0.8
		Atropine and hyoscine	0.04
		DW	0.05
	Hyoscine	Atropine	0.8
		Atropine and hyoscine	0.08
		DW	0.09
	Atropine and hyoscine	Atropine	0.04
		hyoscine	0.08
		DW	0.9
	DW	Atropine	0.05
		hyoscine	0.09
		Atropine and hyoscine	0.9
Apgar score at five minutes	Atropine	Hyoscine	0.4
		Atropine and hyoscine	0.04
		DW	0.01
	Hyoscine	Atropine	0.4
		Atropine and hyoscine	0.2
		DW	0.1
	Atropine and hyoscine	Atropine	0.04
		hyoscine	0.2
		DW	0.6
	DW	Atropine	0.01
		hyoscine	0.1
		Atropine and hyoscine	0.6

accordance with our results. In addition, a study by Shedid et al., in agreement with our results, signified that rectal hyoscine decreased the duration of the first and second stages of labor with no remarkable neonatal and maternal adverse effects (16).

In general, several studies were conducted to evaluate the effect of anti-spasmodic, relaxant, and analgesic agents on labor management, most of which exhibited reduction of labor duration with no or slight adverse effects (11-17). However, most of these studies used hyoscine; as opposed to these findings, a study by Gupta demonstrated that hyoscine could not decrease the length of active phase. Moreover,

cervical dilation in the hyoscine group was not more than the control group (18).The reason for this discrepancy is not clear; however, it might be related to different administration routes (oral, rectal, or IM), study populations, and techniques.

In summary, the results of this trial and the literature indicated that labor management using combination of hyoscine and atropine or hyoscine alone shortened the duration of active phase of labor and led to assuaging severe pain, particularly in primigravid women. In addition, short active phase lowered the frequency of chorioamnionitis and neonatal sepsis that are more common in women with long duration of active phase. Additionally, due to reduced pain and shorter duration of active phase, the use of analgesics and frequency of cesarean section attenuated (19-22).

Two important limitations of the present study include the relatively small sample size and short duration of the study that limit the generalizability of our results.

Conclusion

Combination of atropine and hyoscine reduced the duration of active phase in primigravid women without remarkable maternal and neonatal adverse effects. It is recommended to conduct further investigations with longer follow-ups and larger sample sizes to validate our findings.

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References

1. Cuningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD. Williams Obstetrics. 22nd ed. New York: McGRAW Hill Medical Publishing Division; 2009. P. 153-4, 422-3, 476.
2. Zargari A. Herbal medicine. 5th ed. Tehran: Tehran University CO; 2001. P. 4.
3. Hotwani J, Ainapure SS. Hyoscine butylbromide suppositories. Ind Med Gaz. 2000; 1:217–9.
4. Samuels LA, Christie L, Roberts-Gittens B, Fletcher H, Frederick J. The effect of hyoscine butylbromide on the first stage of labour in term pregnancies. BJOG. 2007; 114(12):1542–6.
5. Anthony JT, Bertram GK, Susan BM. Pharmacology examination and board review. 8th ed. Singapore: McGraw-Hill Medical; 2007.
6. Saatsaz S, Haji Ahmadi M, Basirat Z, Nazari R, Beheshti Z. Comparison of atropine drugs-promethazine and pethidine on the active phase of labor. J Babol Univ Med Sci. 2007; 38(3):39-42
7. Tabarraei Y, Dargahi R, Azari M, Mard A, Rahimi G, Refahi S. The effect of intravenous injection of Atropine with hyoscine on the progress of labor in primiparous women in Alavi hospital, Ardabil, Iran. Life Sci J. 2013; 10(5):649-51.
8. Sirohiwal D, Dahiya K, De M. Efficacy of hyoscine-N-butylbromide (Buscopan) suppositories as a cervical spasmolytic agent in Labour. Aust N Z J Obstet Gynaecol. 2005; 45(2):128–9.
9. Tewari K, Jabeen R, Sabzposh MA, Rabbani T. Comparison of hyoscine-butylbromide and valethamate bromide in shortening the duration of labor. Ind Med Gaz. 2003; 137:15–9.
10. Gupta B, Nellore V, Mittal S. Drotaverine hydrochloride versushyoscine-N-butylbromide in augmentation of labor. Int J Gynaecol Obstet. 2008; 100(3):244–7.
11. Aggarwal P, Zutshi V, Batra S. Role of hyoscine N-butyl bromide (HBB, buscopan) as labor analgesic. Ind J Med Sci. 2008; 62(5):179–84.
12. Frigoletto FD Jr, Lieberman E, Lang JM, Cohen A, Barss V, Ringer S, et al. A clinical trial of active management of labour. N Engl J Med. 1995; 333(12):745–50.
13. Sadler LC, Davison T, McCowan LM. A randomised controlled trial and meta-analysis of active management of labour. BJOG. 2000; 107(7):909–15.
14. Mortazavi F, Rakhshani MH. The effect of atropine, hyoscine and promethazine on the duration of labor stages and rate of labor progress in multiparous women. J Gorgan Univ Med Sci. 2005; 6(2):92-6.
15. Qahtani NH, Hajeri FA. The effect of hyoscine butylbromide in shortening the first stage of labor: a double blind, randomized, controlled clinical trial. Ther Clin Risk Manag. 2011; 7:495–500.
16. Shedid AA. Rectal hyoscine-N-butylbromide safely accelerates progress of labor in primipara: a placebo-controlled study. J Am Sci. 2012; 8(8):517-22.
17. Makvandi S, Tadayon M, Abbaspour M. Effect of hyoscine-N-butyl bromide rectal suppository on labor progress in primigravid women: randomized double-blind placebo-controlled clinical trial. Croat Med J. 2011; 52(2):159-63.
18. Gupta B, Nellore V, Mittal S. Drotaverine hydrochloride versus hyoscine-N-butylbromide in augmentation of labor. Int J Gynaecol Obstet. 2008; 100(3):244-7.
19. Zhang J, Troendle J, Mikolajczyk R, Sundaram R, Beaver J, Fraser W. The natural history of the

normal first stage of labor. Obstet Gynecol. 2010; 115(4):705-10.
20. Maharjan SK, KarkiCB. Painless delivery--a short experience. Kathmandu Univ Med J (KUMJ). 2003; 1(2):128-31.
21. Capogna G, Camorcia M, Stirparo S, Valentini G, Garassino A, Farcomeni A. Multidimensional evaluation of pain during early and late labor: a comparison of nulliparous and multiparous women. Int J Obstet Anesth. 2010; 19(2):167-70.
22. Myles TD, Santolaya J. Maternal and neonatal outcomes in patients with a prolonged second stage of labor. Obstet Gynecol. 2003; 102(1):52-8.