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Original Article

A comparative study of Hyoscine butylbromide versus Drotaverine hydrochloride in first stage of labor.

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Abstract

Objectives: To compare the efficacy of hyoscine butylbromide with drotaverine hydrochloride for increasing the rate of cervical dilatation in first stage of labor. *Methods :* A randomized comparative study was carried out on one hundred women in labor. They were randomly allocated to one of the two groups. Group A included 50 women who were given injection drotaverine hydrochloride and Group B included 50 women who were given injection hyoscine butylbromide intravenously in the first stage of labor. The main outcome measures were the time taken for full dilatation, rate of cervical dilatation, the duration of first and second stages of labor and blood loss in third stage of labor, all calculated separately for nulliparas and multiparas of the two groups. *Results:* The two groups were comparable with regards to the gestational age, parity, and average dilatation of cervix at injection of the antispasmodic agents. Average time to full cervical dilatation was significantly less in Group B in both nulliparas ($P<0.01$) and in multiparas ($P<0.05$). Similarly, the average rate of cervical dilatation was significantly more in Group B, both in nulliparas ($P<0.007$) and in multiparas ($P<0.02$). The same findings were obtained when Bishop's score was taken as baseline. No significant difference in the side effects of either drug was observed. The difference in the duration of second and third stages of labor and the blood loss were statistically insignificant. Students 't' test was used for statistical analysis. *Conclusion :* Hyoscine butylbromide is more efficacious than drotaverine hydrochloride for cervical effacement and dilatation with no increase in the side effects, duration of second and third stages of labor and the third stage blood loss.

Key words : labor, active management, hyoscine butylbromide, drotaverine, cervical dilatation.

Introduction

Both the obstetrician and the laboring woman would like to accomplish the delivery in the shortest possible time without compromising the maternal and fetal safety. Hence, along with early amniotomy and early administration of oxytocin, to accelerate labor many advise the use of antispasmodic agents like drotaverine, hyoscine butylbromide, dicyclomine valethamide bromide etc. to hasten the first stage of labor. While valethamide and drotaverine have been the subject of a number of studies a study comparing hyoscine butylbromide has not been done, to the best of our knowledge. The present study was conducted to find whether hyoscine butylbromide shortens the first stage of labor more efficaciously than drotaverine.

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Methods

This randomized controlled trial was undertaken at our tertiary level teaching hospital from June 2005 to January 2006. The study was conducted on 100 women in labor, who were randomly allocated to Group A or Group B. The women in Group A were injected drotaverine 40mg (one ampoule) intravenously at 3-5cm dilatation, if admitted in latent labor or at first examination if already more than 5 cm dilatation. The women in group B were injected one ampoule of hyoscine butylbromide (hyoscine butylbr) - 20 mg instead of drotaverine. Exclusion criteria were preterm labor, absent membranes, abruptio placentae, history of cervical encerclage, breech presentation and intrauterine death. Active, but not aggressive management protocol was followed for all women in labor. Latent phase of labor was accepted as upto 3cm dilatation. No intervention was done till the patient reached 3cm dilatation after which oxytocin infusion was started at a rate of 6 mU/mL and titrated according to the uterine contractions. Artificial rupture of membranes was done under antibiotic cover at 4-5cm dilatation along with an intravenous injection of either of the two drugs being tested. A second dose of the antispasmodic was not allowed for the course of the study. Cervical assessment was performed every 2 hours or earlier if otherwise indicated. The various timings were noted - admission to 3cm dilatation, injection of antispasmodic and full dilatation of the cervix. The duration of second and third stages of labor were noted and amount of bleeding in the third stage of labor was also taken note of. The woman's pulse rate was monitored hourly and every 15 minutes for one hour after injection of the antispasmodic. Continuous fetal heart rate (FHR) monitoring for high risk and intermittent monitoring at 15 minutes was done for the low risk patients, after an admission NST was taken.

For calculation of the efficacy of action of both the drugs, each group was further divided into one of nulliparas (excluding nulliparas with previous histories of second trimester abortions or cervical encerclage) and one of multiparas and within these two subgroups, further division was done depending upon whether the antispasmodic was given at less than 5cm dilatation or more than 5cm dilatation. Bishop's score was also calculated for each woman and division done on the basis of Bishop's score $\leq$10 and > 10. Calculations of the time taken for full dilatation and the rate of cervical dilatation for each of the eight subgroups was calculated. Enquiry was also made into the side effects of the respective drugs. Statistical analysis of the data was done by the student 't' test.

Results

Maternal characteristics were comparable in the two groups (Table 1). The average time taken from time of injection of antispasmodic to the full cervical dilatation of cervix in nulliparas with baseline dilatation <5cm in group A was 103.45 minutes and in group B was 59.88 minutes ($P<0.01$) while with baseline dilatation >5 cm it was 115.38 minutes in group A and 66.67 minutes in group B ($P<0.05$). In multiparas with baseline dilatation <5cm, the time to full dilatation in group A was 117.09 minutes and in group B it was 60.48 minutes ($P<0.05$) while with baseline dilatation >5 cm, the average time to full dilatation was 104.53 minutes in group A and 61.22 minutes in group B ($P<0.05$) (Table 2).

The rate of cervical dilatation in the nulliparas with baseline cervical dilatation <5 cm in group A was 2.9 cm/hour and in group B it was 5.06 cm/hour ($P<0.007$). With cervix >5cm dilatation, the average rate in group A was 2.6 cm/hour and in group B it was 4.5 cm/hour ($P<0.001$). In multiparas, the rate with cervix <5cm dilated in group A was 2.56 cm/hour and in group B it was 4.97 cm/hour ($P<0.02$) while with baseline dilatation >5 cm/hour, in group A it was 2.87 cm/hour and in group B 4.94 cm/hour ($P<0.03$) (Table 3).

In the subgroups taking the Bishop's score as baseline, in nulliparas with Bishop's score $\leq$10, the rate of cervical dilatation in group A was 2.23 cm/hour and group B was 3.80 cm/hour ($P<0.03$) while with bishop's score >10, the rate was 2.68 cm/hour and 4.7 cm/hour in group A and B respectively ($P>0.05$). In multiparas, taking the Bishop's score as the baseline the rate of cervical dilatation in subgroup with Bishop's score $\leq$ 10 in group A was 2.34 cm/hour and in group B it was 4.7 cm/hour ($P<0.01$), while in subgroup with bishop's score >10, the rate in group A was 2.78 cm/hour and in group B, it was 4.38 cm/hour ($P<0.02$) (Table 4).

The differences in durations of second and third stages were statistically insignificant (Table 5).

The differences in the amount of blood loss in the third stage of labor in the two groups was also statistically insignificant (Table 5).

A rise in the maternal pulse rate of upto 8-10 beats per minute was detected within 10 minutes of injection of

Table 1. Comparison of the two groups.

Sl. No.	Variable	Group A (Drotaverine) n=50	group B (Hyoscine) n=50	't' Value	'p' Value
1.	Average gest age (days)	278.29 ± 5.73	277.77 ± 7.48	0.27	P>0.05 N.S.
2.	Average dilatation < 5cm	3.595 ± 0.625	3.586 ± 0.606	0.41	P>0.05 NS
3.	Average dilatation > 5 cm	5.857 ± 0.476	6.60 ± 1.39	0.57	P>0.05 N.S.
4.	Average dilatation at injection (cm)	4.16 ± 1.16	4.18 ± 1.33	0.54	P>0.05 N.S
5.	Average Bishop's score ≤ 10	8.18 ± 1.07	8.129 ± 0.756	0.76	P>0.05 N.S
6.	Average Bishop's score > 10	10.636 ± 0.809	10.125 ± 0.641	1.47	P>0.05 N.S

Table 2. Average time from Injection to full dilatation (in minutes).

Baseline Dilatation	Group A (Drotaverine hydrochloride)	Group B (Hyoscine buty1 bromide)	't' Value	'p' Value
Nulliparas				
< 5 cm	103.448 ± 13.2	59.88 ± 63.6	3.22	<0.01
> 5 cm	115.38 ± 21.5	66.67 ± 15.2	2.14	<0.05
Multiparas				
< 5 cm	117.09 ± 91.3	60.483 ± 59.5	2.18	< 0.05
> 5 cm	104.53 ± 68.7	61.22 ± 20.0	2.07	< 0.05

Table 3. Average rate of Dilatation in cm/hour.

Baseline dilatation	Group A	Group B	't' Value	'p' Value
Nulliparas				
< 5 cm	0.049 ± .0332 = 2.9 cm/hour	0.844 ± 0.0402 =5.06 cm/hour	2.91	0.007 H.S
> 5 cm	0.0446 ± 0.0493 =2.6 cm/hour	0.0757 ± 0.0629 = 4.5 cm/hour	5.2	<0.001 S.D.
Multiparas				
< 5 cm	0.0427 ± .0204 =2.56 cm / hour	0.0828 ± 0.0495 =4.97 cm/hour	2.54	<0.02 S.D.
> 5 cm	0.0478 ± 0.036 =2.87 cm/hour	0.0824 ± 0.047 =4.9 cm/hour	2.27	< 0.03 S.D.

S - Significant HS - Highly Significant NS - Not Significant SD - Significant Difference

Table 4. Average rate of dilatation with Bishop's score cm/hour.

Baseline Bishop's score	Group A	Group B	't' Value	'P' Value
Nulliparas				
< 10	0.0372 ± 0.022 =2.23 cm/hour	0.0636 ± 0.0383 = 3.8 cm/hour	2.29	<.03 Significant
= 10	0.0447 + 0.176 = 2.68 cm/hour	0.079 ± 0.0132 = 4.7 cm/hour	0.31	> 0.5 N.S
Multiparas				
< 10	0.0397 ± 0.0178 = 2.34 cm/hour	0.0797 ± 0.0431 =4.7 cm/hour	3.14	< .01 H.S. < .01 H.S.
≥ 10	0.0464 ± 0.0278 = 2.78 cm/hour	0.0809 ± 0.0423 =4.38 cm/hour	2.45	< .02 S.D.

Table 5. Duration of II and III stage and blood loss.

Average duration (minutes)	Group A	Group B	't' Value	'p' Value
2nd stage				
Nulliparas	36.62 ± 6.61	36.58 ± 5.53	0.54	> 0.05
Multiparas	21.51 ± 4.9	21.46 ± 1.82	0.42	> 0.05
3rd Stage				
Nulliparas	5.6 ± 1.91	5.4 ± 1.82	0.51	> 0.05
Multiparas	4.4 ± 1.9	4.4 + 1.56	0.44	> 0.05
Average blood loss				
in 3rd stage (mL)				
Nulliparas	105.46 ± 38	106.22 ± 37	0.76	>0.05
Multiparas	90.05 ± 11.9	90.01 ± 11.5	1.47	> 0.05

hyoscine butylbromide. It rapidly subsided within the next 15 minutes. The woman did not have any complaints during this time. With drotaverine hydrochloride, an inconsistent rise in the pulse rate of upto 5-6 beats per minute was seen which also settled down within the next 10-15 minutes with no complaints noted.

Discussion

Cervical ripening, expressed as a remodeling of the cervical connective tissue, has been proven to be necessary for an uncomplicated vaginal delivery [1].

Rigidity of the cervix, as a cause of poor progress was often cited by obstetricians previously. Inability of the cervix to ripen and dilate or cervical dystocia is still acknowledged as a cause for nonprogress of labor and nonachievement of vaginal delivery. Recent biochemical evidence also suggests that the cervix could obstruct labor by a sustained spasm due to insufficient connective tissue remodeling. While various immunohistochemical studies concentrate upon collagen type remodeling and stabilization, it is a known fact that upto 10-15% of the nonpregnant cervices is constituted by smooth muscle fibres[2]. Hughesdon[3] reveals the probability of the existence of an outer muscular layer in the cervix corresponding to the smooth muscle of the vagina. Studies have also shown that besides a decrease in fibrous connective tissue in

the cervix at term, there is an increase in the proportions of smooth muscle fibres, which also become dissociated and hypertrophic, and are aligned in a particular direction[2].

These studies, relating to the presence of smooth muscle fibers in the cervix logically support the role of antispasmodics and smooth muscle relaxants in helping the cervix to dilate. Drotaverine hydrochloride and hyoscine butylbromide are two such smooth muscle relaxants with different mechanisms of actions.

Drotaverine hydrochloride or isoquinolone 1,2,3,4-tetrahydro 6,7 diethoxy-1-(C-3,4 - diethoxy phenylmethylene) hydrochloride is a highly potent spasmolytic agent, acting on the smooth muscle but is devoid of anticholinergic effects as it acts through inhibitory effect on phosphodiesterase enzyme, mainly PDE IV. Near term, human myometrium contains a higher proportion of rolipram sensitive type IV PDE isoforms. Drotaverine inhibits them and in turn increases the intracellular concentration of cAMP and cGMP and causes smooth muscle relaxation. It does not cross the placenta and hence has no side effects on the fetus[4].

Hyoscine butylbromide or Scopalamine hydrochloride is 6,7- Epoxy-8-butyl-3((S)- tropoyloxy) tropamine bromide and is a quaternary derivative of atropine which acts as an anticholinesterase. It acts on the muscarinic receptors of the smooth muscles and competes for the receptor sites with acetylcholine. Being a quaternary ammonium derivative, it does not readily cross the blood brain barrier, so central effects, if any, are rare. Also, there are no known fetal effects of this compound.

In our series, it was consistently noted that the time taken to full dilatation was more and the rate of cervical dilatation was consistently less with both the drugs when given in the latent phase of labor (data not included). This finding can probably be explained by recent studies which indicate that the cervix may contract in response to oxytocic stimulation during the latent phase of labor. Cervical contractions are present only during the first 3-4 cm dilatation, and these contractions are synchronous with the uterine contractions[2]. At this stage of labor, the physical state of the cervix modulates uterine wall tension and the intrauterine pressure. Any increase in the cervical compliance causes a decrease in the intrauterine pressure in the latent phase of labor[5]. Hence, as also suggested by the findings in our study, any relaxation of the cervix by smooth muscle relaxants in the latent phase of labor, will also delay progress of labor by effectively decreasing the intrauterine tension. This could also give the basis of why, when given in the latent phase of labor, hyoscine butylbromide sedates the uterus and the cervix, when the uterine contractions are not too strong.

Another observation made in this study was that the progress of labor was markedly faster once the cervix was ≥4 cm dilated (data not included). Further studies are required to prove this, but our study favors a latent phase upto 4 cm dilatation instead of 3 cm.

The action of hyoscine butylbromide was consistently found to be much better than that of drotaverine hydrochloride without an increase in any untoward maternal or fetal side effects, with all but one of the beneficial effects achieving statistical significance.

Conclusion

There is a distinct advantage in using hyoscine butylbromide as an antispasmodic of choice for expediting the first stage of labor.

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