

INTRA CERVICAL INJECTION OF HYLASE TO HASTEN CERVICAL RIPENING

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SUMMARY

A study of 72 primigravidae showed that labour could be accelerated and shortened by an average of 9.54 hours in Group A (all cases) and 9.38 hours in Group B (18-25 Years age group). It showed a significant change in the latent and active phases of both the groups and the rate of dilatation was 3.77 cm/hrs in Group A and 3.71 cm/hrs in Group B as compared to the control (2.95 cm/hrs).

Hyaluronidase hydrolyses hyaluronic acid which helps in moving the fluid from the cervical tissue. This loss of fluid causes loss of turgor or rigidity and it become "soft", distensible and capable to dilation.

Introduction

Acknowledgement of the cervix as a functional organ in its own right is one of the major advances in reproductive physiology. The uterus must remain closed during pregnancy to maintain the pregnancy, yet open during parturition. It must perform at the right time and in the right sequence within a reasonable period of time. The process that co-ordinates these activities is labour and it is an equal mixture of uterine contractions, cervical effacement and dilatation.

For the purpose of cervical ripening the cervix has been treated to various drugs, hormones, catheters bougies, balloons etc. None of these have proved satisfactory to hasten the ripening of the cervix or bring about a rapid dilatation without problems to the mother or the fetus.

There are certain bio-chemical changes which take place in the cervix during pregnancy and at term. The ripening of the cervix depends on collagen content, water, hyaluronic acid and sulphated glycosaminoglycans. Hyaluronidase has the ability to depolemerize and hydrolyse hyaluronic acid, one of the principal constituents of the extracellular material of connective tissue. This molecular re-

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arrangement lowers the viscosity of the extracellular substance, thus relaxing the tissues and permitting free passage of fluid.

We, at the B. Y. L. Nair Ch. Hospital and T.N. Medical College undertook a study to evaluate the effect of intracervical injection of hyaluronidase (Hylase*) in primigravidae during labour.

Material and Methods

Seventy primigravidae were selected with vertex presentation and were in early labour with good uterine contractions and with a 2-2.5 cm dilatation of the cervix. 3 cases were excluded from the analysis as they underwent caesarean section due to obstetric indications.

Age distribution is given in Table I. The cases were divided into 2 groups. All cases in Group A and those in the age group between 18-25 years in group B.

TABLE I
Age Distribution

Parameter	All cases (70)	18.25 Yrs. (58)
Mean (x)	21.27 Yrs.	20.79 Yrs.
S.D. (\pm)	2.89 Yrs.	1.92 Yrs.
S.E. (\pm)	0.34 Yrs.	0.25 Yrs.
n	70	58

Table II shows the type of pregnancy. In Group A 57 cases (81.42%) were normal, whilst in Group B 50 (86.20%) were normal. Twelve cases (17.14%) of Group A and 7 cases (12.06%) of Group B had pre-eclampsia. There was 1 case of sickle-cell Thalassaemia.

To evaluate whether the cervix was ripe or not, the Bishop's 1 score was given to each of the cases. Table III shows that in Group A and Group B, majority of the

TABLE II
Type of Pregnancy

Type	All cases		18-25 Yrs.	
	Nos.	(%)	Nos.	(%)
Normal	57	(81.42)	50	(86.20)
Pre-eclampsia	12	(17.14)	7	(12.06)
Sickle cell thalassaemia	1	(1.44)	1	(1.74)
Total	70	100	58	100

cases, 45 and 37 respectively had a score between 8-9. The average Bishop's score was 8. This score takes into consideration the dilatation, effacement, station, consistency and position. With his evaluation method we were able to predict an optimal time to begin the injection as well as to predict how long it would take a patient with a given score to go into spontaneous labour.

1,500 I.U. of Hylase diluted in 20 ml of saline was injected in the substance of the cervix at 2 O'clock, 6 O'clock and 10 O'clock position. Oxytocin was not administered to any of the cases. Partogram in the form of a graph showing the cervical dilatation against the time was plotted. Fifty cases were taken as a control group with similar parameters and did not receive any drugs during labour.

Table IV shows the length of the various phases viz. the latent phase active phase, phase of maximal dilatation (slope), length of the 2nd stage and the total duration of labour. The mean length of the latent phase in Group A was 2.45 hrs., Group B 2.58 hrs. and control Group 8.5 hrs. The mean length of the active phase in Group A was 2.02 hrs., Group B 2.08 hrs., and in the control 4.46 hrs. The maximal rate of dilatation or slope in Group A was 3.77 cm/hr., Group B 3.7

*Supplied by Rallis (India) Pvt. Ltd.

TABLE III
Bishop's Score

Bishop's	All cases Group A		18-25 yrs. Group B	
	Nos.	%	Nos.	%
6	2	(2.88)	2	(3.44)
7	19	(27.14)	15	(25.86)
8	31	(44.28)	27	(46.55)
9	14	(19.94)	10	(17.27)
10	4	(5.76)	4	(6.88)
11	—		—	
Total	70	100	58	100
Average Bishop's score		8	8	
S.D.		± 0.76	± 0.76	

TABLE IV
Post-Treatment Analysis

Phase Statistics		Expl. Group		Control Group
		All cases	18-25 Yrs.	
Total length of Labour (Hrs.)	x	4.96	5.12	14.5
	SD (±)	2.79	2.84	3.5
	SE (±)	0.334	0.374	—
	n	70	58	50
Length of Active Phase (Hrs.)	x	2.02	2.00	4.46
	SD (±)	0.84	0.85	3.6
	SE (±)	0.100	0.111	—
	n	70	58	50
Length of Latent Phase (Hrs.)	x	2.45	2.58	8.5
	SD (±)	2.37	2.48	5.1
	SE (±)	0.28	0.33	—
	n	70	58	50
Length of 2nd stage (Hrs.)	x	0.4218	0.4156	1.25
	SD (±)	0.375	0.3649	0.8
	SE (±)	0.0448	0.0479	—
	n	70	58	50
Slope (cm/Hrs.)	x	3.77	3.71	2.95
	SD (±)	1.79	1.83	1.9
	SE (±)	0.21	0.24	—
	n	70	58	50

n = Number of cases. SD = Standard deviation. SE = Standard error.

cm/hr. and in the control Group 2.95 cm/hr.

The mean duration of the 2nd stage was 0.42 hrs. in Group A, 0.41 hrs in Group B and 1.25 hrs. in control. The total length of labour in Group A was 4.96 hr. in Group B is 5.12 hrs. and 14.5 hrs. in the control.

Group A and B are statistically compared by applying the '+' test and no significant change is noted (Table V).

Table VI and VII show the significance of various parameters in Group A and

Group B with the control group respectively. In both the groups there is a highly significant change ($p < .01$) as compared to the control in respect of the various phases viz. latent and active phase, length of the 2nd stage of labour. The slope or the rate of dilatation in both the groups is significant ($p < .05$) as compared to the control.

Mode of delivery (Table VIII)

Sixty-four cases (91.36%) in Group A and 53 cases (91.39%) in Group B had a

TABLE V
Significance Between Expt. Groups

Phase	Mean values Expt. Group		Mean change between Expt. groups
	All cases (70)	18-25 Yrs. (58)	
Total length of labours (Hrs.)	4.96	5.12	0.16 NS
Length of Latent Phase (Hrs.)	2.45	2.58	0.13 NS
Length of Active Phase (Hrs.)	2.02	2.08	0.06 NS
Length of 2nd stage (Hrs.)	0.4216	0.4156	0.0062 NS
Slope (cm/Hrs.)	3.77	3.71	0.06 NS

NS: $P < .05$ non-significant. Statistical test applied: Non-pair t. test.

TABLE VI
Significance Between Expt. and Control Group
(A) Between Expt. (All 70 cases and Control group).

Phase	Mean Values		Mean change	% Difference W.E.t. Control Group
	All 70 (cases)	Control group		
Total length of labour (Hrs.)	4.96	14.50	9.54*	- 65.79
Length of Latent Phase (Hrs.)	2.45	8.50	6.05**	- 71.18
Length of Active Phase (Hrs.)	2.02	4.46	2.44**	- 54.70
Length of 2nd stage (Hrs.)	0.4218	1.25	0.8282*	- 66.26
Slope (Cm/Hrs.)	3.77	2.95	0.820*	+ 27.79

* (Significant)

** (Highly significant)

-

+

$P < .05$

: $P < .01$

: Decrease

: Increase

TABLE VII
Between Expt. (19-25 Yrs.) 58 Cases and Control Group

Phase	Mean values		Mean change	% Difference W.E.t. Control group
	18-25 Yrs. (58 cases)	Control Group		
Total length of Labour (Hrs.)	5.12	14.50	9.38**	- 64.68
Length of Labour Phase (Hrs.)	2.58	8.50	5.92**	- 69.64
Length of Active Phase (Hrs.)	2.08	4.46	2.38**	- 53.36
Length of 2nd stage (Hrs.)	0.4156	1.25	0.8344**	- 66.75
Slope (Cm/Hrs.)	3.71	2.95	0.76*	+ 25.76

* (Significant) : P<.05
 ** (Highly significant) : P<.01
 - : Decrease
 + : Increase

TABLE VIII
Mode of Delivery

Mode	All cases		18-25 yrs.	
	Nos.	%	Nos.	%
Outlet forceps for prolonged 2nd stage	4	(5.76)	3	(5.17)
Outlet forceps for fetal Distress	2	(2.88)	2	(3.44)
Normal	64	(91.36)	53	(91.39)
Total	70	100	58	100

normal delivery. Outlet forceps for prolonged second stage was applied in 4 cases (5.76%) in Group A and in 3 cases (5.17%) in Group B. For foetal distress forceps was applied in 2 cases (2.88%) in Group A and 2 cases (3.44%) in Group B. There were no complications in the post-partum period.

Discussion

Hyaluronidase for clinical use is prepared from mammalian testes and is available in either liquid or powder form.

The drug acts by producing the degradation of hyaluronic acid and n-acetyl-

glucosamine. This reaction occurs instantly and is completely reversible. Following a single injection of the enzyme, 24-48 hrs. are required to complete reconstitution of the intercellular cement substance by the mesenchymal cells.

Britton and Habib (1953) reviewed the clinical uses of hyaluronidase explaining the mechanism of its lytic action. The enzyme, obtained from the bovine testicular extract depolymerizes hyaluronic acid, thus immediately but only temporarily destroying the connective tissue cement or ground substance.

Seifter (1950) has reported that animals receiving 2,00,000 times the maximum

human therapeutic dosage showed no local or systemic evidences of toxicity.

Banks (1949) found the drug to be non-antigenic.

In this series of hylase that there was a remarkable significant change in the course and duration of labour. The duration of labour was shortened by more than 9 hours which is statistically significant. The effect of hylase is seen on both the phases viz. the latent and active phase. The rate of dilatation is accelerated significantly ($p < .05$) as is seen from the slope. This shortening of labour is a welcome advantage to a primigravida where one can reduce the medications and sedation which is in the interest of the welfare of the new born.

This method is safe and rational as it conforms to the physiologic scheme, as labour normally progresses, an increasing amount of hyaluronidase is known to accumulate in the cervix uteri.

Iversen (1960) found less hyaluronic acid in the post partum cervix.

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