

CERVIX-HYALASE ALONE AND IN COMBINATION WITH OTHER DRUGS

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Cervical factors play a very important role in determining the progress and duration of labour. Conditions like uterine action, malpresentation and cephalopelvic disproportion are other factors of paramount importance which go a long way to determine the length of labour but fortunately we have adequate means to diagnose and treat these conditions, whereas we have not very many ways to improve the cervical factors like rate of dilatation and consistency etc., probably because the factors favouring cervical dilatation are not yet understood. A ripe cervix has always been considered a good omen for commencement of labour and it is noted a few days before the onset of labour.

Cervix is composed mainly of involuntary muscle and fibrous tissue along with the stroma. Below the level of internal os the main component is only fibrous tissue, muscle being only 15% (Danforth, 1947). The stroma contains hyaluronic acid, chondroitin and two acid mucopolysaccharides (Voustas *et al* 1963). These substances serve as the mesodermal "Cement" for binding cells together to form the organ frame-work. All these compounds are depolymerized by hyaluronidase, the so called "Spreading factor"

described by Hoffman and Duran-Reynal (1931).

It is presumed that local injection of hyaluronidase may reduce the adhesions of the cervical cells by neutralising the hyaluronic acid and thus help in softening the cervix and favouring cervical dilatation and in turn shortening the duration of labour.

The present study has been planned to see the effect of intracervical injection of hyaluronidase alone and in combination with other drugs like pethidine and diazepam.

Material and Methods

Three hundred and thirty patients from U.I.S.E. Maternity Hospital and other Nursing homes of Kanpur were selected for this study. A complete history with special reference was taken and a thorough clinical examination to exclude malpresentation, cephalopelvic disproportion and uterine inertia was done.

These cases were randomly assigned to one of the 5 groups and drugs were given as:

- Group I Intracervical hyalase,
- Group II Hyalase and Diazepam,
- Group III Hyalase & Pethidine,
- Group IV only saline, and
- Group V was left untreated.

Saline was taken as blind control.

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Cervices of these patients were visualized and degree of dilatation was noted. Patients with cervical dilatation of 3-4 cm were selected for this study. A solution containing 30 units of hyalase per ml of normal saline was prepared and 4 ml of this (120 units of hyalase) solution was injected into the substance of cervix at 2, 6 and 10 o'clock positions. The dose of diazepam and pethidine injected were respectively 20 mg and 100 mg intramuscularly. The time of administration of all these drugs was noted meticulously. Since it was difficult to note the precise time of full dilatation, the delivery time was taken as the end point of observations.

To maintain uniformity only primigravidae were included in this study. If uterine inertia was noted soon after the injection, oxytocin was administered by the I/V drip and the commencement of active uterine contractions was taken to be the time of beginning the experiment. But if oxytocin had to be given at a later stage of dilatation (After 7 cm), the time was counted from the very beginning.

Observations

Our saline group behaved as "no injection" group and as such these patients were also included later in controls. The Table given below shows the labour time taken by patients from 3-4 cm cervical

dilatation to the time of normal delivery.

Duration of labour thus ranged between 3 to 16.20 hours in hyalase group, 3.16-16.56 hours in hyalase and diazepam group, 3.32-16.58 hours in hyalase and pethidine group and 3.13-17.35 hours in control group. Mean duration of labour as such was minimum in hyalase group (6.48 ± 0.35) and maximum in control group (8.52 ± 0.97). Emotionally patients belonging to the group II (hyalase & diazepam) behaved better but greater analgesia was observed in hyalase and pethidine group. The difference in duration of labour being highly significant in hyalase ($P < 0.01$) and hyalase and diazepam group ($P < 0.05$).

No side effects or adverse drug action was observed by hyalase administration. In the group I, 3 patients ultimately had to have L.S.C.S., 2 because of foetal distress which occurred when the cervix was already about 8 cm dilated and in both cord round the neck (two rounds) was seen at the time of L.S.C.S. In the third L.S.C.S. was done for cephalopelvic disproportion which we had failed to detect. We had excluded these cases from our study because we could neither get full dilatation nor the time of normal delivery which we had decided to take as the end point but in these three cases also the rate of cervical dilatation was good.

We tried hyalase injection in some

TABLE I
Duration of Labour in (Hours/mts.) in Various Groups

Cases	Hyalase (100)	Hyalase & diazepam (150)	Hyalase & Pethidine (150)	Control (30)
Range	3.0 — 16.20	3.16 — 16.56	3.32 — 16.58	3.13 — 17.35
Mean	6.48 ± 0.35	6.52 ± 0.57	7.09 ± 1.12	8.52 ± 0.97
't'	1.85	2.22	1.08	—
'P'	.01	.05	0.1	—

(total 7) patients of pre-eclamptic toxæmia also in whom the cervix was only one or two cm. dilated, firm and almost uneffaced. All these patients were also primigravida. A good ripening effect on cervix was observed and labour later proceeded normally and without delay but mid-cavity forceps had to be applied in two of the cases for foetal distress. We have not included these cases also in our study because we thought the series to be too small to be statistically significant.

Discussion

Efforts have continuously been made to make the labour short and painless by giving various drugs (diazepam, pethidine etc.). Intracervical injection is just one more step in the same direction. We, in the present study, have tried to see the effect of hyalase alone and in combination with diazepam and pethidine on the cervical dilatation and shortening of duration of labour. Hyalase causes enzymic lysis of intercellular mucopolysaccharides and thus seems to be a simple, practical and safe approach for causing ripening of cervix. The method is based on the normal physiology in that an increasing amount of hyaluronidase accumulates in the cervix as labour progresses (Iversen, 1960). Moreover Zachariac (1959) has already pointed out that the ratio between hyaluronidase and acid mucopolysaccharide is an important factor in the softening and dilatibility of the cervix.

We observed that intracervical injection of hyalase alone decreases mean duration of labour as compared to the control group. Our findings are in conformity with Bhatt *et al* (1971).

Diazepam has a beneficial effect in reducing the duration of labour by preventing the fear-tension syndrome and by its relaxant action on uterine muscula-

ture (Beplo and Lowe, 1968; Lee, 1968; Kaur, 1976; and Sharma *et al*, 1979). Diazepam when added with hyalase shortened the labour hours by 25% similar to that of hyalase alone. Pethidine, an analgesic of repute makes the labour bearable and easy by increasing the pain threshold and also breaking the fear-tension syndrome but it did not show any effect on duration of labour when given with hyalase group. These various combinations have not been tried by any other worker to the best of our knowledge and so a comparison has not been possible on this score.

Summary and Conclusions

1. Three hundred and thirty primigravidae with vertex presentation were chosen and given intracervical injection of hyalase (about 390 I.U.) after the cervix was already 3-4 cm dilated. Hyalase caused softening of the cervix and reduced duration of labour by about two hours.

2. Diazepam and pethidine although otherwise had beneficial effects on labour duration and alleviation of pain, yet failed to show any additive effect in combination with hyalase. As such hyalase alone is a simple, effective and safe means of reducing the mean duration of labour.

3. No side effects or adverse reactions of the drug on mother or foetus were observed.

4. In 7 toxæmic patients, who although have not been included in this series for the number was too small to be statistically significant, also showed quick ripening of cervix after which the labour proceeded normally.

5. In 3 patients who had L.S.C.S. for foetal distress and undetected cephalopelvic disproportion also had rapid cervical dilation upto 8 cm after which the operation was done. These cases have also been excluded from the study.

