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REFERENCES

Premature Labour at Groote Schuur Hospital

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SUMMARY

The management of premature labour at Groote Schuur Hospital is reviewed. Aggressive treatment with β-adrenergic agents is attempted. This has not been highly successful, mainly as a result of patients, doctors and midwives not realizing that premature labour is an obstetric emergency.

Other approaches to the problem are discussed. It is concluded that a new concept of obstetric practice is necessary, entailing the recognition of a stressed foetus.


Recent advances in the understanding of premature labour have suggested that the foetus is usually responsible for the onset of labour by means of an adrenocorticotropic hormone (ACTH)-mediated stress reaction. As this is a non-specific mechanism and as the noxious stimulus is often limited in time, premature labour can often be prevented by utilizing the normal defence mechanism against premature labour—the largely β-adrenergic uterine innervation—provided that the stage of rapid dilation of the cervix has not been reached or a maternal life-threatening situation does not pertain.

The high incidence of prematurity and enormous amount of equipment, space and staff required to care for the premature baby motivated the decision to treat premature labour aggressively in the latent phase in an attempt to prevent progression.

This communication describes the methods used and the results obtained during a trial period as well as recent changes that have been instituted in this field.

METHODS

All cases presenting with premature labour between 24 and 36 weeks and where no obvious evidence in favour of interference was available, were treated over a 3-month period at Groote Schuur Hospital.

An attempt was made to exclude cases where delivery was considered advisable. These were severe accidental haemorrhage with a dead foetus, ruptured membranes for 36 hours with no re-accumulation of liquor amnii, severe antepartum disease (e.g. Rhesus disease, toxaemia), or a cervix more than 3 cm dilated in a primiparous patient (4 cm in a multiparous). Great care was similarly
exercised in attempting to exclude the light-for-dates foetus on clinical grounds, which is all that is available in the acute situation.

Intravenous diazepam 10 mg and a similar dosage intramuscularly were administered. If contractions did not subside within 20 minutes an intravenous solution of 5 mg orciprenaline in 500 ml of 5% dextrose in water was infused at such a rate that the maternal pulse rate, which was used as a guide, was raised over a period of 5 minutes to at least 130 beats per minute and maintained at this level for 30 minutes.

Unless exceptional circumstances prevailed (e.g. the first pregnancy of a woman with a long history of infertility) the infusion was discontinued and only restarted if contractions recurred within 20 minutes. Three such courses in 24 hours were considered as adequate treatment unless exceptional circumstances prevailed. Extravascular analgesia was included where pain was thought to contribute to an initial tachycardia, as this limited dosage of the β-adrenergic agent.

If the treatment was successful, oral agents were administered for 1 week. An initial cause of failure was the non-recognition of a painlessly contracting uterus which nevertheless showed increased activity and should have been treated.

The pulse and blood pressure were monitored every 5-10 minutes when stable conditions were reached. Uterine activity was recorded preferably by means of a cardiocograph.

The cases over a 3-month period were reviewed in an attempt to assess the success of this regimen. Paediatric assessment of gestational age was made in all viable survivors.

RESULTS

During a 3-month period 810 deliveries took place at Groote Schuur Hospital. One hundred and fifty-three neonates weighing less than 2.5 kg were delivered. The results of treatment can be seen in Table I.

<table>
<thead>
<tr>
<th>Type of Medication Used</th>
<th>No.</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light-for-dates</td>
<td>75</td>
<td>12</td>
</tr>
<tr>
<td>Appropriate for dates (stillbirths)</td>
<td>9</td>
<td>—</td>
</tr>
<tr>
<td>Appropriate for dates</td>
<td>69</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>153</td>
<td>22</td>
</tr>
</tbody>
</table>

Fifteen cases were apparently successfully treated, i.e. they did not respond to sedation but did respond to orciprenaline and were delivered after 36 weeks of a foetus weighing more than 2.5 kg.

COMMENT

It can be noticed that no light-for-dates foetus was treated successfully. This is in keeping with the concept that these foetuses have a persistent stimulus towards labour and should be delivered.

Only 15 out of 37 cases were successfully treated and a large number of cases were not treated at all. Several approaches were made to this problem:

Type of Medication Used

It has been found that tachyphylaxis does not occur with salbutamol, which can, therefore, be administered continuously. Liggins and Vaughan also claim a lesser β1 effect.

No difficulties in monitoring have been encountered once the maintenance has been stabilized.

Reasons for Failure of Treatment were Analysed

During a further 3-month period 951 patients were delivered. Ninety-three neonates weighed less than 2.5 kg and the gestational age of all these was confirmed by the paediatricians.

If the gestational age was judged to be less than 36 weeks, the mother was interviewed in an attempt to ascertain why the prevention of premature labour had failed. Of the 93 cases 46 had a gestational age in excess of 36 weeks. The remainder were divided into two groups.

The first group consisted of those in whom the cervix was too far dilated on admission for treatment to be instituted (arbitrarily defined as 4 cm in multiparous patients, 3 cm in primiparous patients or a rate of dilatation of more than 0.6 cm per hour), and there were 26 cases (with 6 deaths): patient delay 12; midwife delay 2; doctor delay 4; administrative failure 1; rapid labour 7. A delay of 3 hours from the onset of painful contractions was arbitrarily selected as being appropriate to the geographical circumstances.

The second group consisted of 21 cases where it was feasible for treatment to be instituted: failed sedation 2; failed β-adrenergic administration 5 (in only 1 case were β-adrenergics administered adequately, the usual failure being the inability to maintain the maternal pulse rate at a sufficiently high level); maternal condition justifying termination 11 (5 deaths); no treatment 3. During the review period, 15 cases were apparently successfully treated.

Several conclusions could be drawn from this study. Critical assessment of gestational and foetal well-being before initiation of treatment to stop premature labour is essential in view of the high incidence of light-for-dates foetuses.

As prevention is better than cure, it is imperative that the patients, doctors and midwives be made to realize that threatened premature labour is an obstetric emergency. Until this is done, very little impact will be made by the aggressive administration of β-adrenergic agents. However, as this is unlikely at present, a foetal "flying squad" may well be the interim solution in the circumstances prevailing at Groote Schuur Hospital.
Preventing Labour at the Stage of Rapid Cervical Dilatation

Once the stage of rapid dilatation of the cervix has been reached, labour is irreversible. A likely mechanism is that decidual release of prostaglandins' results in an augmented output of oxytocin, thereby accelerating labour. It has also been shown that β-adrenergic agents are less effective in uterine inhibition when prostaglandins are used than when oxytocin is the uterine stimulant. For this reason antiprostaglandins or relaxant prostaglandins may enable the clinician to halt labour at a later stage of cervical dilatation. Preliminary trials of antiprostaglandins have been encouraging.

Prevention of Lethal Sequelae in the Neonate

The major cause of death in the premature neonate is hyaline membrane disease (HMD). A major mechanism in the production of this condition appears to be an inability of the liver of the premature neonate to synthesize lecithin, the major component of pulmonary surfactant, thereby resulting in a secondary alveolar collapse. It has been shown that cortisol is capable of inducing enzymes necessary for the formation of lecithin and hence of preventing hyaline membrane disease from developing in a significant number of cases. This has been applied to clinical practice in a number of circumstances, for instance where an attempt is being made to prevent premature labour in case of failure. Betamethazone 4 mg by intramuscular injection twice daily for 48 hours appears to be an effective form of enzyme induction. This has been used in 20 cases at Groote Schuur and Mowbray Maternity Hospitals. All cases were at less than 34 weeks’ gestation. Three cases developed mild hyaline membrane disease, a much lower incidence than would be expected. These results are so encouraging, and confirmatory of Liggins and Howie's findings, that a full double-blind trial is now under way.

Enzyme induction is also used for termination of pregnancy for maternal reasons and where the foetus is thought to be unaffected. Several investigators have reported that hyaline membrane disease does not occur among light-for-dates neonates. This may be overstating the case, but is nevertheless in keeping with the concept that an unstressed foetus is the one that will develop hyaline membrane disease if 'snatch’d untimely from his mother’s womb'. Adrenal corticoids are administered, as described above, before termination. Experience at Groote Schuur Hospital is too anecdotal for reporting at present, but is likewise encouraging.

Lastly, enzyme induction may be used in cases where doubt exists about foetal well-being. If the foetal condition gives cause for concern (e.g. in a diabetic patient) but the risks of hyaline membrane disease are high, administration of corticoids is indicated.

It should be noted that the presence of bubbles, when liquor amnii is shaken with an equal volume of absolute alcohol in a clean test tube, indicates the presence of surfactant in the amniotic fluid and the virtual absence of hyaline membrane disease in such neonates, whatever the epidemiological risk. It should be noted that the time scale for the development of liquor surfactant appears to be longer than the 48 hours required to prevent the disease.

Gluck and Kulovich have made the opposite contention, viz. that only a stressed foetus will develop pulmonary surfactant and the presence of this activity in the liquor amnii indicates a good reason to deliver a particular foetus, whereas if surfactant activity is absent, that particular foetus is not stressed by a chronic mechanism endangering its life.

In conclusion, it can be seen that the modern approach to premature labour must be active, if it or its sequelae are to be prevented.

Recent developments in this field have suggested sweeping changes with wide application in obstetric practice. This embodies a physiopathological approach to an individual foetus. In essence, the presence or absence of stress—whatever its nature—to a particular foetus, will determine the onset of labour and foetal outcome, rather than the gestational age or epidemiological risk.

REFERENCES