

THE
Journal of Obstetrics & Gynaecology
of India

VOLUME XVI, NO. 4

AUGUST 1966

EXPERIENCES WITH INTRA-AMNIOTIC INJECTION OF
HYPERTONIC GLUCOSE FOR INDUCTION OF LABOUR

by

M. K. KRISHNA MENON*, B.A., M.D., F.R.C.O.G., F.A.M.S.

and

S. N. DESHPANDE**, M.D.

One of the difficult problems which often confront the obstetrician is that of intrauterine death and retention of the foetus. Intrauterine death may occur at any time in pregnancy but those which take place after the full formation of the placenta are the ones which cause concern. It is generally agreed that in most cases spontaneous expulsion without serious complications occur within 5-6 weeks of the accident.

However in some, such prolonged retention has given rise to coagulation defects in the mother and at times, even in the absence of any in-

terference, to intrauterine infection. Further there is the added psychological trauma, more evident in a neurotic mother who knows she is carrying a dead foetus.

The fact that early attempts at evacuation of the uterus are not undertaken in these cases but heavy reliance is placed on spontaneous evacuation is due to the difficulty experienced in artificial methods of evacuation and the complications resulting therefrom. If a simple method, which is successful and at the same time gives rise to no or only minimal complication, is available, there could be then no objection to its adoption for the early evacuation of the uterus after intrauterine death has occurred.

At times on medical grounds evacuation of a pregnant uterus becomes necessary. While in the early months and in late pregnancy satisfactory

* Director, Institute of Obstetrics & Gynaecology, Govt. Hospital for Women & Children, Egmore, Madras-8.

**Post-graduate at the Institute.

Paper read at the 13th All-India Obstetric and Gynaecological Congress held at Patna in January, 1966.

methods are available, the evacuation of a pregnant uterus between 20 and 32 weeks still poses a difficult problem. Advantages have been claimed in this respect for the intravenous use of oxytocin as a drip with increasing concentration of oxytocin—even upto 100 units have been reported. It is often efficacious but failures are not uncommon. Artificial rupture of membranes in cases of foetal death with prolonged retention is not advocated as a routine because of greater chances and dangers of infection.

In 1962 Bengtson and Csapo used intrauterine hypertonic 20 per cent sodium chloride to induce abortion successfully in women between the 16th and 24th weeks. In a carefully planned series of experiments they produced evidence that the induction of labour after this procedure was due to diminution of placental progesterone production. Although oxytocin alone at infusion rates as high as 70 units for two consecutive days did not terminate normal pregnancy between 16 and 24 weeks a single intra-amniotic injection of 20 per cent saline did so within 38 hours. They also noted that after intra-amniotic injection of hypertonic solution there was a marked fall in blood and placental progesterone level while systemic or local progesterone therapy delayed the onset of labour following the procedure from 31-68 hours. Carl Wood, Booth and Pinkerton

(1962) reported successful results with this procedure using 50% glucose instead. Struck by the favourable results and the innocuousness of the procedure it was decided to try it out in cases of intrauterine death and where termination of pregnancy after 20 weeks was indicated on medical grounds. The solution chosen for intra-amniotic injection was 50% glucose. What follows is our observation on 56 patients so treated. The 56 patients were distributed as follows:—

| | |
|---|----|
| 1. Intrauterine death | 44 |
| 2. Pre-eclamptic toxæmia and controlled eclampsia | 8 |
| 3. Vesicular mole | 2 |
| 4. Foetal anencephaly | 2 |

Patients with intrauterine death (44) cases

The details of the 44 cases are shown in the following statements:

TABLE I

Age

| Age | 16-20 | 21-25 | 26-30 | 31-35 | Total |
|--------|-------|-------|-------|-------|-------|
| Number | 4 | 12 | 12 | 16 | 44 |

One of the difficulties experienced has been the assessment of the time of foetal death and duration of its retention. While full accuracy is not claimed the figures given are not very inaccurate.

TABLE II

Parity

| Parity | 0 | I | II | III | IV | V | VI | VII | VIII | IX | Total |
|--------|---|---|----|-----|----|---|----|-----|------|----|-------|
| Number | 2 | 4 | 10 | 12 | 6 | 5 | 2 | 2 | - | 1 | 44 |

TABLE III
Period of pregnancy at the time of foetal death

| Period in weeks | 20-24 | 24-28 | 28-32 | 32-36 | Over 36 | Total |
|-----------------|-------|-------|-------|-------|---------|-------|
| Number | 8 | 12 | 14 | 8 | 2 | 44 |

TABLE VI
Interval between foetal death and induction

| Duration in weeks | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Total |
|-------------------|---|---|----|---|---|---|---|---|---|----|-------|
| Number | 8 | 9 | 12 | 4 | 2 | 2 | 2 | 2 | 1 | 2 | 44 |

Procedure

After detailed history taking and examination of the cases the intra-uterine death was diagnosed and confirmed in all cases by the male frog test and in 30 cases by x-ray evidence also in addition. In 40 cases blood fibrinogen was estimated and vaginal cytology and urinary pregnandiol estimated in 26. Prior to injection in all cases a vaginal examination was made to note the nature of the cervix. Amniotomy per abdomen under local infiltration anaesthesia was done using a thick aspirating needle (gauge 18 length 4"). No attempt was made to locate the placenta by placentography prior to amniotomy. As much liquor as possible was withdrawn — the amount obtained varying according to the period of pregnancy and duration of intrauterine death. Fifty per cent glucose-mixed with 100,000 units of penicillin and 1 gm of streptomycin was then injected into the amniotic cavity. The amount injected varied according to that withdrawn. But a quantity more than that withdrawn was always injected. No specific difficulty was encountered in the amniotic puncture. In 12 cases no liquor could

be drawn. In spite of this, it was possible easily to make out that the needle was in the amniotic cavity by its free play and when glucose was injected it could be aspirated back. When no liquor was aspirated it was difficult in decide as to how much to put in. As a rule as much as possible was injected without causing any discomfort to the patient and making the size of the uterus bigger than at the start. After the injection the patient was kept in bed till the pains started. Blood pressure and pulse were recorded every half an hour. After delivery the patients were followed through puerperium till discharge.

Observations

The latent period—This is the time lag between the intra-amniotic injection and the onset of uterine activity. It ranged from a minimum of 4 hours to a maximum of 72 hours, the average being 15.8 hours.

The duration of labour

The time taken for complete expulsion of the foetus and placenta from the onset of uterine activity ranged from a minimum of 2 hours to a

TABLE V
Latent period

| Duration of hours | 4-8 | 8-12 | 12-24 | 24-48 | 48-72 | Total |
|-------------------|-----|------|-------|-------|-------|-------|
| No. of cases | 10 | 22 | 7 | 3 | 2 | 44 |

maximum of 24 hours, the average being 6 hours.

TABLE VI
Duration of labour

| Duration in hours | 0-6 | 6-12 | 12-24 | Total |
|-------------------|-----|------|-------|-------|
| Number | 32 | 10 | 2 | 44 |

The Induction/delivery interval

It ranged from 7 hours to 80 hours the average being 20 hours.

An attempt was made to find out correlation if any between the duration of foetal death and induction/

delivery interval. When the duration of foetal death was over six weeks the average induction/delivery interval was 36 hours. It was 19 hours when the retention period was from 1-6 weeks.

While it may not be correct to arrive at a definite conclusion from a small series, it is suggested that the longer a dead foetus is retained in utero the greater the difficulty of quick expulsion. Probably the same factors which are responsible for prolonged retention of a dead foetus are also responsible in preventing its easy expulsion.

TABLE VII
Induction/delivery interval

| I./D. interval in hours | 0-12 hours | 12-24 | 24-48 | 48-72 | 72-80 | Total |
|-------------------------|------------|-------|-------|-------|-------|-------|
| Number | 28 | 7 | 6 | 2 | 1 | 44 |

TABLE VIII
Comparative

| Series | No. of cases | Period of gestation in weeks | Duration of foetal death in weeks | Latent period average in hours | Duration of labour average in hours | I. D. interval average in hours | Failures |
|--------------------------------------|--------------|------------------------------|-----------------------------------|--------------------------------|-------------------------------------|---------------------------------|----------|
| Carl Wood Booth and Pinkerton (1962) | 22 | 28-40 | 1-5 | 21-3 | 6.7 | 28.5 | Nil |
| Csapo (1963) | 17 | 15-37 | 1-5 | 13 | 2.7 | 15.7 | Nil |
| Present series | 44 | 20-36 | 1-10 | 15.8 | 6 | 20 | Nil |

The amount and type of liquor

This varied according to the term of pregnancy and duration of retention of the dead foetus. In long-standing cases of foetal death only small quantities or sometimes no liquor could be aspirated.

The quantity of liquor aspirated varied from 10 ml-400 ml. Except in 8 cases the liquor was clear. In 4 of these cases the liquor was heavily stained with meconium while in the remaining 4 it was dark brown. No correlation was seen between the amount aspirated and induction/delivery interval.

The volume of glucose injected

TABLE IX

| Size of the uterus in weeks | Amount of glucose injected in ml. |
|-----------------------------|-----------------------------------|
| Over 32 weeks | 600 |
| 32 | 500 |
| 28 | 400 |
| 24 | 320 |
| 20 | 200 |

In one case the injection had to be repeated. In 2 cases where 400 ml. of glucose was injected with 26 weeks' uterus the patients complained of severe pain and backache when uterine activity started at the end of 20 hours. When sedation failed to relieve the pain a vaginal examination was done which revealed a tense bag of membranes. This was ruptured and the pain was relieved. The patients aborted soon after.

Induction/delivery interval and nature of the cervix

It is a well established fact that with a favourable cervix most methods of induction are often

successful and in many the induction/delivery interval also is short. The same has been found in this series also — the longest duration being in those with closed uneffaced cervix and shortest with effaced ones — 24.7 hours as against 10.2 hours. There were 36 cases with an unfavourable cervix and 8 with favourable ones.

Glycosuria

Maternal hyperglycaemia and glycosuria was noted in 38 cases — the sugar appearing in the urine within one hour of injection. In no case did it persist for more than 6 hours. The maternal blood sugar in 10 cases rose to 500 mgs% but returned to normal in 3 hours.

Blood pressure and pulse

No appreciable variations in blood pressure or pulse rate were noticed. The blood pressure did not rise above the starting level in those with pre-eclamptic toxæmia.

Urinary pregnanediol and vaginal cytology

Progesterone has an inhibiting action on uterine activity in undisturbed pregnancy. Unless the progesterone block on the myometrium is removed uterine activity may be absent or minimal. At times retention of a dead foetus for long periods may be due to the progesterone levels in the blood or at the placental site remaining high. If this is so, normal or high levels of progesterone for that period of pregnancy may foretell failure of induction or prolongation of induction/delivery interval. These hormonal changes would be reflected in vaginal cytology and urinary pregnanediol excretion. It is well known

that vaginal cytology is difficult of correct interpretation. All the same we have made an attempt to correlate vaginal cytology, pregnanediol estimation and induction/delivery interval.

Urinary pregnanediol and vaginal cytology were determined in 26 patients. In all the patients except one the values were well below the established minimal range for that period of pregnancy. No correlation was found between pregnanediol level and induction/delivery interval.

Table X shows the urinary pregnanediol values, vaginal cytology and induction/delivery interval.

In studying the vaginal smear apart from the general characteristics, Karyopyknotic Index was the one taken into consideration for purposes of correlation. And index above 20 was taken to mean poor pregnanediol excretion and hence poor progestational effect. It has not been possible to establish any correlation between pregnanediol values, vaginal cytology and induction/delivery interval. Discrepancy was occasionally noted between pregnanediol values and the K.P. index.

Plasma fibrinogen

Plasma fibrinogen before and after amniotomy (prior to delivery) was estimated in 40 cases. The values ranged from 210-430 mgs%. There was no significant difference in values after the injection and prior to delivery (206-436 mgs%).

Delivery

No complications followed spontaneous delivery in 42 patients and assisted delivery in 2. The puerperium in all was uneventful.

TABLE X

| Cases No. | Urinary pregnanediol in mgs. | Vaginal smear K.P. index % | I./D. interval in hours |
|-----------|------------------------------|----------------------------|-------------------------|
| 1 | 3.03 | 25 | 12.5 |
| 2 | 5.8 | 20 | 21 |
| 3 | 3.2 | Cytolytic | 12.5 |
| 4 | 5.8 | 22 | 4.5 |
| 5 | 16.4 | 4 | 15 |
| 6 | 3.2 | Cytolytic | 14 |
| 7 | 5.8 | 4 | 27 |
| 8 | 4.3 | Cytolytic | 14 |
| 9 | 1.9 | 55 | 44 |
| 10 | 3.3 | 24 | 42 |
| 11 | 4.3 | Cytolytic | 12 |
| 12 | 8.9 | 80 | 27 |
| 13 | 5.4 | 30 | 17 |
| 14 | 69.8 | 30 | 72 |
| 15 | 10.6 | 28 | 13.5 |
| 16 | 8.4 | 26 | 10.5 |
| 17 | 7.2 | 31 | 9.5 |
| 18 | 6.0 | 26 | 7.6 |
| 19 | 3.2 | 42 | 12.0 |
| 20 | 3.6 | Cytolytic | 11 |
| 21 | 5.6 | 20 | 19 |
| 22 | 4.8 | Cytolytic | 9 |
| 23 | 3.2 | 29 | 7.0 |
| 24 | 3.0 | 33 | 9.4 |
| 25 | 2.4 | 48 | 5 |
| 26 | 8.6 | 24 | 13.2 |

There were no maternal complications requiring attention except headache and abdominal cramps due to uterine distension in 2 cases. There was no maternal mortality or morbidity.

Vesicular mole

There were 2 cases diagnosed prior to passage of vesicles. The size of the uterus varied from 18-28 weeks. The os was closed in both cases. Bleeding was intermittent and mild. 200-400 ml. of 50% glucose was injected into the uterine cavity without any complication. The mole was expelled spontaneously in an average time of

28.6 hours -range 18-72 hours. In one case brisk bleeding commenced when an oxytocin infusion with 20 units in 500 ml was set up. The mole was expelled spontaneously in 12 hours.

Pre-eclamptic toxæmia and controlled eclampsia

There were 8 cases with severe pre-eclamptic toxæmia where it was decided to terminate the pregnancy. The duration of pregnancy ranged from 30-34 weeks with foetus alive in all. Two of them were primigravidae in whom the eclamptic convulsions had been controlled for a week. In all patients the cervix was unfavourable. After amniotomy and injection all delivered spontaneously within an average time of 22 hours—range 16-46 hours. Following the injections the foetal heart disappeared in all cases within 10-26 hours.

Foetal anencephaly

In two patients anencephalic foetuses were diagnosed at 32 weeks. After intra-amniotic injection of 500 ml. of 50% glucose both patients expelled the foetuses in 22 and 46 hours.

In all these patients the puerperium was uneventful.

From this limited experience it is observed that intra-amniotic injection of glucose is a reasonably safe and fairly certain method of evacuation of a pregnant uterus at a time when other measures are likely to be uncertain in effect.

Discussion

Fuchs (1961) Bengtson and Csapo (1962), Carl Wood, Booth and Pinkerton (1962) all have confirmed the effectiveness of intra-amniotic injection of hypertonic saline or glu-

cose as a method of induction of labour. Our experience in 56 patients using intra-amniotic injections of 50% glucose for induction of labour confirm the experience of other workers. The procedure was technically simple and produced no complications.

John Peel (1962) reported a case of fatal staphylococcal septicaemia which occurred in 1933 after induction with uroselectan and hypertonic glucose injected into the amniotic cavity. B. Welchii infection has also been reported following intra-amniotic injections. We have combined the hypertonic glucose solution with 10 lakhs units of penicillin and 1 gm. of streptomycin and have not had any infection in this series.

It is not proposed to discuss the mode of action of the hypertonic glucose in producing uterine activity. From our experience we are to conclude that this method is satisfactory and free from major risks. It invariably kills a live foetus and hence should not be used in cases where a normal foetus has a chance of survival after birth.

References

1. Bengtson, L. P. Stormly: *Acta. Obstet. Gynaec. Scand.* 12: 114, 1962.
2. Bengtson, L. P. and Csapo: *Am. J. Obst. & Gynec.* 1963.
3. Csapo, A. I. & Bengtson, L. P. *Am. J. Obst. & Gynec.* 83: 1083, 1962.
4. Wood, C. Elstein, M., Pinkerton, J. H. M.: *J. Obst. Gynec. Brit. Comm.* 70: 396, 1963.
5. Wood, C., Booth, R. T. and Pinkerton, J. H. M.: *Brit. Med. J.*, Sept. 15: 706, 1962.