

TERMINATION OF MIDTRIMESTER PREGNANCIES BY INTRA-AMNIOTIC INJECTION OF HYPERTONIC SALINE

by

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Amniocentesis and intra-amniotic injection of hypertonic saline to terminate pregnancy in the second trimester has attained great importance in recent years. That such a method was not accepted or currently used in leading obstetric institutions can be easily demonstrated. In Scandinavia, where an average of 3,354 pregnancies were legally terminated annually from 1955 to 1965, abdominal hysterotomy was the method of choice. At the Mayo Clinic from 1959-62 the management of missed abortion was active, surgical in 62% of the cases (Csapo, 1965).

This is an opportune time to review briefly the historical development of application of hypertonic solutions for termination of midtrimester pregnancy. Abruel (1934) in Bucharest studied the problem of induction of labour when survival of the foetus need not be considered e.g. cases of therapeutic abortion, intra-uterine death and lethal foetal anomalies. He found that introduction of 33% saline into the amniotic cavity was effective in terminating pregnancy. His method con-

tinued to find favour in many East European countries. Boero (1935) was impressed by the clinical observation that when pregnancy was accompanied by some serious medical complication like heart disease, toxæmia and tuberculosis, spontaneous death of the foetus led to marked improvement in the patient's condition. He, therefore, sought a method of killing the foetus without causing its immediate expulsion. He achieved this by injection of 2-3 ml of 10% formalin into the liquor by amniocentesis. The foetus was killed immediately and depending on the exact dose, it was either retained for a variable time or expelled within 24 hours.

In England, Burke (1935) investigated the application of amniography in the diagnosis of placenta prævia. He used Uroselectan B for this purpose and found that it frequently led to the onset of labour. Following the publication of his work, Playfair (1941) attempted to induce labour in 115 normal full term pregnancies with 10 ml of Uroselectan B and succeeded in all but 4 cases. Dextrose in a 50% solution in the amniotic cavity was described by Brosset (1958).

The present study was undertaken after the liberalized abortion law in India which became operative on the 1st of April, 1972 permitting abortion upto 20

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Received for publication on 2-10-73.

weeks of pregnancy. The purpose of this report is to describe the clinical observations in 80 women who received intra-amniotic injection of hypertonic saline and to evaluate the reliability, safety and efficacy of this method for induction of second trimester abortion.

Material and Methods

The present study was conducted in the Department of Obstetrics and Gynaecology, Irwin Hospital, New Delhi. Eighty cases were selected from the outpatients department and Family Planning Clinic from April 1972 to April, 1973.

More than half of the patients (60%) were terminated at a period of gestation of 18-20 weeks. The remaining were attempted at 14-16 weeks and included 5 cases of 14 weeks gestation. All cases were admitted a day before the injection. A detailed history and examination were carried out to exclude any systemic or organic disease with particular attention to kidney function, cardiac damage or severe hypertension. If any of these diseases was suspected, the case was considered unfit for saline injection. Routine preliminary investigations like blood for haemoglobin percentage, blood urea and routine urine examination were carried out in all cases. Special investigations were performed as and when indicated.

No premedication was considered necessary except a sedative in the form of tablet Luminal Gr. II the night prior to injection.

Method

1. The patient was placed on the table in a supine position after she had passed urine and her pulse and blood pressure were recorded prior to the injection.

2. The site of puncture selected was

a point 1" below the fundus when the uterine size was 16 weeks and it was midway between the symphysis pubis and height of the fundus in the midline when the period of gestation ranged between 18-20 weeks.

3. Under all aseptic precautions the selected site was first infiltrated with 2-3 ml of 1% xylocaine solution.

An 18 gauge spinal needle with the stylette in place was used for amniocentesis. If a bloody tap was obtained or the liquor was heavily stained with blood hypertonic saline was not injected. Before each injection aspiration was carried out to ensure that there was a free flow of clear liquor. The quantity of amniotic fluid withdrawn ranged from 60-200 ml.

4. After amniocentesis, 20% freshly prepared sterile saline solution was injected slowly through the needle with a 50 ml syringe. The volume instilled did not exceed 200 ml in any case. Normal saline was pushed in before and during withdrawal of the needle.

Before introducing hypertonic saline, the patient was asked to report a sensation of heat in the face, headache, flushing, severe abdominal pain, intense thirst, prickly sensation in the hands and face or anxiety, which are the warning signs of intravascular injection. If any of these symptoms occurred, the procedure was discontinued immediately. Her pulse and B.P. were recorded at the end of the procedure and at one hourly interval. A careful watch was kept on her urinary output. The average hospital stay was 3-4 days, ranging from 2-9 days except in one case, who had a prolonged stay of 20 days. All the patients were asked to report for follow-up at an interval of one month for 3 months.

Maximum number of abortions (76.3%) were performed in the age group of 14-25

years with a mean age of 22.5 years. Single nulliparous women formed nearly 80% of the total. Parous women comprised about one fifth of the series ranging from para 1-6. Racial distribution was Hindus (90%), Mohamedans (7.5%) and Christians (2.5%). The majority of the patients (68.8%) belonged to a low socio-economic status. 25% of the patients were illiterate, while 30% had put in some years at school. 45% had completed school or had had some higher education. The indication for termination were mainly psychological and eugenic.

Table I shows the correlation between the period of gestation and successful amniocentesis. With a gestation period of 17 weeks and over, the failure rate was 4.1%, while a four fold increase in the failure rate was encountered when the pregnancy was less than 17 weeks.

TABLE I

Correlation Between the Period Gestation and Successful Amniocentesis

Size of uterus in weeks	No. of cases	Successful amniocentesis		Failed amniocentesis	
		No.	%	No.	%
14-16	32	26	81.3	6	18.7
17-20	48	46	95.9	2	4.1

The onset of cramping was delayed in multiparae as compared to nulliparae (26.5 and 21.8 hours) respectively, but the duration of labour was prolonged in nulliparae i.e. 7.5 hours compared to 5.1 hours in multiparae. No significant correlation could be observed between parity and I/A (Instillation-abortion) time.

Table II shows that common complications encountered were failed amniocentesis, fever (more than 38°C persisting for more than 24 hours after the injection) and retained placenta. One patient suffered from acute septic arthritis.

TABLE II

Complications Following Saline Instillation

Complications	No. of cases	Percentage
Failed amniocentesis	8	10.0
Failed to abort	3	3.7
Retained placenta	4	5.0
Required manual removal	1	1.2
Fever	10	12.5
Readmitted for D & C	2	2.5
Pelvic Inflammation	1	1.2
Required blood transfusion	1	1.2
Others*	1	1.2

Acute septic arthritis

Amniocentesis was considered a failure when it was not successful after three consecutive attempts in the same sitting. This occurred in 8 cases in the series—5 were 14-16 weeks, two 16-18 weeks and one 20 weeks gestation. In 7 of these

cases, amniocentesis was successful at the second sitting and one case required a third attempt. Ultimately successful instillation was possible in 100% cases.

Three cases failed to abort after instillation. All these cases were injected again in the same manner. One patient aborted about 23 hours after the second injection. The second was a young primigravida with a history of right sided partial nephrectomy. Her microscopic examination of urine, blood urea, creatinine and I.V.P. were within normal limits. 50% glucose was instilled into the amniotic cavity in view of her renal condition

but without any result. Injection syntocinon 5 units in 540 cc of 5% glucose was infused 24 hours after the intra-amniotic injection but without any success. Four days after the first instillation she was re-injected with 20% saline. This time pains started after 16 hours, and the labour was completed within 23 hours. The reason for failure following induction could be observed at the time of completion of labour when she gave birth to 2 fetuses—one macerated and the other a fresh stillbirth. This may indicate that the first injection was made into one amniotic sac leaving the other intact. Third case was a multipara with 18 weeks gestation. She started leaking on the second day following saline instillation and went into missed abortion. She was given oral stillboestrol followed by intravenous syntocinon (5 units) in 540 cc. of 5% glucose for 2 days consecutively, but failed to abort. Subsequently 2 sterile rubber catheters were introduced into the uterine cavity. After about 24 hours she developed moderate uterine contractions and aborted.

Placenta was retained on 4 occasions. In each injection Syntocinon 5 units in 540 cc of 5% dextrose was infused. With the onset of good uterine contractions the placenta and membranes were expelled in 3 out of 4 cases within 1-4 hours. One case required manual removal under general anaesthesia.

Two cases had to be readmitted for excessive bleeding due to incomplete abortion. Both of them required D & C and one of them required blood transfusion.

Pelvic inflammation was noticed in a multipara about one month after the injection but she responded to conservative treatment. Seven cases reported with menstrual disorders in the form of a delayed or a heavy period for the first two

or three cycles after the abortion, but all of them responded well to conservative treatment. Cyclical hormonal therapy in the form of Tab. Lyndiol 5 mg. for 3 cycles was required in one case. One case reported later with another pregnancy.

Discussion

In this series a clinical evaluation of the procedure of intra-amniotic injection of hypertonic saline has been attempted to judge its safety and reliability for termination of second trimester pregnancies.

Majority of patients were young (73% between 14-25 years) Single (76.3%) and nulliparous (80%). This probably reflects their inexperience in recognising the symptoms of pregnancy, hesitation and fear in seeking medical advice and thus presenting themselves late. 16% were multiparae who found themselves pregnant after the husband had been vasectomized. Most of them could not believe they were pregnant and thus the cause of delay. Second trimester abortions formed only 7.5% of the total induced abortions—92.5% of patients coming in the first trimester.

It was observed that 68% of the cases belonged to lower socio-economic status but this did not vary appreciably when all gynaecological and obstetric admissions were taken into account. This indicated that abortions were not restricted to any class of patients which was also experienced by Lewis (1969) and Tietze (1971).

The main reason for termination of pregnancy was psychological which was also found in the series reported by Lewis (1969), Tietze (1971) and many others also.

The average instillation-abortion time (I/A) and latent period recorded were

26.7 hours and 22.1 hours, respectively. No significant correlation could be observed between parity and I/A time. Weingold *et al* (1965) and Ruttner (1966) recorded an almost similar I/A time of 24.9 and 29.6 hours, respectively, but Kerenyi (1971) in his ambulatory series found a higher average time of 36.5 hours. This time difference could not be explained as all the factors concerned with the technique were almost the same and the exact mechanism of action still remains obscure. Csapo (1967) and Mackenzie *et al* (1971) also tried but failed to observe any correlation between the parity and I/A time. It has been unanimously agreed by all workers that once clinical labour starts it lasts for a short while and becomes completed within one to 8 hours. This has been confirmed in the present study. Amniocentesis failed in 4.1% of the cases when attempted at 17 weeks and over but the failure rate jumped upto 18.7% during 14-16 weeks of gestation. Thus, a significant correlation could be established between the period of gestation and successful amniocentesis. Mackenzie *et al* (1971) reported successful amniocentesis in 50% of their cases between 12-15 weeks, but it increased to 95% during 16-18 weeks and 100% between 19-28 weeks. A similar result of 96% success rate was reported by Kerenyi (1971) using the method at 18 weeks and above with intra-amniotic saline.

Failure to terminate pregnancy was encountered in 3 cases (3.7%). It has been reported in 11.7 and 2.5% by Alpern *et al* (1968) and Mackenzie *et al* (1971), respectively. This variation in the results could not be explained, as the exact mechanism of action is not known. Placenta was seen to be retained in 5% of the cases and one of them required manual removal. Retained placenta was encoun-

tered in 4.6% and 3% of the cases in the series reported by Walton (1971) and Kerenyi (1971) but the incidence was higher (10%) with Mackenzie *et al* (1971). Two patients (2.5%) required D & C for incomplete abortion as against that of 2.5% and 1.7% reported by Kerenyi (1971) and Schulman *et al* (1971), respectively.

Fever was a common complication following saline instillation. It was found in 12.5% of the cases though all of them responded to antibiotics except one who developed acute septic arthritis later. Postabortal fever was reported in 7.5% of the cases by Wagner *et al*, (1962), and 23.3% by Schiffer (1969) in his small series of 30 cases. Pelvic infection was noticed in only one case in this series. It was reported as 2.35% by Wagner *et al* (1962) which included one case of pelvic abscess.

One case suffered from persistent intermittent fever and joint pains. She was a young unmarried girl of average built and nutrition without any systemic disease and was admitted with 18-20 weeks gestation. She was injected successfully with 20% saline and labour was uneventfully completed within 25 hours. She started slight bleeding after the abortion which could be easily controlled by oxytocin infusion. On the second post-abortal day she had a rise of temperature 39°C with generalised bodyache. At that time her differential blood count showed polymorphonuclear leucocytosis. Meanwhile, she was put on Cap. chloromycetin and other supportive treatment. The temperature was controlled but the pain gradually centered around her right shoulder joint. Culture of high vaginal swab showed the presence of staphylococci. On the 12th day she felt excruciating pain around her sacro-iliac joints with

slight swelling of the affected joints. On the 18th day her blood sedimentation rate was recorded 65 mm/1st hour with high rise of ASO titre (Antistreptolysin titre) to 500 Todds unit and 'C' reactive protein was positive upto 1 to 20 dilutions. At this point question was raised about the precipitation of rheumatic arthritis following the stress and strain of abortion. Finally, she was diagnosed as a case of acute septic arthritis. Pain was later relieved by Cap. Indocid and physiotherapy. No case of this type has been reported in the literature so far. There was no case of coagulation failure in the series.

Comments

Abortion by intra-amniotic injection of hypertonic saline is a procedure of merit, although the risks to the patient must be recognised and all possible steps taken to guard against them.

Wagatsuma in 1965 reviewed a large experience using hypertonic saline in Japan after abortion was legalised in 1948. Many complications and maternal deaths were associated with the large number of abortions performed and he explained these deaths on the basis of four errors. The first was caused by technical failure that resulted in infection or direct instillation of saline into the blood stream. The second consisted of aggravation of the general complications already present. Third category was secondary to postpartum haemorrhage, laceration of the cervix and uterine rupture and the fourth class were unknown aetiology.

Cameron and Dayan (1966) reported two startling deaths in patients who had therapeutic abortion induced by instillation of hypertonic saline. Both patients had widespread cerebral infarction. The first patient had been given 400 ml. of

20% saline and the second had received 150 cc. of 30% saline.

Sabeti and de Watteville (1967) recorded two deaths related to either the technique failure or the solution used. One death was due to septicaemia which occurred 48 hours after the injection. The second occurred 8 days after salt instillation and was attributed to an inadvertent intravascular injection of 10% solution.

Pathak (1968) described his experience with 78 patients with one death in his series. The patient who died was a known diabetic with an anencephalic foetus and hydramnios. The first instillation of 300 ml. of 20% saline replaced 300 ml. of amniotic fluid, 24 hours later 1500 ml. of amniotic fluid was withdrawn and another 300 cc. of 20% saline instilled. During labour, 11 hours later, the patient went into shock and died and the case was diagnosed as amniotic fluid embolism.

A case of acute renal failure was reported by Eisner and Piver (1968) following this procedure in a patient who showed presence of a trace of protein on urine analysis prior to injection.

Recently, reports have been published regarding coagulation disorders following hypertonic saline injection. Goodlin *et al* (1971) reported one case with disseminated intravascular coagulation associated with amniotic fluid embolism and later in another paper he mentioned one patient with hypofibrinogenaemia. Walton (1971) and Standard *et al* (1971) confirmed defibrination as well as reduced levels of factors V, VIII and IX.

It appears from the above data that some of the poor results in the various series were due to over-enthusiasm and lack of adequate technical knowledge. This can be supported by observ-

ing two deaths from central nervous system damage reported by Cameron and Dayan and large number of deaths reported by Wagatsuma. All the three deaths reported by Sabeti and de Watteville occurred in the early part of their work prior to the use of a special technique which provided many precautionary measures. Pathak used this method in a diabetic patient with poor general condition and in whom two instillations were made with a total of 600 ml. of 20% saline within 24 hours.

Thus, some of the aforesaid mishaps and added risks might have been avoided if more technical information had been available. The proper technique must follow the detailed and careful steps described by Jaffin and Kerenyi (1962) and Alpern *et al* (1968). It is important that the uterus be larger than 15 weeks size as the chances of failed amniocentesis and intravascular injection is more likely in a smaller uterus. Patients should be constantly observed for vital signs of intravascular injection with cessation of the procedure if any adverse sign or symptoms is noted. The method should include selected patients eliminating those with medical complications like heart disease, diabetes, toxæmia or abdominal scarring. Not more than 200 ml. of 20% saline should be injected at a time which carries 40 gms. of sodium chloride.

Summary and Conclusions

Eighty patients were subjected to intra-amniotic injection of hypertonic saline. Average I/A time recorded was 26.7 hours. Common complications encountered were fever, failed amniocentesis, failure to terminate pregnancy and retained placenta. Method has been shown to be useful when the uterus is of

TABLE III
Results of saline instillations

Type of patients	No. of cases	Average age (years)	Parity (Mean)	Gestation Mean (Weeks)	Liquor withdrawn Mean (ml.)	Saline injected Mean (ml.)	Latent period Mean (hrs.)	Labour Mean (hrs.)	I/A time Mean (hrs.)	Range of I/A time (hrs.)
Nullipara	64	18.7	0	17.8	118.6	135.9	21.8	7.5	24.8	0.6-48.6
Multipara	16	26.3	2.9	18.6	132.4	141.8	26.5	5.1	26.7	8.10-53.3
All cases	80	22.5	0.5	18.2	125.5	138.8	22.1	6.3	26.7	6.00-53.3

16 weeks size or more. The solution used was 20% saline and the amount instilled never exceeded 200 ml. The relevant literature has been reviewed.

The method is easy and reliable. It is emphasized that a meticulous technique should be carried out with careful attention to selection of patients and complete knowledge of the possible complications that may arise during and after the injection.

Acknowledgement

We are grateful to the Director-Principal, Dr. S. Padmavati for permission to publish this paper. We are thankful to Dr. P. N. Ghei, Medical Superintendent, for providing the necessary facilities. To Mr. Sapra we are thankful for typing the script.

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