HISTOPATHOLOGICAL CHANGES IN THE PLACENTA, MEMBRANES AND UMBILICAL CORD FOLLOWING MID-TRIMESTER SALINE ABORTIONS

by

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Introduction

Intra-amniotic instillation of hypertonic saline solution is now considered to be an effective and reasonably safe procedure for induction of abortion in the mid-trimester of pregnancy. But, inspite of its wide use the exact site and mechanism of action remain unknown. Recently, several papers describing the histological changes in placenta, membranes and umbilical cord have been published in world literature. The reported results are controversial and confusing. The objects of the present study were (1) to describe in a systematic manner the histological changes in the membranes, placentae and umbilical cords following mid-trimester saline abortions and to compare these appearances with those cases where the same structures were removed by abdominal hysterotomy (2) to study whether the changes in the former group can throw any light upon the mechanism of action of hypertonic saline solution in initiating uterine contractions.

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Material and Methods

A. Study group (25 cases): Pregnancy was terminated by intra-amniotic instillation of 200 ml of 20 per cent saline solution per abdomen.

B. Control group (25 cases): Pregnancy was terminated by abdominal hysterotomy (duration of gestation being identical with study group of cases).

The duration of gestation in above groups varied from 16-20 weeks. The mean ages in groups (A) and (B) were 25.1 and 27.2 years respectively. The average Hb level in group (A) was 10.2 and in group (B) was 9.8 grams per cent. Cases with any systemic disease, with history of bleeding P/V or with any associated pelvic pathology were carefully excluded from this study.

The specimens were at first examined macroscopically, using 10 per cent formal saline as a preservative. Three blocks were taken from each placenta from areas which looked abnormal (each block included a portion of normal looking placenta also). Two blocks were taken from the membranes and another two from the placental end of the umbilical cord. Sections were cut at 4 micron thickness and were stained with haematoxylin and eosin.

Results

A. Study group: taking 72 hours as the "action time" 24 cases (96 per cent) aborted successfully, the mean induction—abortion interval being 33.4 hours. One case aborted 92 hours after I.A.H.S. instillation. Antibiotics were used prophyllactically in all cases and none showed any clinical evidence of infection during induction-abortion interval.

Macroscopic Examination: The changes observed are shown in the table below (Table I).

TABLE I
The Changes Observed in the Study Group of Cases

Changes	No. of cases	Percentage
FOETAL SURFACE		
(i) Oedema of the membranes with or without fluid filled bullae distributed irregularly	25	100
(ii) Scattered areas (of various shape and size) of haemorrhage underneath the membrane	4	16
(iii) Umbilical cord	Looked normal	
MATERNAL SURFACE	Looked normal	
CUT SECTION		
(i) Scattered areas of haemorrhagic necrosis	6	24
(ii) Formation of red thrombus underneath the membranes	9	36
(iii) Areas of haemorrhagic necrosis and red thrombus	4	16

Thus, except oedema of the membranes no other constant change could be observed. Areas of damage were restricted close to the foetal surface of the placenta. Most of the placental tissue looked normal.

Microscopic Examination: The changes noted are shown in the table below (Table II).

The duration of gestation and induction-abortion interval failed to show any significant influence upon the histopathological changes found in this study.

B. Control group: Except intervillous space fibrin deposition (amount being within normal limit) in 4 (16 per cent) cases no other significant change could be found. Foci of calcification and small infarcts were noted in all cases.

Discussion

The exact mechanism causing the histological changes in the membranes, placentae and umbilical cords remain unknown. Patchy nature and variability of the changes in different specimens are still more difficult to explain. Hypertonic saline solution can reach the placenta by (1) diffusion through the membranes, (2) hypertonic saline is swallowed by the foetus and thereby reaches the placenta via the foetal circulation. But this is unlikely as the effect of hypertonic saline solution is to produce circulatory stasis (Meyers *et al*, 1974). Moreover, the amount of damage to the placenta is minimum and in some cases no damage to the placental tissue can be demonstrated. Hence, diffusion is the possibility. But considering the direction of fluid transport following I.A.H.S. the whole thing

TABLE II

The Microscopical Changes Observed in the Study Group of Cases

Changes	No. of cases	Percentage
Membranes		
(i) Oedema of the membranes. The tissues failed to take up stains properly	25	100
(ii) Degeneration of the cells of amniotic epithelium in the form of cytoplasmic vacuolation and nuclear pyknosis (Fig. 1)	12	48
Similar changes in the cells of chorion but less marked	3	12
The changes affecting the amniotic epithelium were patchy in distribution. Vacuolation, when present, appeared as clear spaces displacing the nuclei, desquamation of epithelial lining was absent		
(iii) Scattered areas of haemorrhage underneath the membranes	6	24
(iv) Subchorionic zones of red thrombosis (Fig. 2)	9	36
(v) Thrombosis in chorionic blood vessels	12	48
Chorionic villi (Fig. 3)		
(i) Degeneration of chorionic villi in form of eosinophilic coagulative necrosis or vacuolar degeneration of cytoplasm and nuclear pyknosis of syncytiotropoblasts. Such degeneration changes were patchy, affecting a segment of a villus. The villi showing such changes were located in the areas of haemorrhage and thrombosis. Rest looked normal	21	84
Intervillous space		
(i) Areas of red thrombosis	11	44
(ii) Leucocytic exudate (Fig. 4)	9	36
(iii) Haemorrhage	6	24
(iv) Fibrin deposition (Fig. 5)	4	16
(v) Calcification	4	16
Decidua		
Leucocytic infiltration	3	12
Umbilical cord		
Thrombosis in cord vessels	12	48

appears paradoxical. The direction of flow of water is likely to be from the maternal side to the amniotic cavity. This diffusion of water should continue until the induced hyper-osmolarity is reduced equal to that of the maternal serum. It may be that following I.A.H.S. instillation, while this particular process of diffusion from maternal side goes on, the immediate effect of the instilled hypertonic solution upon the amnion is degeneration of its cells at places and this degeneration is probably due to the chemical effect of hypertonic saline solution. This damage to amniotic epithelium possibly alters the permeability resulting in leakage of hypertonic saline through these areas to the deeper tissues. Thus it fails to cause any uniform damage to the placental tissue underlying the membranes. It is obvious that greater the distance from the sac, lesser is the salt concentration and minimum is the damage. This explains the scantiness of damage to the placental tissue and its location restricted mainly towards the foetal surface of the placentae. Oedema of the membranes is probably due to osmotic effect of hypertonic saline solution. It has been shown that following I.A.H.S. there is fall in maternal blood volume (Wagner, 1966). Leucocytic infiltration probably occurs as a reaction to degeneration and thrombosis is possibly due to (a) increased stickiness of R.B.C. to vessel wall (Meyers *et al*, 1974) (b) loss of water from plasma (Meyers *et al*, 1974) and (c) circulatory stasis.

In this study evidences of infection were absent both clinically and histopathologically. Christie *et al* (1966) had also similar observation and stated "it is improbable that the histological changes could have resulted from infection".

Despite much research the mechanism of onset of uterine contractions following I.A.H.S. to induce abortion in mid-pregnancy remains unknown. However, these cases provide suitable models for studying the mechanism of uterine contractions —a problem of great theoretical and clinical significance still remaining unsolved. Of the various theories Csapo's (1966-67) theory of withdrawal of progesterone block received wide acceptance. Csapo (1966-67) suggested that I.A.H.S. produces marked necrosis in the placenta and membranes. This removes the progesterone block in a mid-pregnancy uterus enabling the circulating oxytocin to stimulate myometrial contractions. This hypothesis was based mainly upon the following observations: (1) Necrotising asceptic placentitis (Bengtsson and Stormby, 1962) (2) Fall in progesterone concentration in peripheral venous blood (Klopper *et al*, 1966) (3) Decrease in urinary excretion of pregnandiol (Bengtsson and Stormby, 1962) (4) Significant prolongation of induction-abortion interval by oral treatment with gestagens (Bengtsson and Stormby, 1962).

But judging by the results of this study and many similar recent studies it can be said that intra-amniotic instillation of 20 per cent saline solution does not cause any gross damage to the membranes and placenta. The amount of necrosis seen in the placenta is minimum and most of the placenta looks histologically normal which has also been proved by immunofluoresent (Christie *et al*, 1966) and electron microscopic studies. Hence it is very difficult to believe that I.A.H.S. removes the progesterone block and thereby it initiates uterine contractions.

Although Csapo's (1966-67) findings of drop in blood progesterone level following I.A.H.S. instillation have been confirmed by other workers (Bengtsson and Stormby, 1962: Luukkainess, 1966-67),

yet many others have failed to demonstrate any such reduction. Klopper *et al* (1971) found that for most of the induction-abortion time, pregnandiol stayed at 80-90 per cent of the pre-induction levels. Short *et al* (1965) commented that "it has remarkably little effect upon the production of progesterone by the placenta. Holmdahl *et al* (1971) could not confirm any corelation between the decrease of progesterone level and the onset of abortion. As to the effects of gestagens, some (Galen *et al*, 1974; Ruttner, 1969; Wiest *et al*, 1973) claim that they delay abortion while others have failed to demonstrate such an effect. Thus, it appears that the target of action of hypertonic saline solution must be located somewhere else and the mechanism of its action may be a completely different one. Recently, it has been suggested that hypertonic saline does not induce abortion by acting on the tissues within the amniotic sac or in the foetal portion of the placenta but rather by acting upon the extra-amniotic tissues. The decidua which lies outside the foetal sac is probably the target. The release of prostaglandin F2 alpha into the amniotic fluid is probably caused by damage to the decidual cells, and diffusion of lysosomal enzymes into the decidual calls may be the triggering mechanism for the release of prostaglandins (Gustavii 1973).

Summary and Conclusion

This paper describes the results of histopathological study of membranes, placenta and umbilical cord in 25 cases following intra-amniotic instillation of 200 c.c. of 20 per cent saline solution for induction of abortion in mid-trimester of pregnancy. The results are compared with a control group of 25 cases where these structures were removed by abdominal hysterotomy. The duration of gestation in both the groups was identical. It has been shown that following such I.A.H.S. instillation only a small amount of placental tissue underlying the chorion is damaged. Affection of chorionic villi is mild, patchy and segmental in distribution. Most of the placental tissue appears normal histologically. Gross necrosis of the placenta upon which Csapo based his theory of "uterine defence mechanism" could not be confirmed from this study.

Judging by the results of this study it can be concluded that I.A.H.S. does not induce abortion by causing extensive placental damage. The site of its action appears to be somewhere else and consequently the mechanism too, may be a completely different one.

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See Figs. on Art Paper II-III