

HORMONAL AND CLINICAL STUDIES IN PATIENTS UNDERGOING TERMINATION OF MIDTRIMESTER PREGNANCY WITH DIFFERENT ABORTIFACIENTS

by

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Introduction

Since late sixties, when intra-amniotic injections of saline shot into prominence as an abortifacient, considerable amount of work poured in, bringing into light the possible hazards associated with its use. This led to renewed interest in Ethacridine Lactate an acridine dye derivative with uterotonic action. The last to join the race is prostaglandin, which have gained widespread acceptance, due to its unique ability to excite uterine action at any stage of gestation. We present here our observations on the serum hormonal levels and the prostaglandin level changes in amniotic fluid in abortions induced by these three abortifacients and discuss them in the light of our clinical experiences.

Material and Methods

Two hundred and sixty-two patients included in this study were between 13-20 weeks of gestation.

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Extra-Amniotic Saline (99 cases): A Foleys catheter No. 14 F for nulliparous and No. 16 F for multiparous was passed transcervically and the bulb was inflated with 20 ml. of distilled water to hold the catheter in place and prevent the leakage of the drug back into the vagina. 20 ml. of 20% saline was injected between the membrane and the myometrium through this catheter at an interval of 3 hours for maximum 9 doses or till the abortion, whichever was earlier. Once the os was dilated, the catheter was expelled and the process of abortion followed. Following the insertion of catheter one vaginal anti-septic suppository of chlorquinaldol was inserted each night till abortion.

Extra-Amniotic Ethacridine Lactate (68 cases): As mentioned before, a Foleys catheter was passed and the bulb kept inflated. 100 ml. of 0.1% ethacridine lactate with 300 mgm of spartein sulphate was injected through the Foleys catheter into the extra-amniotic space. 4 hours later, the catheter was withdrawn and the patient was observed. No vaginal anti-septic was administered.

In both the above procedures if the patient did not show progressive signs of

abortion, the trial was considered failure at the end of 48 hours.

Vaginal Suppository (98 cases): A single 3.0 mgm suppository of 15MePGF_{2a} me ester was inserted high up in the posterior fornix, following which patients were asked to lie on bed for 6 hours. 10 mgms of Diphenoxylate chloride was administered orally every 3 hours for 3 doses to counteract the hypermotility induced by prostaglandin.

The trial was considered a failure if the patient had not aborted at the end of 30 hours.

Details of Collection of Blood and Amniotic Fluid Samples: The samples of blood and amniotic fluid were collected at the following intervals: 0, 2, 6, 12, 18, 24, hours and one post abortal (blood sample). These sera samples and amniotic fluid were preserved in deep freeze at -15°C till they were analysed.

In order to reduce the baseline variability, the patients for hormonal studies were selected between gestation weeks of 14 to 17. The three hormones were measured by a specific and sensitive radio-immunoassay, the details of which have been

earlier described (Laumas *et al* 1974). Amniotic fluid prostaglandin was also estimated by radioimmunoassay.

Results

All the three abortifacients induced abortion successfully in large percentage of cases almost to the same extent between 82% to 87%. However, with prostaglandin patients aborted much quicker almost in about half the time of that required for either with saline or ethacridine lactate.

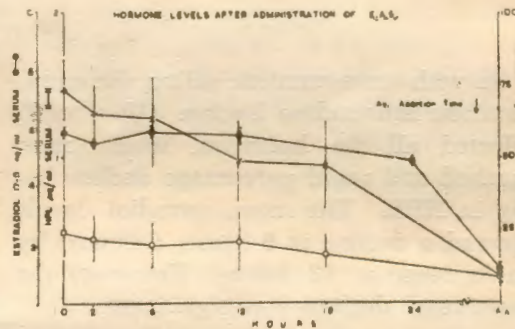


Fig. 1

Significant drops in serum estradiol 17 B, progesterone and HPL were observed with extra-amniotic saline. In three patients there was an increase in estradiol

TABLE I
Comparable Clinical Data of Extra-Amniotic Saline, Ethacridine Lactate and P.G. Suppositories

	Total cases	Success rate	Mean Abt. interval	Incomplete abortion
E. A. Saline	99	87%	30.8 hrs.	39.4%
E. A. Ethacridine Lactate	68	82%	29.5 hrs.	16.0%
P. G. Vaginal Suppository	145	86%	16.6 hrs.	16.75%

levels upto 12 hours, but the postabortal fall was significant.

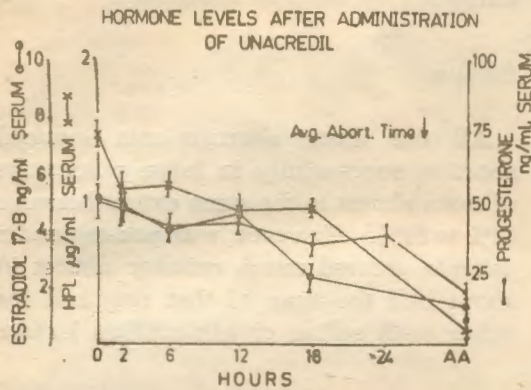


Fig. 2

As with extra-amniotic saline, the extra-amniotic Ethacridine Lactate (Unacredil) affected all the hormonal levels, most marked and rapid percentage decline being in HPL. The mean estradiol levels showed a decline at 6 hours, followed by an increase at 12 hours. However, the postabortal decline was significant.

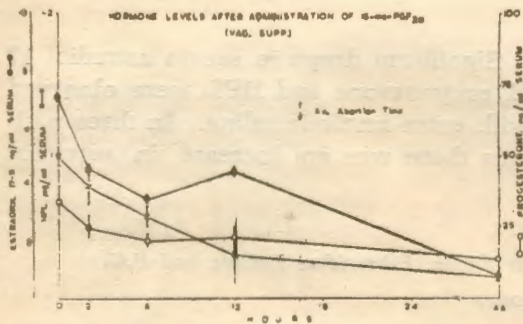


Fig. 3

Prostaglandin suppositories caused consistent decline in all the three hormonal levels which was most marked with estradiol and HPL. The serum hormonal decline was the quickest with suppositories.

Endogenous PGF_{2a} in amniotic fluid was analysed by radioimmunoassay (RIA). The levels varied between 190 to 3294 pg/ml at 0 hours and between 639 to 8718 pg/ml around the time of rupture of membranes in all the 3 abortifacient groups. The values showed increase in PG levels with the progress of abortion. The changes were faster, where patients aborted quicker. Where patients failed to abort, PG levels did not show any appreciable change.

However, the rise in PG levels were not consistent in all cases that aborted. Three patients started with higher levels of PG and the levels of PG declined during the process of abortion. Thus our findings were not conclusive.

Discussion

A single intra-amniotic injection of 20% saline though found successful in 85% of cases within 48 hours (Brenner, 1975) for termination of pregnancy, has been reported to have serious potential complications like coagulation (Brenner, 1975) disorders or hypernatremia. Recent works on the extra-ovular route has been believed to minimise the risk of accidental intravasation of a large volume of saline. We found it useful in approximately 88% of cases with an average abortion interval of 30.8 hrs. which is comparable to the result of most of the intra-amniotic (Brenner 1975) reports. Later, we have even terminated 482 pregnancies similarly and have not come across any problem.

Ethacridine lactate alone, though successful in large number of cases, has slow cumulative abortion rate and long abortion interval.

Although the Foley's catheter is retained longer in cases of extra-amniotic saline as compared to extra-amniotic ethacridine

lactate, it does not shorten the abortion interval. This might be due to a lesser uterotonic potency of saline.

Although the PG single suppository has a net success rate marginally lower as compared to the other method, they preclude the need of surgical expertise and make the procedure self administerable. Besides a low incidence of incomplete abortion, the other salient feature has been the short abortion interval.

It was earlier reported (Laumas *et al*, 1974) that single shot of intra-amniotic 200 ml. of 20% saline affects mainly the foetus, as reflected by a marked fall in oestradiol 17B, due to reduced availability of foetal precursors of oestrogens, while the progesterone and HPL levels were not much affected.

However, the multiple small doses of the 20% saline, but by extra-amniotic route affect the HPL levels also, in addition to oestradiol fairly early and significantly, implicating impairment of placental functions too. The same abortifacient through a different route might affect the foeto-placental biosynthesis differently.

The rather persistent rise in the serum oestradiol level in 3 patients of saline prior to abortion is difficult to explain. Could it be due to the stress induced increase in circulating maternal dehydroepiandrosterone sulphate precursors of adrenal origin?

As with extra-amniotic saline, the extra-amniotic ethacridine lactate affected all the hormonal levels, most marked being the oestradiol and HPL. The fluctuating levels may indicate episodic release of the hormone.

Prostaglandin 15 Methyl F_{2a} me ester suppositories caused consistent decline in all the three serum hormonal levels, which was once again sharper with

oestradiol and HPL. This is at variance with the findings of Fraser (1977) in which series both progesterone and HPL levels remained only marginally affected with the use of PGE. But that was with PGE₂. Could the difference in primary prostaglandin effect the hormonal pattern differently?

On the whole, the hormonal changes had set in fastest with prostaglandin, with extra-amniotic saline the last and with extra-amniotic ethacridine lactate in between. The mechanism of exciting uterine contractions with extra-amniotic procedure has been thought (Gustavi and Green 1972) to be mediated through damaging the decidual lysosomes and release of endogenous prostaglandins. Since it perhaps occurs late in the course of clinical events with saline and ethacridine lactate, the endocrine changes and effective uterine contractions tend to set in later thereby prolonging the abortion interval.

On the whole, the large fall in the oestradiol level in all the three abortifacients perhaps can be explained on the basis of the foetal death leading to decreased biosynthesis of the precursor. The next affected is HPL which is produced entirely by the placenta. The least affected is progesterone which is synthesised by the placenta and has a significant contribution from maternal cholesterol.

Fraser (1977) has shown that the hormonal changes occur much later with extra-amniotic procedure as compared to intra-amniotic, as with intra-amniotic procedures foetal death occurs early due to high intra-uterine pressures. The increasing anoxia as a result of induced increasing uterine contractions considerably impair the foeto-placental perfusion. With extra-amniotic procedures such changes set in very gradually and hence placental

perfusion continues for long. He further noticed that the hormonal changes were related to foetal death. However, there was no clear correlation between foetal death and the time of abortion. The rising values of amniotic fluid prostaglandin with progress of abortion perhaps indicate endogenous release of prostaglandin, as a determinant in the process of successful abortion. However, this observation need further investigation as the result has not been very considerable.

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