PLACENTAL FUNCTION FOLLOWING THE INTRA-AMNIOTIC INJECTION OF GLUCOSE

by

SUJATA MOHANTY,* M.S.

Several studies on the mode of action of intraamniotic injection of hypertenic solution demonstrated that hypertonic saline triggered the onset of uterine activity by affecting placental production of progesterone (Csapo 1961, 66; Bengtssone, Csapo 1962; Wiest *et al* 1966; Wiest 1967; Gensen *et al* 1968).

Placental damage in the form of separation of trophoblast from basement membrane with disruption of endoplasmic reticulum and swelling of mitochondria was substantiated by electron microscopic studies (Wynn 1965).

But conflicting view that there was no significant change in the progesterone production was put forward by Short *et al* (1965) and Klopper *et al* (1966).

The effect of glucose induction in the placental production of oestrogens has attracted relatively little attention.

Most of the studies were in urinary excretions of hormones which is not highly accurate as 24 hours urine collection is difficult to obtain. In view of this it was decided to investigate the placental functions of glucose induction by plasma oestriol essay and also by estimating heat stable alkaline phosphatase (HSAP) in blood. Changes in the blood glucose levels were also observed at the same time.

Material and Methods

Intra-amniotic injection of 50% glucose was being used for termination of pregnancy in Oxford. Ten patients were studied; their ages, parity and age of gestation were recored. The following clinical details were also noted:—

(1) Volume of amniotic fluid removed from the uterus and the volume of glucose injected.

(2) The time interval between the injection of glucose and abortion.

(3) The details of any oxytocin infusion employed.

(4) The total duration of stay in hospital.

An 18 gauge needle was inserted into the amniotic sac, midway between the symphysis pubis and umbilicus. The needle was held in position when liquor was aspirated and 50% glucose and I mega unit of benzyl penicillin were injected. The blood samples collected were as follows:—

(1) 2 cc. in a *fluride* tube for blood glucose.

(2) 4-5 cc. in a heparin tube for heat-stable alkaline phosphatase.

(3) 3 cc. of blood in a heparin tube for blood oestriol estimations.

Venous samples were taken at the following times for blood glucose and blood oestriol levels:—

(i) A fasting venous blood sample prior to the injection of intraamniotic destrose.

(ii) Blood samples were repeated at ½ hour, 1 hour, 2 hours and 3 hours following the intraamniotic dextrose, and there-

*Associate Professor of Obst. & Gynaecology S.C.B. Medical College, Cuttack.

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after fasting specimens were taken daily till 12-34 hours after the abortion.

Blood samples for heat stable alkaline phosphatase were taken in conjunction with fasting specimens until 24 hours after the abortion and presence and absence of uterine contractions were noted when specimens were taken.

Plasma oestriol was measured by the method (Corker and Naftolin, 1970) using competitive protein binding analysis. It was possible using the method to measure oestriol levels by taking only 3 cc. of blood. There were 5 collections in the first 24 hours.

Results

Details of the age of the patient and their parity and gestation times, together with volume of liquor removed, and glucose injected are given in Table I.

Fig. 1

at 72 hours, which is 36 hours after the the mean induction abortion interval.

A Spearman ranking test was applied to the mean oestriol values over a period of 0-72 hours, and this gave a R value (0.9761), which gave a P value = LL 0.01 which is statistically significant, (Spear-

TABLE I

Parameter Measured	Mean Value ± Standard Error
Number of patients	10
Parity	0.7 ± 0.3
Age (Years)	23.6 ± 2.3
Gestation (weeks)	17.5 ± 0.8
Volume of liq. removed (ml.)	227 ± 39
Volume of glucose (ml.) injected	300 ± 48
Induction abortion interval (hours) excluding 108 hours value	36.2 ± 3.2
Duration of stay in hospital (days)	3.9 ± 0.7

The serial values of plasma oestriols of each patient, except one, are recorded graphically in figure I. The gestational age of each patient has also been shown, and the arrow indicates the time of abortion. In the majority of cases the oestriol values show a significant downward trend.

The mean oestriol values of each serial estimation are shown in Table II and figure 2 with their mean standard errors. The falling levels of oestriol are evident, reaching the lowest mean value

TABLE II

Time	Oestriol Mean Value ± Standard Error of Mean
0 hour	2.51 ± 0.46
½ hour	2.68 ± 0.60
1 hour	2.31 ± 0.45
2 hours	1.83 ± 0.37
3 hours	1.58 ± 0.38
24 hours	1.31 ± 0.29
48 hours	0.98 ± 0.24
72 hours	0.68 ± 0.25

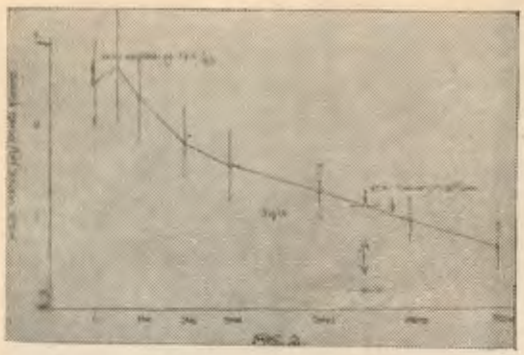

Fig. 2

man ranking formula ($P = \frac{1\text{-}6ED^2}{CN^2\text{-}I}$). The percentage of drop of oestriol at 3 hours of induction were correlated with induction abortion interval. Definite correlation was found. The coefficient of correlation, R was 0.72 giving a P value = 0.02, which is statistically significant. The regression equation is Y = I-06 x + 2.51 (where x is the percentage of oestriol drop, and y is the induction abortion interval).

The serial estimations of HSAP are plotted graphically in figure 3. The

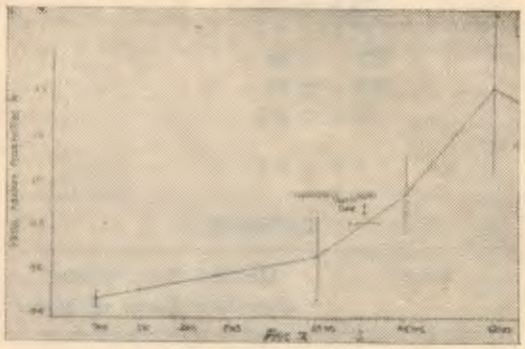

Fig. 3

arrow indicates the time of abortion. There are rising levels of HSAP in most of the patients 24 hours after induction.

The values of HSAP before induction and at 1st, 2nd and 3rd day after induction were correlated with those of oestriols. Significant correlation could be observed. The coefficient of correlation R was 0.86 giving a P value = 0.02, which is statistically significant. The regression equation was y = 1.67 x + 2.85) (where x is the plasma oestrid level and y is HSAP concentration).

The mean values of oestriol and the mean values of alkaline phosphatase are together plotted graphically in figure 4.

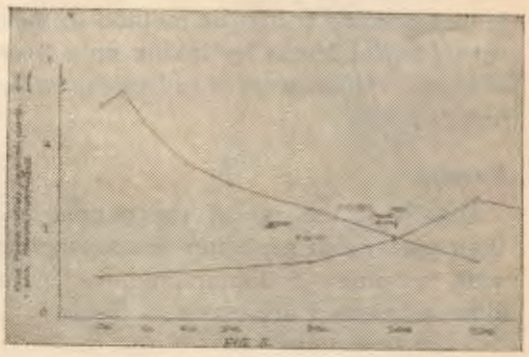

Fig. 4

The fall of oestriol and rise of HSAP are clearly visible, and both of them cross at the mean induction abortion interval.

Figure 5 shows serial values of plasma

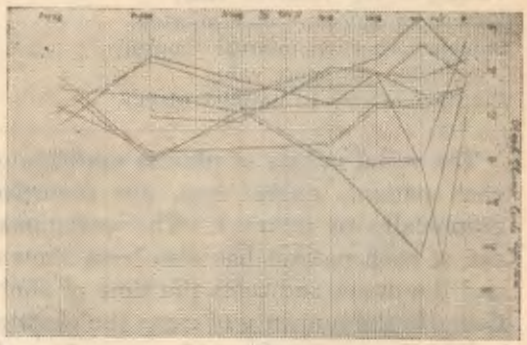

Fig. 5

glucose in each patient. There have been little changes in plasma glucose level after glucose instillation into the amniotic

cavity, except two cases, and one of them had a single high value which could have been due to contamination.

Discussion

The mean induction abortion time was shorter than that reported by Lewis *et al* (1969). This could be due to oxytocin infusion in 9 out of 10 cases.

Significant drop of oestriol and oestrone excretion in the urine after instillation of hypertonic solution was demonstrated by Timonent *et al* (1962), Klopper *et al* (1966).

Kerr *et al* (1966) studied urinary levels excretion and blood levels of sex steroid at 12 hourly interval after glucose induction. There was some fall in urinary excretion of oestrone and oestriol in first 12 hours. The blood levels of oestrone and oestriol were only temporarily reduced, and tended to recover by the time of abortion.

In the present study, significant fall in plasma oestriol after induction, and the maintenance of a downward trend throughout the post-induction period is in variance with that observed by Kerr *et al* (1966).

It is possible that the fall in plasma oestriol level is due to a change in the production of the steroid in the foeto-placental unit. Moreover, Kerr *et al* (1966) measured blood oestriol levels at 12 hourly intervals, and postabortion estimations were not done. The serial estimations of oestriol in the present study gave a consistent result.

The significant positive correlation of the percentage drop of oestriol at 3 hours, and induction abortion interval reflects the high sensitivity of oestriol assay employed.

HSAP originates in the placental trophoblast (Wislocki and Padykula 1961; Lobel *et al* 1962; Mc Master *et al* 1964). In the normal patient there is linear rise of serum HSAP as pregnancy progress towards term, and characteristic fall 3-6 days after delivery (Hunter 1969). Abnormal levels of HSAP occur in pregnancy when there is placental damage (Curzen and Morris 1965; Hunter 1969).

Rising HSAP values in most patients after induction and significant difference in value of HSAP between pre-induction level and the level at 48 hours may be due to placental damage by the intra-amniotic glucose. Though the serum levels of HSAP in early pregnancy are low, the present study shows that there is a significant place for HSAP estimations in assessing the placental function in the middle trimester. Hunter (1969) stressed the necessity of HSAP estimation in cases of bad obstetric history from the midtrimester.

Stamm and Watteville (1954) found enhanced urinary excretion of indigocarmine in cases of saline inductions supporting the functional impairment of amnion. Nolle (1948) and Kosowski (1949) made a similar observation using methylene blue, and indigocarmine following intra-amniotic injection of formalin.

Minimal changes in plasma glucose levels in the present study do not substantiate the functional impairment of amnion. The glucose remains inside the uterus, and there was little absorption of glucose into systemic circulation, except in 2 cases and in 1 where glucose might have been injected into the blood vessel inadvertently.

Most of the studies on placental functions are in late pregnancy. Besides determination of parameters of assessing placental function the clinical progress in pregnancy also helps to great extent in diagnosis of placental insufficiency. But

the cases with bad obstetric history or I.U.D. who have sad experience of repeated abortions and I.U.D., really pose a difficult problem and in them assessment of placental functions are highly necessary right from early weeks. From the present experience it is hoped that estimations of plasma oestriol and HSAP may be worthwile in investigating and treating the cases of placental insufficiency in the midtrimester.

Summary

Termination of pregnancy in middle trimester was attempted in 10 patients with intra-amniotic glucose. Serial estimations of plsma oestriol, heat stable alkaline phosphatase, and blood glucose were undertaken. Significant fall in oestriol level was observed, and HSAP showed a significant rise after induction. No significant alternation in plasma glucose level could be observed.

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