DIGOXIN LIKE IMMUNO-REACTIVE FACTOR IN PREGNANT SUBJECTS

By

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SUMMARY

Digoxin like immuno-reactive factor (DLIF) has been estimated in 38 patients in labour and cord blood levels of DLIF of their newborns were also simultaneously estimated. Twentyone out of 38 patients were normotensive and 17 were hypertensive by the criteria of 140/90 mm of Hg. The estimation of DLIF was carried out by RIA. The mean DLIF level in hypertensive mothers was 0.224 ng/ml while in the normotensive mother it was 0.202 ng/ml. The difference was not significant. The mean DLIF level of 0.283 ng/ml in the cord blood of infants of hypertensive mothers did not differ significantly from that of 0.315 ng/ml in the cord blood of the infants of normotensive mothers. But in the hypertensive group the mean DLIF level 0.291 ng/ml in 7 patients giving birth to infants of birth weight less than 2.5 kg was significantly higher than the mean maternal DLIF level of 0.149 ng/ml of 10 hypertensive patients giving birth to infants of more than 2.5 kg birth weight (t 15, 5% = 1.753).

It is concluded that serial longitudinal DLIF estimation in hypertensive patients may be of value in suspecting the failure of weight gain of foetus.

Introduction

It has been observed recently that some subjects not on digoxin therapy have a circulating substance which reacts with antibody to digoxin by Radio Immuno Assay (RIA). Goodlin (1987) reported DLIF in the serum of patients with renal failure. He also detected DLIF in pregnant women particularly with hypertension (Goodlin, 1986) It has been found in the cord blood and serum of newborn infants for 2-8 days (Ebara *et al*, 1986). The level of DLIF of patients in preterm labour before 34 weeks has been found to be the same as that of patients in labour at term (Goodlin, 1987).

Friedman *et al* (1987) reported on DLIF in fairly large amounts in the urine of pregnant subjects. These authors found the DLIF level to increase progressively during pregnancy. We now report on the results of our study comprising of 38 pregnant subjects and 38 newborns in whom the DLIF was estimated.

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Material and Methods

Thirtyeight patients admitted in Tata Main Hospital, Jamshedpur, India, were randomly selected for study. All of these patients were in labour. The newborn babies soon after delivery had their cord blood estimated for DLIF. The clinical details were not supplied to Research Laboratory where the DLIF was estimated. 3 ml of maternal venous blood and 3 ml of cord blood were collected and DLIF was estimated by RIA.

Seventeen out of these 38 patients had hypertension. A blood pressure record of 140/90 mmHg or more was accepted as hypertension. Twentyone normotensive patients were also included in the study. Five non-pregnant patients were investigated for DLIF for comparison. None of these five had any detectable level of digoxin like substance. All patients except two were at term between 38-40 weeks. Two patients delivered preterm at 30 and 34 weeks.

Assay Method

DLIF was measured by Radio Immuno Assay (Biotext Lab. Texas, USA). The lowest detectable level of digoxin that could be distinguished from the zero standard was 0.18 ng/ml at the 95% confidence limit. The cross reactivity with progesterone was 0.02 per cent as per the manufacturer's report.

Statistical analysis

In the hypertensive group two populations were separately scrutinised. Seven patients gave birth to infants weighing less than 2.5 Kg at birth and 10 patients gave birth to infants of more than 2.5 Kg birth weight. Since the sample sizes were small before performing the small sample t-test for both the samples of mother and child, it was necessary to ensure that standard deviation of the populations being compared did not differ significantly. With a view to this F-test for comparing variances was performed. For population 1 (mothers whose babies weight was 2.5 Kg) s value was 0.16580 and population 2 (mothers whose babies weight was 2.5 Kg) the s value was 0.12998. Computed statistic was 1.62770 and $F_{6,9}$, 5% = 3.37. So it could be concluded that the two populations did not have significantly different variances. Similarly for babies of the two populations the computed statistic was 2.72550, $F_{5,10}$, 5% = 3.37, so we may conclude that the two populations do not have significantly different variances. The final comparison of DLIF level of mothers giving birth to infants of more than 2.5 Kg birth weight with DLIF level of mothers giving birth to infants of less than 2.5 Kg birth weight was done by small sample t-test.

Results

Seventeen hypertensive patients had mean DLIF level of 0.224 ng/ml. The mean DLIF level of the 21 normotensive patients was 0.202 ng/ml. The difference was not significant. The mean cord blood level of DLIF in seventeen infants of hypertensive patients was 0.283 ng/ml while the cord blood level of DLIF of infants born to normotensive group showed a mean of 0.315 ng/ml. This difference was also not significant (Table I). Amongst the 17 hypertensive patients, the mean DLIF level of 10 patients giving birth to infants of 2.5 Kg birth weight or more was 0.149 ng/ml while the 7 mothers delivering infants of less

than 2.5 Kg birth weight had a mean DLIF level of 0.291 ng/ml. This difference was highly significant (t_{15}, 5% = 1.753) (Table II). The mean level of DLIF in the cord blood of infants of higher birth weight group was 0.249 ng/ml as compared to the DLIF level of 0.289 ng/ml of the infants in the lower birth weight group (Table III). This difference was also not significant. Further studies to assess the value of DLIF level as a marker in hypertensive pregnancy to predict and detect the poor weight gain of fetus-in-utero are warranted.

Discussion

Since Goodlin (1986) reported on DLIF, the interest on this subject has remained concentrated on several areas. Attempt has been made to explain the occurrence and level of DLIF in some abnormal conditions like hypertension and renal failure (Goodlin, 1987; Friedman *et al*, 1987). Even though the exact physiological process resulting in the formation and circulation of DLIF has not been clearly understood it is believed that this substance may be the expression of the adaptation mechanism in response to the abnormal conditions like hypertension and renal failure where control of plasma volume is of great importance. The inhibition of Na-K-ATPase by this substance leading to prevention of Na efflux from intra cellular to extracellular space (Goodlin, 1987; Friedman *et al*, 1987) may be the physiological mechanism to check the dangerous increase of plasma volume (Gonzalez *et al*, 1987). Pregnancy shows almost same DLIF levels as in salt loaded experimental animals (Friedman *et al*, 1987). On the other hand there is a possibility that

TABLE I

Mean DLIF Level in Ng/ml. of Patients According to Blood Pressure

	Hypertensive	Normotensive	Significanie test
Maternal	0.224 n=17	0.202 n=21	Not Significant
Cord Blood	0.283 n=17	0.315 n=21	Not Significant

TABLE II

Mean DLIF Level of Hypertensive Patients According to the Birth Weight of Infants

	Birth Wt. more than 2.5 kg.	Birth Wt. less than 2.5 kg.	Significance
Mean DLIF in ng/ml.	0.149 n=10	0.291 n=7	Highly significant t15.5% = 1.753

TABLE III

Mean DLIF Level in Cord Blood of Infants According to Birth Weight

	Birth Wt. more than 2.5 kg.	Birth Wt. less than 2.5 kg.	Significance
Mean DLIF in ng/ml.	0.249	0.289	Not significant

DLIF by increasing intracellular Na & Ca may predispose to arteriolar spasm and hypertension (Goodlin, 1987; Gonzalez *et al*, 1987). There has been discussion as to the question whether this substance can be used to monitor the advent of pathological conditions like pregnancy induced hypertension. As to the utility of DLIF as a marker for prediction of hypertension or for prognostication in established hypertension, some workers like Gusdon *et al* (1984) have found significant differences between the levels of DLIF in hypertensive patients as compared to normotensive patients. We have not found any significant difference between mean DLIF levels of hypertensive and normotensive patients. It should be remembered that the rise of DLIF in mother and newborn in hypertension takes place only in very severe degree of hypertension with possible target organ change (Goodlin, 1987). This may explain the lack of significant difference between the hypertensive and normotensive levels in our study as no case of severe hypertension with renal or cardiac change has been included. Gonzalez *et al* (1987) have failed to find any difference between mean DLIF level of 41 hypertensive patients as compared to mean DLIF level of same number of normotensive patients.

Relation of DLIF with foetal weight

Some workers have found a significant rise of DLIF in cord blood of preterm babies. Also there has been the suggestion that DLIF levels may vary according to foetal weight (Gonzalez *et al*, 1987). In our study we have not found any significance in mean DLIF levels of infants of low birth weight as compared to normal birth weight in the normotensive group of mothers. But we observed a significant difference in the mean DLIF level of hypertensive mothers giving birth to infants of low birth weight (less than 2.5 Kg) as compared to the mean DLIF level of hypertensive mothers giving birth to infants of birth weight above 2.5 Kg. This observation raises a very interesting question as to whether a serial study of DLIF as a marker for monitoring foetal weight in established case of hypertension in pregnancy would be a justifiable approach in management. Only a longitudinal study on pregnant patients with hypertension may answer this question which appears to be relevant at this stage of research.

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