Plasma pancreatic glucagon and insulin : glucagon ratio at birth

Recent evidence (Girard, Bal, and Assan, 1972) indicates that pancreatic glucagon may play an important role in the mobilization of hepatic glycogen in the neonatal rat by activating phosphorylase. Glucagon has been described as a hormone which is secreted at times of intracellular glucose need; and Unger (1971) has emphasized the importance of considering, in fasting and post-prandial states, not the absolute concentrations of insulin and glucagon, but the ratio of the two, arguing that it is the net balance of insulin and glucagon which determines the cellular uptake or production of glucose. In the present study we have measured plasma pancreatic glucagon levels in mother and infant at birth and related these to the insulin levels at this time.

Methods

All 30 infants studied were normal term vertex vaginal deliveries and were of normal size for their gestational age. The range of birthweights was 2740 to 4230 g, and of gestational ages 37 to 42 weeks. 14 of the mothers were receiving intravenous infusions containing hexose at the time of delivery. At delivery, blood, 10 ml, was collected from a maternal arm vein, the umbilical artery, and umbilical vein, and placed in chilled tubes containing 20 mg EDTA and 4300 U Kallikrein inhibitor (Trasylol) in 0.6 ml. Plasma was separated within 30 minutes by centrifugation and stored at -20°C until analysed for glucose, insulin, and glucagon, as described previously (Milner *et al.*, 1972b). Plasma was thawed once only. In the expression of results no correction was made for the dilution factor (approximately 1.12) caused by the anticoagulant.

Results

The mean ($\pm$ SE) plasma concentrations of glucose, insulin, and glucagon in the maternal and umbilical blood specimens are shown in the Table.

TABLE

Mean ($\pm$ SE) plasma concentration of glucose, insulin, and glucagon at birth

Source of blood	Glucose (mg/100 ml)	Insulin ($\mu\text{U/ml}$)	Glucagon (pg/ml)
Maternal vein (30)	99 $\pm$ 5	30 $\pm$ 3	177 $\pm$ 9
Umbilical artery (30)	72 $\pm$ 5	19 $\pm$ 3	162 $\pm$ 10
Umbilical vein (30)	80 $\pm$ 4	20 $\pm$ 3	174 $\pm$ 13

Note: Number of observations in parentheses.

In mothers receiving hexose infusions at the time of delivery (14) the mean ($\pm$ SE) plasma concentration of glucose was 99 ± 7 mg/100 ml, insulin 32 ± 6 $\mu\text{U/ml}$, glucagon 183 ± 17 pg/ml. These levels were similar to those occurring in mothers who did not have an i.v. infusion, permitting pooling of the two groups for further analysis.

The 't' test for paired data was used for statistical comparison of plasma concentrations of metabolite or hormones. The mean ($\pm$ SE) difference between maternal and umbilical venous plasma glucose was 22 ± 3 mg/100 ml, and between umbilical vein and artery 8 ± 1 mg/100 ml. The mean ($\pm$ SE) maternal venous plasma insulin level was 10 ± 3 $\mu\text{U/ml}$ higher than that in the umbilical vein. There was no significant difference between any pair of samples in plasma glucagon levels.

Analyses of linear correlation were performed between plasma glucose and plasma insulin, glucagon and the insulin : glucagon ratio. Maternal plasma glucose and insulin levels were significantly correlated ($r = 0.411$ $P < 0.05$) as were umbilical venous plasma glucose and insulin levels ($r = 0.512$ $P < 0.01$). Plasma glucagon levels were not significantly correlated with insulin or glucose levels in any of the three blood samples. The insulin : glucagon ratio correlated significantly with plasma glucose concentration in maternal venous blood ($r = 0.447$ $P < 0.01$), umbilical venous blood ($r = 0.473$ $P < 0.01$), and umbilical arterial blood ($r = 0.389$ $P < 0.05$).

Discussion

Since the human placenta is impermeable to glucagon (Adam *et al.*, 1972), the umbilical and maternal plasma glucagon measured in this study were of fetal and maternal pancreatic origin, respectively. This interpretation is supported by the finding that the mean umbilical arterial and venous plasma glucagon levels were very similar, whereas the mean umbilical venous plasma glucose concentration was higher than that in the artery due to the transplacental passage of glucose from mother to fetus. The similarity of the maternal and fetal mean plasma glucagon levels defy further comment in the absence of information on the control of glucagon secretion at the time of birth. The levels are low in comparison to those found in fasting normal adults and may indicate a basal plasma concentration in the fed state since plasma glucose did not correlate with glucagon in mother or fetus but did with plasma insulin.

The present results, taken in conjunction with those reported earlier (Fekete *et al.*, 1972), agree with the observation that plasma glucagon levels

rise after birth (Johnston and Bloom, 1973; Luyckx *et al.*, 1972). A finding that at present remains unexplained is the fact that infants suffering from haemolytic disease of the newborn have higher plasma glucagon levels than those in comparable normal infants (Milner, Fekete, and Assan, 1972a).

The degree of correlation of plasma glucose and the insulin : glucagon ratio was no better than that of glucose and insulin, indicating that glucagon was a stable denominator in the insulin : glucagon ratio, and suggesting that the concept of the ratio does not have biological meaning at this time in life. This is not surprising for plasma pancreatic glucagon levels are not affected by glucose infusions in erythroblastotic infants (Milner *et al.*, 1972b) or normal infants (Luyckx *et al.*, 1973). It will be of interest to determine the time at which the pancreatic α -cell becomes sensitive to changes in extracellular glucose concentration and to determine the validity of the insulin : glucagon ratio at this time.

Summary

At birth the mean plasma pancreatic glucagon concentration of maternal peripheral venous blood, umbilical arterial and venous blood was similar, and varied between 160 and 180 pg/ml in 30 normal term deliveries. Plasma insulin levels and the insulin : glucagon ratio correlated with plasma glucose in each of the three samples. Plasma glucagon did not correlate with either plasma glucose or insulin. No evidence was found for biological significance of the insulin : glucagon ratio in mother or infant at the time of birth.

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