INSULIN CONTENT OF FETAL BLOOD IN MATERNAL DIABETES

(UDC 616.379-008.64-056.716-06:616.379-008.61-053.1-07:616.154-07-616.379-008.61-053.1-07:616.154-07]-02:616.379-008.64-056.716)

L. L. Liberman

Department of Endocrinology (Scientific Supervisor—Prof. V. G. Baranov, Active Member, Academy of Medical Sciences, USSR), Institute of Obstetrics and Gynecology (Dir.—Prof. M. A. Petrov-Maslakov), Academy of Medical Sciences, USSR, Leningrad

Presented by V. G. Baranov, Active Member, Academy of Medical Sciences, USSR
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 58, No. 9, pp. 46-49, September, 1964
Original article submitted June 15, 1963

One of the characteristic manifestations of diabetes in females during pregnancy is high fetus weight; this symptom is customarily attributed to hyperfunctioning of the fetal insular apparatus. Such hyperfunctioning may be the result of hyperglycemia in the mother and fetus. However, high fetus weight and hyperplasia of the fetal insular apparatus are also noted in prediabetic mothers, when there is still no hyperglycemia [6]. This may result from intensified formation of an insulin antagonist, which passes through the placenta to the fetus, in the prediabetic state [8].

At present there are no direct data on the insulin content of human fetal blood in maternal diabetes. The results obtained in experiments involving alloxan diabetes in rabbits [3] cannot be applied to humans, in whom diabetes is usually not the result of absolute insulin deficiency [4].

We studied the insulin content of the fetal blood in maternal diabetes in order to clarify the following problems: 1) whether or not there is a correlation between the severity of the maternal diabetes and hyperglycemia on the one hand and the insulin content of the fetal blood on the other; 2) whether or not maternal diabetes influences the insulin level of the fetal blood; 3) whether or not there is any difference in the insulin activity of the maternal and fetal blood in maternal diabetes.

EXPERIMENTAL METHOD

The insulin activity of serum extracts was determined from the absorption of glucose by isolated rat epididymal fat and expressed in milligrams of glucose absorbed from the serum extract per g of adipose tissue over a 3 h incubation in excess of the quantity absorbed from a buffered solution [1]. All the insulin was extracted from the serum with the strong sulfocationite SDV-3 in its hydrogenous form [2]. For the experiment we took 5 ml of serum and processed it so as to obtain 10 ml of eluate (diluting it by a factor of 2). Blood was drawn from the umbilical cord immediately after it was cut and simultaneously from one of the mother's veins. A number of control determinations showed that the insulin activity of retroplacental blood is equal to that of the mother's venous peripheral blood.

This study was made on 10 diabetes patients; in one the diabetes was compensated by diet, while the others received insulin. Two females received insulin only during pregnancy, three had an unchanged insulin requirement during pregnancy, two had a reduced demand, and two had an elevated demand. All the infants were live births and no complications occurred during the postnatal period.

EXPERIMENTAL RESULTS

The table presents the results of a study of 10 diabetes patient and 20 healthy females. The insulin activity of the blood was somewhat higher in the diabetes patients than in the healthy individuals ($P < 0.05$). The insulin activity of the fetal blood was greater in mothers with diabetes than in healthy mothers ($P < 0.02$). While the insulin activity of the fetal blood did not exceed 2.70 mg/g over 3 h for the healthy females, it was higher in 6 of

Insulin Activity of Maternal and Fetal Blood in Maternal Diabetes

Persons examined	Age (years)	Duration of diabetes (years)	Treatment	Daily insulin dose (units)	General appraisal of compensation for diabetes during pregnancy	Last insulin dose before delivery (units)	Interval between last insulin injection and delivery (h)	Weight of fetal (g)	Blood sugar content in samples (mg-%)		Insulin activity (mg/g) over 3h	
									Mother	Fetal	Mother	Fetal
Z. N	34	1	Diet		Satisfactory	–	–	4550	140	118	1.52	3.19
S. E.	32	1	Insulin	40	The same	20	24	4550	174	153	5.30	9.90
Sh. D	27	3	"	36	" "	8	5	3250	156	121	2.82	2.47
P. S.	32	1	"	52	Unsatisfactory	12	4	4750	150	124	3.78	5.25
Ch. N.	30	14	"	60	The same	36	10	3550	140	100	1.90	3.21
K. G.	31	11	"	76	" "	48	8	3000	187	169	4.64	3.44
S. M.	42	1	"	36	" "	16	60	3200	296	209	2.58	2.73
B. O.	35	3	"	56	Satisfactory	36	13	4000	98	79	0.67	1.53
K. B.	37	7	"	72	The same	16	4	2900	342	184	1.59	1.58
K. E.	33	11	"	114	" "	4	7	4800	368	256	2.24	2.32
						Mean M ± m					2.70 ± 0.46	3.56 ± 0.75
						Mean M ± m for 20 healthy females					1.68 ± 0.14	1.65 ± 0.12

the 10 children of the diabetic mothers. In not a single one of the healthy females were there reliable differences in the insulin activity of the maternal and fetal blood. Such a difference was noted in six of the cases of maternal diabetes; in five of them the insulin activity of the maternal blood was higher than that of the fetal blood. In the one case where it was higher in the maternal blood we were dealing with a patient who had received 48 units of insulin 8 h before delivery and in whom the action of insulin ordinarily lasted longer than this.

The insulin activity of the fetus was correlated neither with the severity of the mother's diabetes nor with her insulin demand or its change during pregnancy. Moreover, a very high insulin activity was noted in the children of mothers suffering from moderately severe and mild diabetes, including the one patient who did not require insulin therapy. In a number of patients with high fetal-blood insulin activity diabetes was so well compensated that repeated blood sugar tests over a 1-day period did not show hyperglycemia. The complete lack of any correlation ($r = -0.05$) between the sugar content and insulin activity of the fetal blood and between these indices in the mother ($r = -0.006$) is extremely interesting. At the same time, there was a strong positive correlation between the insulin activity of the fetus' blood and its weight ($r = +0.444$; $P = 0.05$) and between the insulin activity of the maternal and fetal blood ($r = +0.789$; $P < 0.001$).

The data obtained indicate that the insulin activity of the blood is somewhat higher in mothers with diabetes than in healthy females, which is in complete accord with our data and those in the literature on the insulin activity of young diabetes patients. In this work we were interested in the insulin activity of the fetal blood. It was found that this activity increases reliably when the mother has diabetes; maternal diabetes consequently leads to hyperfunctioning of the fetal insular apparatus. We are naturally faced with the problem of whether we can attribute this to hyperglycemia in the mother, since the blood sugar content of the fetus develops in parallel with that of the mother, although at a slightly lower level [7]. The absence of any correlation between the severity of the diabetes, the extent to which it is compensated, and the blood sugar level on the one hand and the insulin activity of the fetal blood on the other, indicates that the elevated value of the latter results both from maternal hyperglycemia and apparently some other disorder which develops in diabetes. Considering the peculiarities observed and the well-known fact that prediabetic mothers deliver children with insular hyperplasia, we are inclined to believe that transmission of an insulin antagonist through the placenta occurs in maternal diabetes [8].

We found no reports in the literature regarding determination of the insular activity of umbilical blood in maternal diabetes. Studies made 3-5 h after delivery revealed the same activity as in the children of healthy females, but a substantially more marked insular reaction to administration of glucose was noted [5]. In this connection we

may assume that in maternal diabetes the fetal insular apparatus not only functions intensively (as may be seen from the high insular activity of the blood with a normal blood sugar content), but also has an elevated reactivity to the physiological stimulus presented by glucose.

The problem of the passage of insulin through the placenta is also of great importance. As was pointed out, the insulin activity of the maternal and fetal blood differed materially in six cases. This bears a great deal of weight in refuting hypotheses regarding any substantial passage of insulin through the placenta.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
