FREE AND BOUND INSULIN IN PREGNANCY AND LABOR

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Until recently, investigations had been conducted only on the total insulin content in the blood during pregnancy; an increase in its level was established in this case [10, 12]. In our investigations conducted during labor, in which insulin was isolated from the blood on ion exchange resins, followed by testing for insulin activity according to the glucose uptake of the rat epididymal fat pad, the average insulin activity was equal to 1.680±0.145 mg/g in 3 h [3]; these indices do not differ reliably from the indices of the insulin activity of the blood in nonpregnant women. In the same work, in contrast to previous data obtained by the method of glucose uptake by the rat diaphragm [6, 11], no difference could be detected in the insulin activity of the blood of the mother and fetus.

Recently it was established that insulin exists in the blood in 2 forms—free (active with respect to all insulin-sensitive tissues) and bound (active with respect to adipose but not muscle tissue) [5].

In this work we attempted to determine which form of insulin—free or bound—varies in content during pregnancy Moreover, we were interested in the question of whether the content of the insulin fractions differs in the blood of the mother and fetus.

METHOD

The insulin activity of the blood was determined according to the glucose uptake by the rat epididymal fat pad and was expressed in milligrams of glucose supplementarily absorbed from an extract of blood serum in comparison with the glucose uptake of another sample of tissue from a buffered solution in 3 h of incubation, converted to 100 mg of tissue weight (Δ of glucose in mg/g in 3 h) [1].

The separation of free and bound insulin in the blood was performed by the method that we developed [2]. The blood serum (5 ml) was first passed through the resin IR-120 (grain size 16-50 mesh, divinylbenzene content in the resin 6-8%) in the sodium form; this resin adsorbed only bound insulin. Then the effluent was passed through the resin SDV-3 (grain size 50-100 mesh, coefficient of swelling of the resin 3) in the hydrogen form; this resin sorbed free insulin. The method made it possible to obtain eluates of the same ionic composition, practically devoid of all other proteins. Blood was taken for investigation from the ulnar vein of fasting pregnant women during the period of pregnancy from 24-36 weeks. During labor, blood was obtained from the ulnar vein of the mother immediately after the birth of the fetus; blood was taken from the umbilical vein at the same time. All the women examined had a normal sugar curve during pregnancy.

RESULTS

As the data presented in Table 1 show, in pregnant women the content of bound insulin is the same as in nonpregnant women of child-bearing age ($P > 0.5$), but the free insulin level is reliably increased ($P < 0.02$). At the moment of labor, the amount of bound insulin (Table 2) is reliably decreased ($P < 0.01$), while the free insulin content is

TABLE 1. Free and Bound Insulin Content in the Blood During Normal Pregnancy

Last name of patient	Insulin activity (in Δ glucose mg/g in 3 h)	
	Free insulin	Bound insulin
Aks.	3.89	4.03
Il'.	5.30	3.73
Smi.	3.31	4.41
Kosh.	6.75	4.22
Leb.	3.46	6.22
Ras.	3.71	3.94
Kva.	3.12	3.26
Svi.	3.42	3.15
Vas.	1.19	1.37
Koz.	2.87	2.13
Ski.	1.42	1.47
Kri.	3.50	4.47
But.	2.85	2.82
Dom.	1.08	0.87
Man.	1.63	1.94
Kut.	1.54	1.68
Kon.	0	0.98
Tom.	0	3.00
Average (M± m)	2.724± 0.410	2.983± 0.342
Average in nonpregnant women (M± m)	1.391± 0.282	3.162± 0.267

somewha reduced in comparison with that in pregnant women, but remains higher than the indices obtained in nonpregnant women; however, these differences are statistically unreliable ($P<0.1$). In the fetus, the free insulin content in the blood is the same as in the blood of the mother, while the bound insulin level is higher, although this difference is also statistically unreliable ($P> 0.2$). Noteworthy is the fact that, just as in our previous work on the determination of the summary insulin activity [3], the activity of the individual insulin fractions of the blood of the fetus did not differ on the average from the activity of these fractions in the blood of adult nonpregnant women.

In our investigation, an increased insulin content was established in the blood during pregnancy, on account of an increase in the most active free fraction. This may be evidence of a true increase in the function of the insular apparatus. Of course, this question could not be answered in a determination of the summary insulin activity, since the increase in the latter may be explained by a change in the bonding of insulin by proteins, as is observed with respect to thyroxin and cortisone. During pregnancy, the decomposition of insulin is increased on account of the high insulinase activity of the placenta [9]. It is clear that the rather high insulin level in the blood may be maintained in the presence of its intensified decomposition only on account of an increase in the function of the insular apparatus. Indirect evidence of this is the frequent appearance of previously latent insular insufficiency during pregnancy [7, 8].

During labor, the insulin activity of the blood of the mother did not differ on the average from the activity of the blood of the fetus. However, during labor the hormonal changes are so great that we cannot now explain the existence of large individual differences in the content of individual fractions of insulin in the blood of the mother and fetus. The purpose of these investigations was to determine whether a correlation exists between he content of each insulin fraction in the blood of the mother and in the fetus. Statistical treatment of the material (calculation of the correlation coefficient and its reliability according to the Fisher formula for small numbers $t = Z\sqrt{n-3}$ [4] showed that with respect to bound insulin, a positive correlation exists between its level in the blood of the mother and that of the fetus ($r = +0.440$) at the limit of reliability ($t = 2.16$; $P = 0.05$). In the ratio of the free insulin, the correlation even proved negative ($r = 0.404$), but unreliable ($t = 1.94$;

TABLE 2. Free and Bound Insulin Content in the Blood of the Mother and Fetus During Labor

Last name of patient	Insulin activity (in Δ glucose in mg in 3 h)			
	Blood of mother		Blood of umbilical vein	
	Free insulin	Bound insulin	Free insulin	Bound insulin
Vas.	2,00	1,01	1.23	0,77
Nech.	2,48	2.42	2,11	1,76
Sol.	3,34	1.27	1.81	4,25
Mikh.	0,71	3.68	2,95	2.44
Kon.	1,22	2.83	2.43	5,92
Kol.	1,32	2.85	6,43	4.57
Il'.	2,97	1.07	1,55	2,70
Ser.	4.17	0	0	2,42
Ose.	0,80	0.57	2.66	1.75
Ale.	2,33	0.15	1,58	3,17
Ber.	0,70	1,14	0,69	0,76
Iva.	1,34	0,22	0,92	0,66
Average (M± m)	1,948±0,313	1.434±0,352	2,030±0.470	2,597±0,476

P> 0.05). The absence of a positive correlation between the free insulin content in the blood of the mother and fetus is evidence for the theory of almost complete impermeability of the placenta for insulin [9]. This is also indicated by observations of a number of subjects (Sol., Kon., Kol., Ser., Ose., Ale.), in which extremely substantial differences were noted between the content of individual fractions of insulin in the blood of the mother and fetus.

SUMMARY

The plasma insulin was fractionated on strong sulfocationites: IR-120 in sodium form and SDV-3 in hydrogen form; the insulin bio-assay was carried out according to the glucose uptake of rat epididymal fat pad. The results were expressed as extra glucose uptake in mg/g/3 h. In 12 nonpregnant fasting females of child-bearing age the activity of free insulin was 1.391± 0.282 and that of bound insulin-3,162± 2.267 mg/g/3 h. In 18 women at 24-36 weeks of pregnancy the values were 2.724± 0.410 and 2.983± 0.342 mg/g/3h respectively. At the time of delivery in 12 women the content of free insulin in maternal venous blood was 9.948± 0.313 and that of bound insulin - 1.434± 0.352; in the blood of umbilical vein the values were 2.030± 0.470 and 2.597± 0.476 mg/g/3 h respectively. The increased level of free insulin in pregnancy is significant (P< 0.02). There was a positive correlation of bound insulin in pregnancy is significant (P< 0.02). There was a positive correlation of bound insulin levels in maternal and fetal blood (r = 0.440; P = 0.05) and a negative and not significant correlation of free insulin levels (r = 0.404; P> 0.05). The latter fact points to the insulin impermeability of placenta.

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