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Relationship between placental perfusion and endocrine parameters of pregnants in cases of intrauterine growth retardation

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The placental perfusion index (PPI) measured 1–27 days before delivery was compared with maternal urinary and serum oestriol (OT) and serum human chorial somatomammotropine (HCS) levels in the mothers of 24 newborns born with intrauterine growth retardation. No significant correlation between placental perfusion and the above endocrine parameters was found. Placental perfusion was not reduced in every case of intrauterine growth retardation. Mathematical analysis has shown that hit accuracy can be increased by the use of more endocrine parameters in pathological pregnancy.

Measurement of certain endocrine parameters is useful in the prenatal diagnosis of placental insufficiency and in monitoring pathological pregnancies. Determination of urinary steroid excretion offers information about the fetoplacental unit and the maternal serum level of some proteohormones may supply information concerning the condition of the placenta. In our department the daily excretion of oestriol and of maternal serum oestriol levels (OT) and of maternal serum human chorial somatomammotropin (HCS) is a routine measurement. Earlier we have shown that serum HCS and OT levels were lower in pregnant mothers who subsequently gave birth to babies with intrauterine growth retardation.

Measurement of placental perfusion is another method which has proved useful in prenatal diagnosis of intrauterine malnutrition. Decreased placental perfusion has been incriminated for placental insufficiency and regarded as the first sign of incipient placental failure [1, 2].

In the present study we have attempted to clarify whether there was a relationship between changes in endocrine parameters and in placental perfusion in pregnant mothers giving birth to malnourished babies.

Materials and Methods

A retrospective comparison of maternal serum and urinary oestriol excretion, and serum HCS with placental perfusion values was performed in mothers of babies born with intrauterine growth retardation between 1 June, 1981, and 31 May, 1982, in whom placental perfusion had been determined 1–27 days prior to delivery. Only cases with an exactly known gestational age were included in the study.

Among the 24 cases, in 8 mothers gestosis of variable severity was the cause of the intrauterine malnutrition, one mother had diabetes mellitus. Fifteen mothers were free of symptoms and complaints. Grading of the severity of gestosis was carried out by the gestosis index recommended by the World Health Organization.

All retarded babies had a birth weight lower than the 10 percentile value for the corresponding gestational age and neonatological examination revealed physical signs of intrauterine malnutrition in every case.

In additional 12 cases similar measurements were carried out because of suspected intrauterine malnutrition but subsequent intrauterine development was normal and all babies proved to be eutrophic at birth: these babies served as control.

Placental perfusion was measured by a method using $^{113}InCl_3$ [3]. A relative number, the placental perfusion index (PPI), can be calculated from the difference between the activity of radiation deriving from the placenta and from the placenta-free myometrium. In our experience values of PPI lower than 2 indicate a restricted placental perfusion and values below 1 point to a situation threatening fetal life.

Oestriol was determined in 24 hour urine samples by our own method uniting the method of Ittrich modified by Kecskés et al and the method of Brown [4]. Serum oestriol was measured by the oestriol (total) RIA kit of Amersham Laboratories, serum HCS by hCS/hPL test RIA kits of Pharmacia Phadebas^R. The results were expressed in SI units.

Evaluation of the serum values was carried out by standard values indicated by the producing firm, for urinary OT we used our own standard value system. Values falling below the 2 SD limit below the mean were regarded as abnormal.

Additional tests (CTG, amnioscopy, repeated echography, amniocentesis for L/S determination, etc.) were done whenever indicated.

Results

Results are summarized in six tables. Tables I to III demonstrate the three groups of the material. Group 1 comprises dysmature cases without maternal toxaemia, Group 2 dysmature cases with maternal toxaemia and Group 3 is the eutrophic control group. In each table birth weight, gestational age at the time of measurement, the value of PPI and of the endocrine parameters obtained at the time of perfusion measurements (serum HCS and OT, daily excretion of OT) are indicated.

In the group comprising 16 dysmature babies whose mothers had no toxaemia, less than 28 days elapsed between determination of endocrine parameters and placental perfusion on the one hand and birth on the other hand. PPI values below 1 were found in one case, values below 2 in four cases. Urinary oestriol excretion was low in 10, serum oestriol in 3 and serum HCS in 8 cases.

In the group of 8 dysmature babies whose mother had toxaemia determinations were carried out also within 28 days prior to birth. Again, a PPI value lower than 1 was encountered in one case, values lower than 2 in four additional cases. Abnormally low oestriol excretion was found in five cases, low serum oestriol in one case while a low HCS value in four cases.

In the control group (12 cases) 1–63 days elapsed between the measurements and delivery. PPI was higher than 2 in all cases, only one case each

TABLE I

Endocrine parameters in dysmatures without maternal toxaemia (Group 1)

Serial number of case	Weight at birth g	Gestational age at time of measurement week	Interval between measurement and delivery day	PPI	HCS µg/ml	SeOT ng/ml	Urinary OT µmol/l
1	1200	33	+ 6	0.98	0.5*	88	24*
2	2500	35	+27	3.02	2.4*	102	52
3	1990	39	+ 6	3.99	2.5*	150	55
4	2500	39	+ 6	3.91	2.0*	28*	35*
5	1970	36	+10	2.25	5.0	136	30*
6	2600	38	+ 1	3.65	2.7*	76	18*
7	1100	37	+ 7	1.41	3.3*	136	25*
8	2550	38	+11	1.71	5.1	147	32*
9	2400	36	+25	3.17	5.0	153	42*
10	2600	38	+ 7	2.07	5.5	55*	62
11	1810	35	+10	1.42	4.4	94	40
12	1850	37	+ 5	2.13	4.0*	176	88
13	2470	37	+17	2.48	3.8*	166	37*
14	2500	38	+10	3.01	4.7	66*	44*
15	2650	34	+24	1.88	4.2	75	23*
16	2600	39	+ 4	3.71	6.2	104	96

* abnormally low value

TABLE II

Endocrine parameters in dysmatures with maternal toxaemia

Serial number of case	Weight at birth g	Gestational age at time of measurement week	Interval between measurement and delivery day	PPI	HCS µg/ml	SeOT ng/ml	Urinary OT µmol/l
17	2550	40	+ 1	2.89	3.8*	84	25*
18	1530	32	+15	0.97	4.2	168	28*
19	2300	34	+18	1.77	5.2	220	47
20	1910	32	+17	1.83	5.0	40	26*
21	2000	34	+27	2.04	2.1*	36*	45
22	1750	33	+ 3	2.23	3.8	62	40
23	2250	36	+ 7	1.19	3.7*	62	40*
24	1280	35	+ 5	1.47	1.2*	85	20*

* abnormally low value

had a low oestriol excretion or a low serum HCS.

In order to establish whether changes in placental perfusion and the hormonal parameters were of the same direction and order, correlation coefficients were calculated. Table IV demonstrates that PPI was not cor-

TABLE III

Endocrine parameters in eutrophic newborns

Serial number of case	Weight at birth g	Gestational age at time of measurement week	Interval between measurement and delivery day	PPI	HCS µg/ml	SeOT ng/ml	Urinary OT µmol/l
1	3600	34	+27	2.72	7.6	—	40
2	3300	35	+ 5	2.57	5.4	—	62
3	3500	38	+12	3.15	8.0	196	94
4	3000	36	+17	2.54	4.0	200	67
5	3950	38	+ 6	3.04	5.2	175	35*
6	3250	35	+34	3.80	5.0	90	63
7	3000	31	+63	2.80	6.6	247	42
8	3100	33	+36	2.95	6.5	67	45
9	2300	34	+11	4.45	4.9	260	49
10	2700	36	+ 7	3.07	7.4	210	84
11	3350	33	+15	3.45	5.1	158	51
12	4100	40	+ 1	3.07	5.6*	143	66

* abnormally low value

TABLE IV

Correlation coefficients between PPI and hormonal values in the three groups

	PPI/HCS	PPI/SeOT	PPI/Urinary OT
Group 1 (n=16)	0.302	0.179	0.342
Group 2 (n=8)	0.459	0.469	0.263
Group 3 (n=12)	0.176	0.019	0.013

The r-values did not significantly differ from zero in any of the cases

TABLE V

Percentage of pathologically low hormone values within each group

	HCS	SeOT	Urinary OT
Group 1 (n=16)	50	18.8	62.5
Group 2 (n=8)	50	12.5	62.5
Group 3 (n=12)	8	0	8

TABLE VI

Distribution according to number of abnormal hormonal findings in the individual patients

	Number of patients with			
	0	1	2	3
	abnormal hormonal findings			
Group 1 (n=16)	2	8	5	1
Group 2 (n=8)	2	1	5	0
Group 3 (n=12)	10	2	0	0

Group 1/Group 2: $\chi^2 = 4.248$ $p < 0.05$
Group 2/Group 3: $\chi^2 = 10.280$ $p < 0.001$
Group 1/Group 3: $\chi^2 = 14.680$ $p < 0.001$
0: all the three values are normal
1: one pathologic value
2: two pathologic values
3: all the three values are pathologic

related with any of the hormone values, i.e., placental perfusion showed no relationship to fetoplacental hormone production or to placental proteohormone levels. Table V shows the percentage of abnormal hormone values within each group. It can be seen that the highest percentage of an abnormal finding was 62.5% low oestriol excretion in the groups with intrauterine growth retardation.

Comparison of the number of cases with simultaneous occurrence of more than one abnormal hormonal finding is represented in Table VI. The χ^2-test revealed a significant difference within each pair of groups in this respect. A much higher percentage of abnormal findings was encountered in dysmaturity as compared to the normal group. Similarly, dysmaturity caused by toxaemia was accompanied by more abnormal hormonal findings than dysmaturity without maternal toxaemia.

All three hormone values were simultaneously low in a single case, in Case 4 of Group 1. In this patient the PPI value was completely normal (3.91). Subsequently a newborn of 2500 g was born during the 39th gestational week, the baby was healthy.

Among the 24 dysmature fetuses 2 intrauterine deaths occurred. In both cases there was a pathologically low PPI value (0.98 and 1.19, respectively) and urinary oestriol excretion and serum HCS were low. In these cases, serum oestriol was normal.

DISCUSSION

We found no significant correlation between placental perfusion and placental endocrine parameters. In certain cases changes in PPI are thus independent of maternal oestriol and HCS changes. The two methods

furnish information on two different aspects of prenatal growth.

It has been anticipated that all kinds of placental insufficiency are introduced by a decrease in placental perfusion, thus in every case a placental hypoperfusion would be the cause of dysmaturity [1, 2, 5]. Our data showed that placental perfusion is not invariably low in cases of intrauterine growth retardation. This may mean that intrauterine malnutrition cannot fully be ascribed to restricted placental perfusion, and other factors must also be taken into consideration.

The level of hormones produced by the placenta is rather independent of placental perfusion, in other words, the quantity of compounds produced by the syncytiotrophoblasts and released into the maternal circulation is not a simple function of placental perfusion. Hormone values may be normal in cases of markedly depressed placental perfusion, or, conversely, normal placental perfusion may be accompanied by low hormone values; of course, both may be simultaneously low. The result is an intrauterine growth retardation in both cases. In some instances the malnutrition may be ascribed to low placental perfusion but normal hormone production in the placenta shows that damage to placental tissue is not irreversible for a long time. In other cases placental insufficiency reflected in abnormal production of surface enzymes may remain unaccompanied by abnormal placental perfusion [6].

Mathematical analysis shows that the more the hormonal parameters examined, the higher the probability of detecting pathological conditions is. In practice, at least urinary excretion of oestriol and maternal serum HCS have to be measured in pregnancies which seem to be pathological.

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