AMNIOTIC FLUID REVERSE TRIIODOTHYRONINE IN NORMAL AND HIGH RISK PREGNANCIES

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SUMMARY

The Authors have dosed by radioimmunoassay the rT_3 concentrations in the amniotic fluid of 12 normal pregnant women and of 25 women with high risk pregnancies at the same period of gestation.

The average of the rT_3 concentrations in the amniotic fluid of pregnant women affected by diabetes mellitus, EPH gestosis and with foetal growth retardation, are not different from those found in the control group.

In the patients affected by Rh isoimmunization, the rT_3 levels are remarkably higher than those found in the control group.

The rT_3 highest levels found in the amniotic fluid of pregnant women affected by Rh isoimmunization, could be due:

1) to a decreased transformation of rT_3 in rT_2 for an accentuated alteration of the sulphidril groups;

2) to a need of blocking the pathway's conversion of T_4 in T_3 (hormone with great catabolic effect) in these foetuses already presenting an accentuated catabolism for the chronic haemolitic anemy and for the severe hepatic alterations.

Triiodothyronine is not produced only by the thyroid, but particularly by the peripheral metabolism of thyroxine (T_4).

In fact, it has been demonstrated that the highest percentage of T_4 (around 85%) is metabolized through monodeiodination ([1]).

By using sensible radioimmunoassay it has been possible to demonstrate that T_4 is peripherally monodeiodinate not only into 3,5′,3′–triiodothyronine, but also into 3,3′,5′–triidothyronine (reverse T_3).

A small part of reverse T_3 is produced at thyroid level too.

T_3 and in particular rT_3 are then metabolized, always through a mechanism of monodeiodination, into 3,5′–diiodothyronine (3,3′–T_2) and 3′,5′–T_2.

3,3′–T_2 is then monodeiodinate into 3′–T_1. Both the last compounds are finally metabolized into T_0 (fig. 1).

In 1973, Sullivan has described a selective lack of T_3 with normal levels of blood and tissutal T_4, in patients who died from various systemic diseases.

Low blood levels of T_3 with normal levels of T_4 are present in many other conditions; besides low blood levels of T_3 and high concentrations of rT_3 are contemporaneously present.

Dauforth ([14]) has observed a decrease in T_3 blood levels and an increase in rT_3 blood levels, in case of prolonged fasting.

Similar results were found in cases of proteinic malnutrition ([7]), of nervous anorexy ([15]), of cirrhosis of liver ([5]), of diabetes out of balance ([17]), of febrile conditions ([19]) and after administration of some drugs as dexamethazone ([4]) and propanolol ([20]).

Chopra ([10]) admits that the amniotic fluid presents low concentrations of T_4 and traces of T_3 and TSH not dosable by the actual RIA methods.

Chopra ([10]) and Burman ([3]) assert that rT_3 concentrations in the foetal blood and in the amniotic fluid, are higher than those of the maternal blood; in fact this is evident in the amniotic fluid from the 15th week of gestation on.

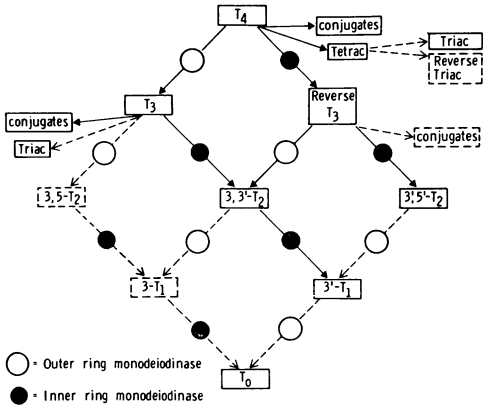

Fig. 1. — A schematic view of a possible cascade of metabolism of T_4. Dashed lines mark those areas where data on the operation of a pathway or the existance of a compound are either not available or insufficient. From Chopra I.J. - Pathways of metabolism of thyroid hormones. In: Recent progress in hormone research. Ed. Greep R.O., Acad. Press, London, 1978, p. 521.

The rT_3 concentration in the amniotic fluid decreases with the evolution of pregnancy; anyhow the values at the end of pregnancy are almost the double of those present in the maternal blood.

An interesting data derives from the finding that T_3 concentrations in the amniotic fluid are very low for the duration of pregnancy.

Recent studies ([11]) have demonstrated that in human, the rT_3 blood levels in the neonate, till the second week of life, are higher than those of the adult.

Since the rT_3 present in the amniotic fluid seems to be prevalently of foetal origin, and since the rT_3 blood levels are high even in non pregnant subjects affected by systemic diseases, we have studied the rT_3 behaviour in the amniotic fluid of high risk pregnant women.

MATERIAL AND METHODS

We have examined 12 normal pregnant women between the 35th and 40th week of amenorrhea and 25 high risk pregnant women at the same period of pregnancy.

The pregnancy's pathology examined included:

EPH gestosis	(6 cases);
Diabetes mellitus	(5 cases);
Foetal growth retardation	(4 cases);
Erythroblastosis foetalis	(10 cases).

The amniotic fluid was drawn by amniocentesis, previous echography, or in course of caesarean section.

The amniotic fluid drawn was immediately centrifugated and stored at −20 °C.

The rT_3 was dosed by radioimmunoassay using Biodata kits.

RESULTS

The rT_3 concentrations (average + SD) present in the amniotic fluid of the 12 women with normal pregnancy between the 32th and 40th week of amenorrhea, range between 55 and 130 ng/dl (90+4).

The rT_3 values, in the patients affected by diabetes mellitus, range between 74 and 110 ng/dl (92+2).

The rT_3 levels in the patients affected by EPH gestosis are between 62 and 125 ng/dl (93+4).

In the patients with foetal growth retardation the rT_3 concentrations vary from 80 to 135 ng/dl (67+5).

As one can notice, the average of the rT_3 concentrations in the amniotic fluid of the pregnant women belonging to the three categories, are not different from those found in the control group at the same stage of pregnancy (tab. 1; fig. 2).

In the 10 patients affected by erithroblastosis foetalis the rT_3 levels in the amniotic fluid are remarkably higher than those found in the amniotic fluid of the control group (181+40) (tab. 1; fig. 2).

DISCUSSION

The difference between the high levels of rT_3 and the low ones of T_3, present in the foetal blood and in the amniotic fluid, is due both to the decreased conversion of T_4 in T_3 and to the increased conversion of T_4 in rT_3 in the foetus.

Table 1. — *Levels of reverse T_3 in amniotic fluid ($AFrT_3$) in women with normal and high risk pegnancies.*

Pregnancies	No. of patients	Gestational age (weeks)	$AFrT_3$ (ng/dl)
Normal pregnancy	12	32-40	55-130
Pregnancy toxemia and hypertensive disease . .	6	32-40	62-125
Diabetes mellitus	5	32-40	74-110
Fetal growth retardation	4	32-40	80-135
Erythroblastosis fetalis	10	32-40	95-280

Wu ([20]) has found that liver and kidney homogenate of foetal lamb, have a lower capacity of deiodination of T_4 in T_3 of the foetal tissues is not due to the absence of the enzyme monodeiodinating the external ring of T_4, but is due to the alteration of the SH–sulphidril groups.

In fact, administration of substances protecting the SH groups, determines, in the foetal tissues, a capacity identical to that of adults, of converting T_4 in T_3.

According to Chopra ([12]), the integrity of the sulphidril groups, would be also important for the conversion of the rT_3 in rT_2.

Hence, the non availability of sulphidril groups would simultaneously reduce the T_3 production and the rT_3 catabolism.

T_3 has a high catabolic action while T_4 has a minimal catabolic power: its catabolic effects can be greatly due to its conversion in T_3 in the peripheral tissues.

rT_3 and its metabolites have no catabolic action.

In most of the cases where the conversion of T_4 in T_3 is inhibited, the tissutal catabolism is superactive, this is true in the calorie deprivations, in the systemic diseases, after pharmacologic doses of dexamethasone.

This does not happen in the foetus, whose metabolism tends toward a predominant anabolism. Anyhow in all these conditions, catabolism is cleary, undesirable.

The inhibition of the T_4 conversion in T_3 and the rT_3 increase could be a defensive reaction of the organism to the undesirable catabolic action.

The rT_3 highest levels found by us in the amniotic fluid of pregnant women affected by Rh isoimmunization in comparison with the levels found in the amniotic fluid of normal pregnant women at the same week of gestation, could be due:

1) to a decreased rT_3 transformation in rT_2 for a more accentuated alteration of the sulphidril groups;

2) to a greater need of blocking the conversion pathway of T_4 in T_3 (hormone with high catabolic effect) in these foetuses having an already accentuated catabolism for the chronic haemolitic anemy and for the severe hepatic alterations.

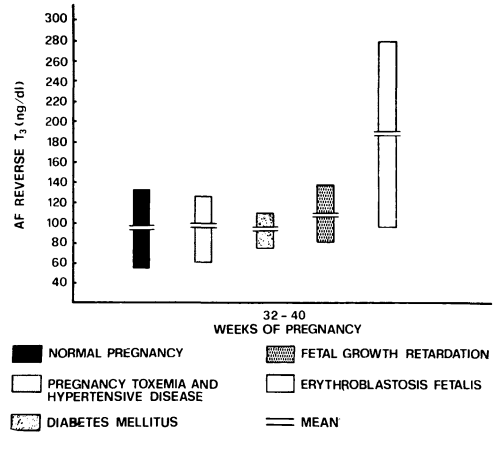

Fig. 2. — Levels of reverse T_3 in amniotic fluid ($AFrT_3$) in normal and high risk pregnancies.

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