EFFECTS OF HYPOTHYROIDISM ON PREGNANCY OF RATS

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Summary: Adult female rats of approximately same age and weight were grouped and thyroidectomized before pregnancy and at different stages of gestation. While studying their pregnancy performances, it was observed that there was a significant ($P<0.05$) increase in the length of gestation in thyroidectomized animals as compared to intact controls. This is possibly due to the smaller litter size. The litter size and foetal weights were significantly ($P<0.01$) lower than the controls and were inversely proportional to the duration of the hypothyroidism during pregnancy. Hypothyroidism did not affect the implantation. The mammary gland growth was significantly ($P<0.01$) reduced in all the experimental groups. Hypothyroidism during pregnancy hardly affected the adrenal weight but significantly ($P<0.01$) decreased the ovarian weight possibly due to the disturbance in hypophysialgonadal axis.

Key words: hypothyroidism gestation litter size litter weight mammary gland

INTRODUCTION

Ample evidence is available to show that normal reproductive functions both in male and female depend to an appreciable extent on thyroid activity. The length of gestation was found to be usually prolonged if hypothyroidism is initiated before pregnancy (1) which may be possibly due to the defect in the ovarian functions and with possible effects on the act of parturition (2) or a reduced litter size (3). It has also been reported that thyroidectomized rats when made pregnant had foetuses with cleft-palate, hare-lip and occular defects. Hypothyroidism has been found not to interfere with the implantation (4,5) even though resorptions resulted in very small conceptus. Maternal hypothyroidism was considered to be the cause of reduced size and foetal weight (6,7) but Greenberg (8) advanced that, although thyroid hormone is necessary for some aspects of prenatal tissue differentiation, it is not required for foetal growth in uterus, Beacuse of such conflicting reports on the role of thyroid in the maintenance of normal pregnancy, this experiment was designed to study the effect of hy othyroidism before and during pregnancy on the various physical parameters associated with it like length of gestation, litter size, litter weight and resorptions along with adrenal, ovarian and mammary gland weights.

MATERIALS AND METHODS

Sixty adult female rats of I.V.R.I. strain of 180-200 *gm* weight and approximately of same age were maintained with food and water *ad libitum*. The animals were thyroidectomized surgically (9), one group before they were exposed to adult males and the other at different stages of pregnancy corresponding to the periods of zygote transport (3rd-4th day), implantation (6th-7th day) and various stages of foetal growth (8th, 10th and 13th days of gestation). Thyroidectomized (Thx) animals were given 1% calcium gluconate

solution to combat the effects of partial parathyroidectomy. Intact control and sham-thyroidectomized animals were maintained similarly except the addition of calcium gluconate to their drinking water. The sham-thyroidectomy involved all the surgical manipulation without disturbing the thyro-parathyroid structures. To make the necessary observations, foetuses, uterus and other tissues were collected from individual animals immediately after parturition or after sacrificing the one where the parturition was incomplete and difficult.

RESULTS

Intact and Sham-thyroidectomized pregnant animals had gestation periods of about 21 days (Table I). But the other groups, either thyroidectomized before or at different stages of pregnancy had significantly longer ($P<0.05$) gestation periods. Average foetal weights of intact and sham-thyroidectomized animals were 6.24 ± 0.3 and 5.6 ± 0.1 gm respectively having no significant difference between them, but the other groups had foetal weights significantly ($P<0.01$) lower than the controls.

Total number of foetuses born to intact and sham-thyroidectomized animals were 8.2 ± 0.7 and 8.5 ± 0.5 respectively without any dead or resorption. On the other hand hypothyroid groups produced significantly ($P<0.01$) smaller litters with significant numbers of deads and resorptions, the smallest size being 2.1 ± 0.1 foetuses born to animals thyroidectomized before mating (Table I).

TABLE I : Effect of thyroidectomy on the length of gestation, weight and total number of foetuses born and foetuses resorbed.

Group No.	Treatment	No. of animals	Length of gestation (days)	Weight of foetuses (g)	Number of feetuses born			Number foetuses resorbed
					Live	Dead	Total	
1	Pregnant (intact controls)	8	21.0±0.4	6.2±0.3	8.2±0.7	—	8.2±0.7	
2	Pregnant Sham Thyroidectomized (Thx)	8	21.5±0.5	5.6±0.1	8.5±0.5	—	8.5±0.5	—
3	Thx first and then made pregnant	6	24.0±0.6	3.5±0.1	2.1±0.1	—	2.1±0.1	1.50±0.1
4	Pregnant Thx on 3rd day of gestation	8	24.0±0.5	3.7±0.1	—	4.1±0.1	4.1±0.1	2.2±0.1
5	Pregnant Thx on 6th day of gestation	8	23.3±0.3	3.9±0.1	6.0±0.2	—	6.0±0.2	3.0±0.1
6	Pregnant Thx on 8th day of gestation	8	23.6±0.2	4.2±0.3	4.2±0.7	2.6±0.7	6.2±1.6	2.1±0.1
7	Pregnant Thx on 10th day of gestation	7	23.0±0.3	4.6±0.0	2.0±1.0	3.0±1.1	4.3±1.2	1.6±0.7
8	Pregnant Thx on 13th day of gestation	7	24.0±0.4	4.0±0.0	1.1±0.2	3.7±0.3	5.0±0.7	2.6±0.1

Each figure is mean±standard error.
Student's t' test has been used for test of sfgnificance.

Length of gestation:	1	vs	3,4,5,6,7,8	(individually)	$P<0.05$
Weight of foetuses:	1	vs	3,4,5,6,7,8,	(individually)	$P<0.01$
Total number of foetuses:	1	vs	3,4,7,8	(individually)	$P<0.01$
Live foetus:	1	vs	3,6,7,8	(individually)	$P<0.01$

Adrenal and ovarian weights of intact pregnant animals were 47.5±2.5 *mg* and 126.0±7.6 *mg* respectively (Table II). Hypothyroidism showed no effect on the adrenal weights of pregnancy, but the ovarian weights of animals thyroidectomized at different stages of gestation were significantly ($P<0.01$) lower than the controls (Table II). The mammary gland weights of intact and sham - thyroidectomized animals were 10.4±0.1 and 9.8±0.1 *gm* respectively. All the hypothyroid groups had significantly ($P<0.01$) lower weights than the control (Table II).

TABLE II : Effect of thyroidectomy on the weights of adrenals ovaries and mammary glands.

Group No.	*Treatment*	*Number of animals*	*Initial body weight (g)*	*Final body weight (g)*	*Weight of adrenals (mg)*	*Weight of ovaries (mg)*	*Weight of mammary glands (g)*
1	Pregnant (intact control)	8	182	193	47.5±2.5	126.0±7.6	10.4±0.1
2	Pregnant Sham Thyroidectomized (Thx)	8	196	212	51.4±1.8	123.7±7.1	9.8±0.1
3	Thx first and then made pregnant	6	206	220	40.5±2.8	46.0±6.1	6.1±0.1
4	Pregnant Thx on 3rd day of gestation	8	185	210	41.5±3.5	70.5±6.9	5.6±0.2
5	Pregnant Thx on 6th day of gestation	8	198	206	41.2±3.6	113.5±6.5	6.6±0.1
6	Pregnant Thx on 8th day of gestation	8	200	207	38.2±3.9	73.0±8.6	5.0±0.8
7	Pregnant Thx on 10th day of gestation	7	180	192	50.5±1.7	81.0±1.6	4.9±0.1
8	Pregnant Thx on 13th day of gestation	7	187	198	51.6±3.8	52.6±4.5	3.1±0.4

Each figure is mean ±standard error
Student's t' test has been used or test of significance.

Weight of adrenals: 1 vs all other (indvidually) no significance difference.

Weight of ovaries: 1 vs 3,4,6,7,8 (individually) $P<0.01$

Weight of mammary glands: 1 vs 3,4,5,6,7,8 (individually) $P<0.01$

DISCUSSION

Thyroid function undergoes complex changes during pregnancy due to the altered hormonal and metabolic demands at that time. On the other hand gestational processes are very much affected by changes in thyroid function as the latter is closely related to fertility(10). It was observed that most of the pregnant animals made hypothyroid for different durations during gestation had significantly smaller ovaries indicating an impairment in the mechanism of feed-back control of gonadotrophins (3,11,14). Although in many species of mammals, the sex steroids elaborated by the fectoplacental unit contribute, to a great extent, in the maintenance and outcome of normal pregnancy, the ovaries

(with the corpus lutea) play indispensible role in the rat (15). The ovaries of hypothyroid rats are usually atrophied (16) and of lower weight and function (17): but in some animals large cystic ovaries have also been reported (18). The present findings in thyroidectomized groups agree with these reports. It is also interesting to note here that all the hypothyroid groups having decreased ovarian weight had smaller litters with lesser number of live fetuses born as compared to intact pregnant animals indicating the importance of ovarian function for both survival and growth of fetuses in utero (15) in rats which might have been derranged by hypothyroidism during gestation. The adrenal weights remained unaffected by thyroidectomy similar to earlier findings (12). There was significant decrease in mammary gland weights of all hypothyroid mothers, the most affected group being the one which was thyroidectomized on the 13th day of gestation. This was possibly due to the absence of circulating thyroid hormone (13). This effect on mammary gland growth is of importance since post-parturient milk secretion and thereby the growth and development of newborn depend entirely on it.

All animals rendered hypothyroid for different lengths of time during gestation, had resorptions with total number of foetuses significantly lower, 56.5% of which were dead. The smaller litter was not due to failure in implantation in thyroid deficiency since mothers made hypothyroid after implantation also bore smaller litters. It is interesting to find that the group, thyroidectomized at preimplantation period (3rd day) had also a smaller litter size and all were dead. This spells out the fact that thyroid hormone is necessary even before implantation for the survival of the implanted embryos to full term. It is found also that the weights of the foetuses born to hypothyroid mothers were significantly lower those of intact ones, the weight of foetuses being inversely proportional to the length of hypothyroidism during gestation. The cause of resporptions and lesser foetal weights resulted possibly from the altered uterine metabolism that created an unsuitable environment for adequate growth and development of foetuses. The increase in length of gestation and difficulty in parturition observed with the hypothyroid mothers may be consequent to the smaller litter size, which gives insufficient mechanical stimulus for initiating uterine contraction or decreased prostaglandin production under altered conditions of uterine metabolism, as it has been thought that thyroid hormone facilitated parturition and required to be present in the later part of gestation (2).

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REFERENCES

1. Lucas, J.J., G. E. Brunstad and S.H. Fowler. The relationship of altered thyroid activity to various reproductive phenomena in gilts., *J. Endocrinol.*, **17** : 54-61, 1958.
2. Hoar, R.M., R.W. Goy and W.C. Young. Loci of action of thyroid hormone on the reproduction in the female guinae pig. *Endocrinol.*, **60** : 337-348, 1957.

3. Bruce, H.M. and H.A. Sloviter. Effect of destruction of thyroid tissue by radio-active iodine on reproduction in mice. *J. Endocrinol.*, **15** : 72-82, 1957.

4. Krohn, P.L. and H.C. White. The effect of hypothyroidism on reproduction in the female albino rat. *J. Endocrinol.* **6** : 375-385, 1950.

5. Currie, R. and R. Schultz. Effect of induced alterations of thyroid function in pregnancy. In proceedings, 3rd Midwest Conference on Thyroid, University of Missouri, U.S.A. pp 114-115, 1967.

6. Parrot, M.W., M.E. Jonston and P.W. Durbin. The effect of thyroid and parathyroid deficiency on reproduction in the rat. *Endocrinol.*, **67** : 467-483, 1960.

7. Stempack, G. Maternal hypothyroidism and its effect on foetal development. *Endocrinol.*, **70** : 444-445, 1962.

8. Greenberg, H.A. In "Hand Book of Physiology" Ed. by Roy O. Greep (Endocrinology), Section 7. III : 377, 1974.

9. Ducommune, P. Note Sur La thyroidectomie chirurgicale chez le rat adulte, *Revue Can Biol.*, **21** : 171-173, 1962.

10. Burrow, G.N. Thyroid and parathyroid function in pregnancy. In Endocrinology of Pregnancy. Ed. by F. Fuchs and A. Klopper, 2nd Edition, Harper and Row Publishers, N.Y., pp 246, 1977.

11. Chu, J.P. and S.S. You. The role of thyroid gland and estrogen in the regulation of gonadotrophic activity of the anterior pituitary. *J. Endocrinol.*, **14** : 115-124, 1944.

12. Heap, R.B., J.S. Perry and J.R.G. Challis. Hand book of Physiology. Ed. by Roy O. Greep. (Endocrinology)) Section 7 : **II** : 217, 1973.

13. Schmidt, G.H. and W.H. Moger. Effect of Thyroactive materials upon mammary gland growth and lactation in rats. *Endocrinol.*, **81** : 14-18, 1967.

14. Florsheim, W.H., P. Rudko, N.L. Corcorran and R.E. Bodfish. On the mechanism of the inhibition of compensatory ovarian hypertrophy by goitrogens. *Endocrinol.*, **81** : 771-777, 1967.

15. Frazer, J.F.D. and D.P. Alexander. The effect of spaying in the pregnant rat. *J. Physiol.*, **124** : 36-37 P, 1954.

16. Leathem, J.H. Hormonal influence on the gonadotrophin sensitivity of hypothyroid rat ovary. *Anat. Rec.*, **131** : 487-489, 1958.

17. Schreiber, V., Z.Z. Kmentova and V. Zbazek. The blocking effect of thyroidectomy on adrenal and ovarian hypertrophy produced by aminoglutethimide in rats. *J. Endocrinol.*, **42** : 349-350, 1968.

18. Bray, G.A. and H.S. Jacobs. In Hand book of Physiology. Ed. by Roy. O. Greep (Endocrinology) Section 7: **III** : 425, 1974.