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Hypervitaminosis-A, Causes Hypothyroidism in Mouse

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Abstract:
Thyroid gland is unique among vertebrate endocrine glands is that it stores its secretory products i.e. thyroid hormone. The thyroid influence reproduction, growth and differentiation.
Retinol Palmitate (RP) is known for its effects on differentiation and morphogenesis during vertebrate development, as it is important for reproduction development and growth, hyper and hypo-vitaminosis- A both provoke epithelial pathologies in animal and human being. So a critical value of RP is required in vivo for the maintenance of normal architecture and function of many body tissues
Thyroid gland is unique among vertebrate endocrine glands is that it stores its secretory products i.e. thyroid hormone. The thyroid influence reproduction, growth and differentiation.
The group of adult mouse was treated 4 IU/ day concentration of RP by intubations for 7 days. This constituted the treated group. A similar number of mice were considered as controlled group, and were not given any RP treatment. The animal were observed for their growth, behaviour and weight, during the period of treatment

1. *On 8th day of the serum thyroxin level analysis was done to both treated as well as controlled mice.In treated case hypothyroidism was seen.*
2. *The studies concluded that RP treatment results in a reduced activity of thyroid follicles i.e. reduced synthesis of thyroxin.*

Keywords: *Hypothyroidism / Retinol palmitate / Thyyroxin / mouse)*

1. Introduction

Vitamin A and its derivatives called retinoids play an important role in maintaining normal growth, regulating proliferation and differentiation of epithelial tissues, and maintaining visual and reproductive functions. Hypovitaminosis –A, leads to night blindness. (Goodman,et al.,1983,184)

Recently many other functions of vitamin-A have been added during the vertebrate development. These includes its role in morphogenesis, maintenance the healthy epithelium, regeneration of limbs (Wolf` 1984). McCollum and Davis (1973) were the first to report that frog tadpoles fed with vitamin-A rich diet showed delayed metamorphosis. Nazi and Sabena (1972) carried out systematic studies on vitamin-A induced delayed metamorphosis in buffo tadpoles and caused many histological changes in the thyroid. Such effects were consistent in other anurans (Sharma and Nazi, 1983)

Farhangi,et.al., (2012) investigated the impact of vitamin A supplementation on thyroid function in obese women.

In Rats Vitamin a Repletion with Concurrent Vitamin A and Iodine Deficiency affects Pituitary TSHβ Gene Expression and Reduces Thyroid Hyperstimulation and Thyroid Size (Biebinger, 2007).

Vitamin A supplementation in human beings has been promoted by much health organization to control night blindness and other diseases related to vision (Food and Nutritional Board, 1980).

It happens quite often due to ignorance that vitamin A supplementation is given overdosing in the young children, which some time leads to death. Even slightly higher dose than the required may cause damage to certain vital organ including the endocrine glands (Drill, 1943). Goswami and Choudhury(1999) established interrelationship between retinoids and thyroxin hormone. This study was carried out to find how RP, ester form of vitamin-A, influence thyroid gland of mouse when given in excess.

2. Material and Method

Experimental work was carried out on adult Swiss albino mouse (4 weeks old). The mice were divided into two groups. The first group of four animals was not given any treatment and was considered as control. The other group of four animals was treated with 4 IU/day concentration of retinol palmitate by oral intubation for 7 days continuously.

2.1. Biochemical Analysis

On the 8th day of experiment, the biochemical estimation of T3, T4 and TSH present in the blood of untreated and RP treated mouse was calculated using ELISA technique. The mean value of T3 was 0.47 ng/ml in the untreated mouse. This value was within the normal value range described by Dr. Mildred.

Table –1 show that RP treatment reduces the value of T3, which was observed 0. 34 ±0.0158 ng /ml after RP treatment for 7 days. Almost similar pattern of effects of RP was observed in the case of T4 and TSH. In these molecules RP caused reduction in the mean values. The mean value of T4 in the untreated mouse was 5.10 ±0.305 µg /dl, whereas this was 3.50±0.305 µg /dl in treated case.

The TSH also showed low value under the influence of RP. It was 1.05±1.458 µIU /ml in the RP treated case as compared to 1.25 µIU /ml of the untreated case.

Test	Control		Treated		t - Value	Degree of Freedom at 5% level
	Sample	**Mean Value**	**Sample**	**Mean Value**		
T3	C1- 0.45 ng /ml	**0.45±0.0158 ng /ml**	t1- 0.33 ng /ml	**0.34 ±0.0158 ng /ml**	**23.2719**	**2.447**
	C2- 0.47 ng /ml		t2- 0.35 ng /ml			
	C3- 0.48 ng /ml		t3- 0.34 ng /ml			
	C4- 0.49 ng /ml		t4- 0.36 ng /ml			
T4	C1- 4.9 μg /dl	**5.10±0.305 μg /dl**	t1- 3.5 μg /dl	**3.50 ± 0.305 μg /dl**	**14.8134**	**2.447**
	C2- 5.2 μg /dl		t2- 4.0 μg /dl			
	C3- 5.1 μg /dl		t3- 3.0 μg /dl			
	C2- 5.2 μg /dl		t4- 3.5 μg /dl			
TSH	C1-1.00μIU /ml	**1.25±1.458 μIU /ml**	t1-1.03μIU /ml	**1.05 ±1.458 μIU /ml**	**0.3879**	**2.447**
	C2-1.50 μIU /ml		t2-1.10 μIU /ml			
	C3-1.00 μIU /ml		t3-1.00 μIU /ml			
	C4-1.50 μIU /ml		t4-1.1 0 μIU /ml			

Table 1: Thyroid function test of adult mouse of control and treated group

±value represents standard error

- Result: Reduction in the levels of T3, T4 and TSH in the RP treated mice indicates hypothyroidism. Similarly, iodination of thyroglobin does not occur.

2.2. Histo-Chemical Analysis

2.2.1. Pattern of Synthesis of Thyroglobulin and Its Iodination

The specific staining technique Domagk (1948) that includes Nuclear Fast Red, Aniline-blue and Orange-G clearly distinguish the de-iodination and iodination area of colloid (Figs.1 & 2). The active thyroids of the control mouse of all age groups showed orange color of the non-iodinated colloid.

The iodination starts at the periphery and the blue color of the colloid marks the iodination of the thyroglobulin.

In the RP treated mouse iodination of thyroglobulin does not take place, which is inferred by the absence of blue color of the colloid. Because RP inhibits the secretion of TSH and TSH stimulate the follicular cells to absorb iodine from blood. So higher dose of RP inhibits the iodination of thyroglobulin and hence the synthesis of thyroid hormone (Figs.3 & 4).

- Result: RP treatment inhibits the iodination of thyroglobulin and hence the synthesis of thyroid hormone.

2.3. Statistical Observation

The decrease in values of T3 and T4 is highly significant when adult male was treated with 4 IU RP for 7 days, as indicated by t value. The values are highly significant at 5% level.

2.4. Conclusion

The biochemical, Histochemical and statistical studies of RP treated mice cases showed inhibition of iodination of colloid and decrease level of thyroxin

On the contrary untreated cases showed iodinated thyroglobulin in the colloid and normal levels of thyroxin.

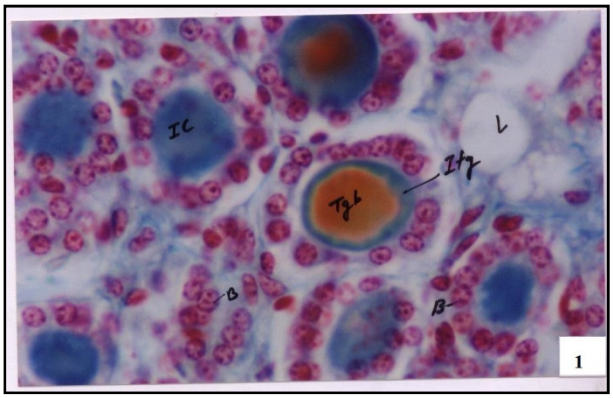

Figure 1: Control, well organized follicles at 100 X. C-Colloid filled with thyroglobulin Itg- Iodination of thyroglobulin

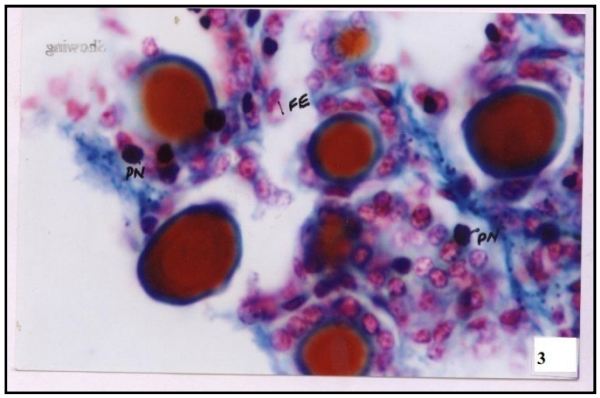

Figure 3: Treated, disorganized follicles at 100 X.

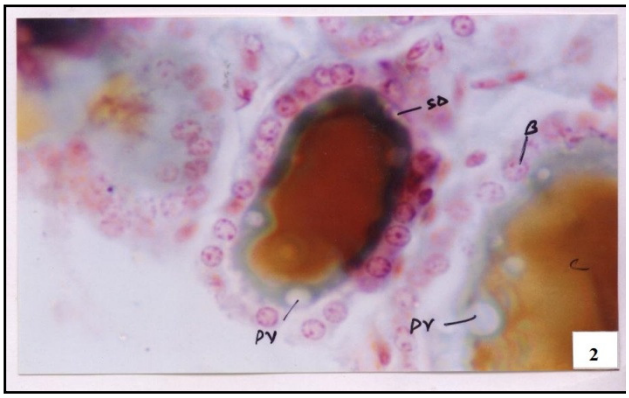

Figure 2: Control, well organized follicles at 400 X. B- Bi-nucleated cell PV- Pinocytosed Vacuole SD- Secretory droplet

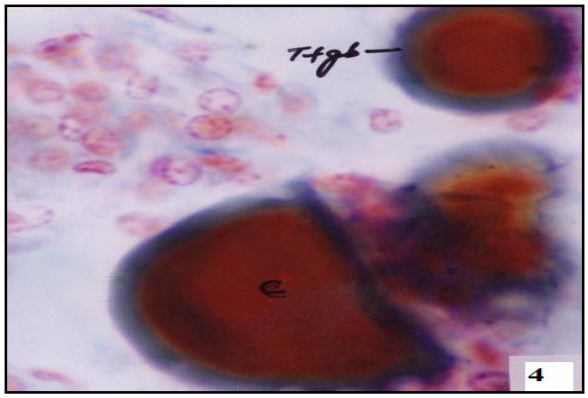

Figure 4: Treated, disorganized follicles at 400 X.

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