

Effect of Iodine Overdose on Thyroid Hyperplasia

Tala A. Abdul Wahab, MSc*

الخلاصة:

الهدف: دراسة العلاقة بين تأثير الوقت (طول المدة الزمنية) مع مادة اليود بتركيز عالي ودراسة تأثيره على فعالية الغدة الدرقية والتغيرات من الناحية الهرمونية والنسجية.

المنهجية: أجريت دراسة تجريبية على (٣٠) جرد أبيض من نوع الاباينو بعمر (٨) أسابيع لمعرفة تأثير اليود بتركيز عالي على فعالية ونشاط هرمونات الغدة الدرقية والتغيرات النسجية التي تحدث فيها وبالارتباط مع المدة الزمنية (الوقت) واستمرت الدراسة لمدة ستة أشهر للمدة من ٢٠٠٧/٢/١ إلى ٢٠٠٧/٧/٣١، وأجريت التجارب في مختبر الدراسات العليا في فرع الباثولوجي التابع لكلية الطب جامعة بغداد.

النتائج: تبين من الدراسة ظهور تغييرات في قراءات هرموني الغدة الدرقية (T3,T4) مع تغييرات نسجية في نسيج الغدة الدرقية في قطر وعدد الجريبات المكونة للغدة وزيادة عدد الجريبات الحارة الفعالة active hot follicles وقلّة في عدد الجريبات الباردة غير الفعالة inactive cold follicles حيث تأخذ الجريبات الحارة اللون الأزرق الفاتح أو الشاحب بعد تصبغ النسيج بصبغة toluiden blue dye، بينما تأخذ الجريبات الباردة اللون الأزرق الغامق في المقطع النسيجي للغدة الدرقية باستخدام نفس الصبغة.

التوصيات: إجراء دراسة مخطّط أو تصميم التجربة لمدة زمنية أطول (سنة أو أكثر) لمعرفة تأثير اليود عالي التركيز على نسيج ووظيفة الغدة الدرقية مع دراسة العلاقة بين نتائج التجربة وسلوك الإنسان (تطبيق هذه الدراسة على الإنسان) كما ويوصى بدراسة تأثير اليود وبتركيز مختلفة مع هرمون الثايروكسين على الغدة الدرقية.

Abstract

Objectives: study the relation between the effect of time (long time duration) with high concentration of iodine and study its effect on the activity of the thyroid gland (hormonal and histological changes).

Methodology: An experimental study was done on (30) albino rats (8 weeks of age) to know the effect of high concentration of iodine on the activity of the thyroid gland (hormonal and histological changes) related with time. The study last for six months for the period of 1/2/2007 to 31/7/2007, the experiment was carried out in the research lab. of pathology department, College of Medicine, University of Baghdad.

Results: The study shows changes in hormonal levels of thyroid hormones (T3 & T4) and also histological changes in the diameter and numbers of thyroid follicles and increase in the numbers of active hot follicles and decrease in the numbers of inactive cold follicles. The hot follicles takes faint blue colour after using the toluiden blue dye to stain the thyroid tissue while the cold follicles takes deep dark blue colour in the thyroid gland section when using the same dye.

Recommendations: Carrying out such a study for long time duration (1year or more), and to study the correlation between the experimental results and the behavior of the human, and study the effect of iodine in different concentrations in mixture with thyroxin hormone.

Key words: Thyroid gland, Hyperplasia, High concentration of iodine.

Introduction:

Thyroid gland is an important organ of the endocrine system in the body which is very important for its activity, weighting about (20gm) in human. It is the earliest endocrine glandular structure to appear in human embryo ⁽¹⁾, it is the site of synthesis, storage and control of the secretion of thyroid hormones; Thyroxin T4, Triiodothyronin T3 and part of reverse Triiodothyronin rT3 ⁽²⁾.

TSH effects directly on the secretion of both hormones T3, T4 from thyroid gland by increasing their secretions ⁽³⁾ then regulate the function of thyroid gland ⁽⁴⁾. If there is any defect in the thyroid gland, this will lead to decrease its hormones (T3, T4), the pituitary gland will increase the secretion of (TSH) to regulate the T3, T4 secretion ⁽⁵⁾. TSH plays an important role in activating the iodine trapping process and releasing thyroid hormones into blood ⁽⁶⁾, also increase the activity of iodide pump and the iodide concentration inside and outside the cells ⁽³⁾.

*Assistant Instructor, Department of Basic Science-Physiology, College of Dentistry, University of Baghdad

Iodine enters to body either from drugs as treatment or food and water or through diagnostic agents⁽³⁾. It effects directly in the regulation of thyroid gland activity , Large doses inhibits the up take of iodine and iodination , and inhibits the synthesis and secretion of thyroid hormones⁽⁷⁾, this effect persist in hyperplastic glands in which the iodide transport is stimulated⁽⁸⁾. Hyperplasia occur in thyroid gland (in experimental animals) by giving antithyroid drugs like carbimazole drug or results from excessive TSH secretion following reduction of T3 and T4 plasma levels⁽⁹⁾. and this study shows the effect of iodine on the function of thyroid gland which appears directly on the hormone levels and the tissue and cause changes in them.

Methodology:

An experimental design was applied on thirty healthy adult female rats of albino strain aged (8) weeks, weight (250) gm. they were kept in cages as groups, (10 rats / cage) housed in the animal house of college of medicine/Baghdad university in proper environmental conditions for animals. Ten rats used as control group (C) and the other (20) rats divided into (2) groups (T1, T2), fed with high iodine diet (HID) and watered with tap water .The study lasts for six months during the period of 1/2/2007 to 31/7/2007. for 10 days (T1 & T2) groups treated with carbimazole drug (2mg / rat) to induce hyperplasia and given normal diet then left for involution then treated with (HID) (10 μ g / day), the animals were sacrificed and dissected after 2 and 6 months to study hormonal and histological changes by taking the thyroid gland and drawing blood directly from heart to measure the hormonal levels of (T3 &T4) and their changes due to the effect of iodine on hormones with time. The results were written as (Mean \pm SE) and analysis of variance (ANOVA) test for statistical analysis was used.

Preparation of thyroid gland tissue:

Thyroid gland after fixation by (10%) formalin followed by tissue processing by passing in different concentrations of alcohol (50, 70, 80, 90, 100%) for (1-2) hours then in xylen for clearing (1-2) hours and imbedded In melted paraffin wax (60C $^{\circ}$) for 30 minuets (2) times concequentivly, casts of paraffin wax were made, then sliced to (5) micrometer in thick by using the microtome, these slices placed on slides, later on stained by haematoxylin and eosin dye (H & E) and toluiden blue dye to differentiat between hot and cold follicles, and examined by light microscope to study the changes⁽¹⁰⁾. Radio immunoassay (RIA) by using gamma counter was used to measure the hormonal changes of (T3& T4) from the serum of the blood to study the changes in there levels. The objective of this study is to notice the effect of high iodine concentration and long time of treatment on the thyroid gland (histological and hormonal changes) in rats.

Results:

Table 1. The Histological Changes in Thyroid Gland Tissue

	Control group (C) Normal diet zero iodine	2 months treatment (HID) Group 1	6 months treatment (HID) Group 2
Diameter of follicle (micrometer)	11.1 \pm 0.63 (μ m)	12.3 \pm 0.59 (μ m)	11.6 \pm 0.23 (μ m)
Hot/Cold follicles	19.8 \pm 2.6	6.3 \pm 0.2	8.5 \pm 0.8

Table 2. The Hormonal Changes in Thyroid Gland

Hormone level	Control group (C) Normal diet zero iodine	2 months treatment (HID) Group 1	6 months treatment (HID) Group 2
T3 hormone (nanogram)	0.57±0.05 (ng)	0.85±0.6 (ng)	0.9±0.3 (ng)
T4 hormone (microgram)	3.18±0.31 (µg)	6.4±0.48 (µg)	7.3±0.21 (µg)

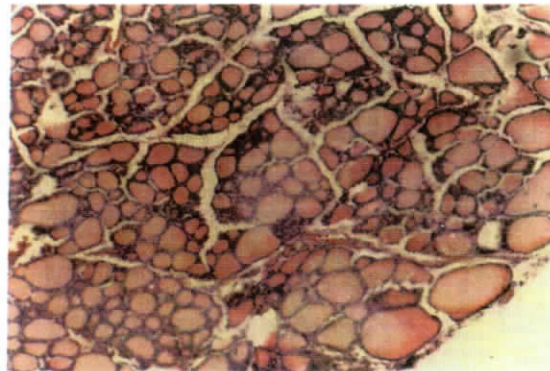


Figure 1. The section of Thyroid gland showing normal structure appearance of follicles

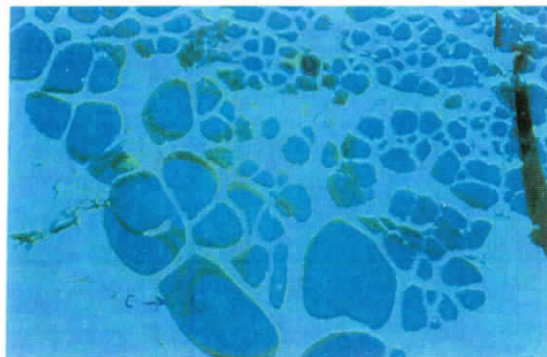


Figure 2. The section of Thyroid gland showing hot follicles, small in size lined by columnar epithelial cells and slightly faint color, and cold follicles with deep color of colloid materials and lined by flat follicular cells

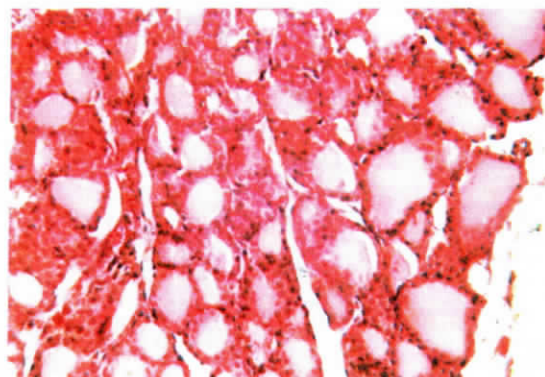


Figure 3. The Thyroid gland looks like normal after long term involution

Discussion:

The data analysis of the experiment's result revealed that the long term of treatment for rats with (HID), shows that the follicles in group (T1) after (2) months of treatment increased in their diameter (12.3 ± 0.59) μm when compared with (C) group, then decreased slightly after (6) months in (T2) group to (11.6 ± 0.25) μm but it is higher in comparison with (C) group (Table 1). Other observations were reported to the hot and cold follicles and the ratio between them shows that hot follicles (active) increased to (8.5 ± 0.8) in group (T2) when compared with group (T1), but its less in number when compared with (C) group as showed in (Table 1). Hot follicles are small in size lined by columnar epithelial cells with slightly faint blue colour, while cold follicles appears big in size and lined by flat follicular cells and deep blue colour of colloid materials as shown in fig. no. 2. T3 hormone increased in (T1) group when compared with (C) group then increased to (0.9 ± 0.3) ng in (T2) group (Table 2), T4 also increased in level in both (T1 & T2) groups when compared with (C) group as shown in (Table 2).

Hyperplasia occurred in thyroid gland tissue because of mitosis in cells which lead to increase in (DNA) mass inside the cells⁽¹¹⁾ and due to the effect of (TSH)⁽¹²⁾, and because of hypertrophy in the follicular size the follicular diameter increased due to the secretion of (TSH) as mentioned by Deneff, et al.⁽¹³⁾. These changes appeared in T1 & T2 groups compared with (C) group which related with the effect of iodine on thyroid gland and its effect on the secretion of (TSH) that causes this enlargement in the size of follicular diameter, these results are similar to that who reported by other investigators as shown above. Also this study shows decrease in cold and partly cold follicles and this reduction can be explained by the transformation of some of these follicles into hot ones. T3 and T4 hormone levels increased in both groups (T1 & T2) treated with (HID), this increase might be explained due to defect in absorption of iodine given with diet from the intestinal cells of animals or the dose of iodine given is not enough to induce an effect in thyroid gland, these results disagreed with other investigators that refers to reduce in hormonal levels with the increase of iodine concentration that inhibit the synthesis and secretion of T3 & T4 related to the inhibition of transforming of inorganic iodine to organic iodine and making thyroglobulin (TG) more resistant to hydrolysis and forming thyroid hormones⁽¹⁴⁾.

Recommendations: According to the early stated results the study recommends to study the design of the experiment for long time duration (1 year or more), and study the correlation between the experimental results and the behavior of the human, and study the effect of iodine in mixture with thyroxin hormone.

References:

1. Pintar, J. and Toran, A.: Normal Development of the Hypothalamic-Pituitary-Thyroid Axis, a Fundamental Clinical Text, 6th. ed. Philadelphia, JB Lippincott, 1992, P.P. 250-254.
2. Gentilo, F., Dilaur, R. and Salvatore, G.: Biosynthesis and Secretion of Thyroid Hormones, **Endocrinology**, 3rd.ed. Philadelphia, W.B Saunders, 1995, P.P.95-98.
3. Guyton, A.: **The Thyroid Metabolic Hormones, TextBook of Medical Physiology**, 11th ed., Philadelphia, 2006: P.P.931-949.
4. Wilber, J.: Human Pituitary Thyrotropin. **Endocrinology**, 1979, (1): P.P.141-147.
5. Fisher, D.: Physiological Variation in Thyroid Hormones: Physiological and Pathophysiological Consideration, **Clin. Chem.**, 1996, (42): P.P.135-139.

6. Garneer, D.: **The Thyroid Hormones, Harpers Review of Biochemistry**, 20th ed., 1985: P.P.530-536.
7. Greer, M. and Haiback, H.: Thyroid Secretion, Handbook in Physiology, Section 7, **Endocrinology**, American Physiological society, Washington D.C., 1974, 3:P.P.135-146.
8. Nagataki, S.: Effect of Excess Quantities of Iodide, Handbook of Physiology, section 7, **Endocrinology**, American Physiological Society, Washington D.C., 1974, 3: P.P.329-344.
9. Greer, M.; Studer, H. and Kendall, J.: Studies on the Pathogenesis of Colloid Goiter, **Endocrinology**, 1967, (81): P.P.623-632.
- ١٠- نوري، ماجدة عبد الرضا: علم تقنية الشرائح المجهرية، الطبعة الثانية، مطبعة جامعة الموصل، ١٩٨٩، الفصل الخامس، ص ١٠٣.
11. Pantic, V.: The Cytophysiology of Thyroid Cell, *Inter. Rev. Cytol.* 1974, (38): P.182.
12. Redmond, O. and Tuffery, A.: Thyroid Proliferation, Bodyweight, Thyrotropin and Thyroid Hormone in Chronic Antithyroid (Carbimazole) Treatment in Rat, **J. Anat.**, 1981, (133): P.37-47.
13. Deneff, J.; Haumont, S.; Cornette, C. and Beker, C.: Correlated Functional and Morphometric Study of Thyroid Hyperplasia Induced by Iodine Deficiency, **Endocrinology**, 1981, (108): P.P.2325-2358.
14. Lamas, L. and Ingbar, S.H.: Effect of Varying Iodine Content on the Susceptibility of Thyroglobulin to Hydrolysis by Thyroid Acid Protease, **Endocrinology**, 1978, (102), P.P. 188-197.