

Study the Effect of Rifampicin in the Level of Thyroid's Gland Hormones and Thyroid - Stimulating Hormone in Rabbits

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Abstract

The aim of this study was intended to study the effect of rifampicin in the level of thyroid's gland hormones (T_4 , T_3) and thyroid -stimulating hormone (TSH) in rabbits.

Eight male rabbits were used through out this study, their weights were measured before the starting of the experiment. Animals were divided into two groups (each group contains 4 rabbits), the first group was administrated daily with 15 mg/Kg physiological normal saline for 35 days and used as a control group, while the second group was administrated with 15 mg /Kg daily for 35 day of rifampicin capsule 300 mg.

At the end of the experiment, all of animal groups were weighted and the sera was prepared to measure the hormones.

The results showed that there was a significant decrease ($P < 0.05$) in the mean of animals weights in the second group that was treated with rifampicin in comparison with the control group. A significant increase ($P < 0.05$) was in T_4 and T_3 hormones level, and a significant decrease ($P < 0.05$) was in TSH hormone level in the second group that treated with rifampicin in comparison with the control group.

From this study, can conclude that rifampicin has a negative effect on thyroid gland function which might disorder on the secretion activity of thyroid gland hormones.

Key words: Rifampicin, Thyroid Gland, Thyroid Hormones.

Introduction

The thyroid is one of the largest endocrine glands in the body. This gland is found in the neck inferior to (below) the thyroid cartilage (also known as Adam's apple in men) and at approximately the same level as the cricoid cartilage(1). The thyroid controls how quickly the body burns energy, makes proteins, and how sensitive the body should be to other hormones (2). The primary function of the thyroid is production of the hormones thyroxine (T_4),

triiodothyronine (T3), and calcitonin. Up to 80% of the T4 is converted in to T3 by peripheral organs such as the liver, kidney and spleen. T3 is about tentimes more active than T4 (3).

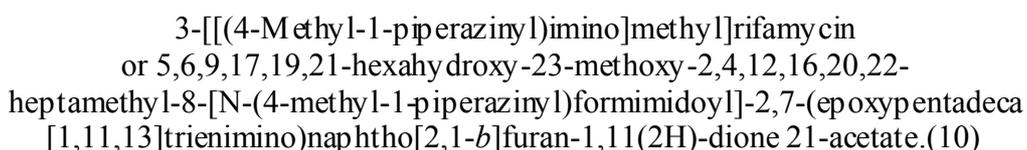
Thyroxine (T4) is synthesized by the follicular cells from free tyrosine and of the tyrosine residues of the protein is called thyroglobulin (TG). Iodine is captured with the "iodine trap" by the hydrogen peroxide generated by the enzyme thyroid peroxidase (TPO) (4) and linked to the 3' and 5' sites of the benzene ring of the tyrosine residues on TG, and on free tyrosine. Upon stimulation by the thyroid -stimulating hormone (TSH), the follicular cells reabsorb TG and proteolytically cleave the iodinated tyrosines from TG, forming T4 and T3 (in T3, one iodine is absent compared to T4), and releasing them into the blood. Diiodinase enzymes convert T4 to T3 (5). Thyroid hormones that are secreted from the gland are about 90% T4 and about 10% T3. (3)

Cells of the brain are a major target for the thyroid hormones T3 and T4. Thyroid hormones play a particular crucial role in brain maturation during fetal development. (6) A transport protein (OATP1C1) has been identified that seems to be important for T4 transport across the blood brain barrier. A second transport protein (MCT8) is important for T3 transport across brain cell membranes (7).

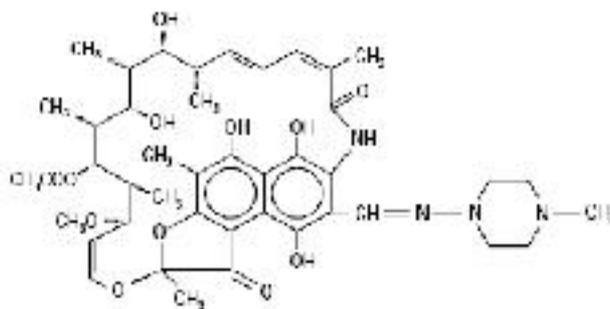
In the blood, T4 and T3 are partially bound to thyroxine-binding globulin. Only a very small fraction of the circulating hormone is free (unbound) - T4 0.03% and T3 0.3%. Only the free fraction has hormonal activity (8).

The production of thyroxine and triiodothyronine is regulated by thyroid -stimulating hormone (TSH), released by the anterior pituitary (that is in turn released as a result of TRH release by the hypothalamus) (8),(9).

Rifampicin, or Rifadin, or Rifampin is a semisynthetic antibiotic derivative of rifamycin SV. Rifampin is a red-brown crystalline powder very slightly soluble in water at neutral pH, freely soluble in chloroform, soluble in ethyl acetate and in methanol. Its molecular weight is 822.95 and its chemical formula is $C_{43}H_{58}N_4O_{12}$. The chemical name for rifampin is either:



Its structural formula is:



Rifampicin drug i.e. (rifampin) Capsules, and (rifampin) for Injection IV an active antibiotic used for tuberculosis and against some gram negative, gram positive, some enteric bacteria, and mycobacterium. Rifampicin binds strongly to DNA dependent RNA polymerase thus it inhibits RNA synthesis in bacteria and Chlamydia (11), (12). Rifampicin has many sides effects for example it causes anemia (13), thrombocytopenia, and leucopenia (14), also rifampicin reduces the level of glutathione, creatinine, WBCs counts and the level of lipid (15) ...etc. Few of researches insinuate that Rifampicin may increase T3 level, and until yet to our knowledge, no study was devoted to the still poorly exploited aspect of the effect of Rifampicin on the level of thyroid gland hormones, i.e. does the Rifampicin has side effects on the thyroid gland function, which is the aim of the present study.

Material and Methods

Eight male rabbits were used in this study were taken from the animal house in the Biotechnology Researches Center / Al – Nahrain University, and their ages were between, (9 – 12) months. Isolated in a relatively controlled environment at a temperature of a bout 37°C, their weights were between (1500 – 1250) gm at the beginning of the experiment ,their weights about and they were given free access for tap water and food adlibitum.

Animals were divided into two groups (each group contains 4 rabbits) as follows:

1. First group was administrated daily with 15 mg / kg physiological normal saline by Orogastric tube for 35 days and used as a control group.
2. Second group was administrated daily with 15 mg / kg of rifampicin 300 mg by Orogastric tube for 35 days.

At the end of the experiment the weights of the animals were taken. and pull up the blood by heart puncture and prepared the sera to measure the thyroid gland hormones (T_4 , T_3) and thyroid -stimulating hormone (TSH) by the (ELISA method) and used the specific ELISA hormones kits for (T_4 , T_3), and (TSH). The experiment and the hormonal assay were done in

the laboratory of the Biotechnology Researches Center / Al – Nahrain University from (20 / November / 2008) to (25 / January / 2009).

Results and Discussion

Animals treated with rifampicin showed a significant ($P < 0.05$) decrease in the body weights (from 1450.00 ± 50.00 to 467.50 ± 46.26) gm in comparison with the animals weights of the control group (from 1250.00 ± 104.08 to 1825.00 ± 85.39) gm (tab-1). These changes reflect the effect of rifampicin administration on the thyroid gland function i.e. increase secretion it's hormones (T_4 , T_3) thus increase the body's basal metabolic rate, stimulate carbohydrate metabolism ,break down fats, and affect protein synthesis.(2), (16),(17), (18).

Also the results showed a significant increase ($P < 0.05$) in T_4 , and T_3 hormone level, and a significant decrease ($P < 0.05$) in TSH hormone level in comparison with the control group (tab- 2). These results show that rifampicin had side effects on thyroid gland function i.e. increase forming and release it s hormones over the normal value especially (T_4 & T_3), that's mean primary hyperthyroidism and the weights results above proved that. May be it s increase thyroxine (T_4) synthesized by the follicular cells from free tyrosine or from the tyrosine residues of the protein called thyroglobulin (TG) (10), (19).

A decrease that happened to TSH it's a result to the negative feed back mechanism (18),(19), i.e. thyroxine T_4 and triiodothyronine T_3 is regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary (that is in turn released as a result of TRH release by the hypothalamus). The thyroid and thyrotropes form a negative feedback loop: TSH production is suppressed when T_4 level is high, and vice versa. The TSH production itself is modulated by thyrotropin-releasing hormone (TRH), which is produced by the hypothalamus and secreted at an increased rate in situations such as cold (in which an accelerated metabolism would generate more heat). TSH production is blunted by somatostatin (SRIH), rising levels of glucocorticoids and sex hormones

(estrogen and testosterone), and excessively high blood iodide concentration (20).

The results concluded that rifampicin had negative effect on thyroid gland function which might have disorder on the secretion activity of thyroid gland hormones.

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Table (1): Explain the effect of administration rifampicin on the Rabbits Mean weights in treated and control group

Groups	Mean weight(gm) (zero time) M ± SE	Mean weight (gm) (end of treatment) M ± SE
1. Control group	1250.00 ± 104.08	1825.00 ± 85.39
2.Group treated with rifampicin	1450.00 ± 50.00	467.50 ± 46.26 *

M ± SE: Mean ± Stander Error

* : Significant Difference (P <0.05)

Table (2): Explain the effect of administration rifampicin in the Level of T₄, T₃, and TSH in Rabbits in treated and control group

Groups	T ₄ µg/ dl M ± SE	T ₃ ng/ ml M ± SE	TSH µu / l M ± SE
1.Control group	6.05 ± 0.16	0.93 ± 0.11	0.80 ± 0.04
2.Group treated with rifampicin	8.80 ± 0.45 *	2.53 ± 0.13 *	0.18 ± 0.05 *

M ± SE: Mean ± Stander Error

* : Significant Difference (P <0.05)

دراسة تأثير عقار الريفامبيسين في مستوى هرمونات الغدة الدرقية والهرمون المحفز للدرقية في الأرانب

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الخلاصة

هدفت الدراسة الحالية الى دراسة تأثير عقار الريفامبيسين في مستوى هرمونات الغدة الدرقية (T_3 , T_4) والهرمون المحفز للدرقية (TSH) في الأرانب. استخدم في هذه الدراسة 8 أرانب ذكوراً أخذت أوزانها ومن ثم قسمت على مجموعتين كل مجموعة مكونة من 4 أرانب. جرعت المجموعة الأولى (مجموعة سيطرة) بالمحلول الملحي الفسيولوجي السوي physiological normal saline يومياً بجرعة 15 مليغرام/ كغم ومدة 35 يوماً ، وجرعت المجموعة الثانية بعقار الريفامبيسين 300 مليغرام وجرعة مقدارها 15 مليغرام/ كغم يومياً ومدة 35 يوماً. في نهاية المعاملة وزنت الحيوانات وتم سحب الدم لتهيئة الأمصال لقياس مستوى هرمون (T_3 , T_4) و (TSH). وأظهرت النتائج وجود نقصان معنوي ($p < 0.05$) في معدل أوزان الحيوانات المعاملة بالريفامبيسين مقارنةً بمجموعة السيطرة وحصول زيادة معنوية ($p < 0.05$) في مستوى هرموني T_3 و T_4 ونقصان معنوي ($p < 0.05$) في مستوى هرمون TSH مقارنةً بمجموعة السيطرة. نستنتج من هذه الدراسة إن لعقار الريفامبيسين تأثيراً سلبياً في فعالية الغدة الدرقية الإفرازية مما يؤدي الى حدوث خلل في الإفراز الهرموني.

كلمات المفتاح: ريفامبيسين، الغدة الدرقية، هرمونات الغدة الدرقية.