Original Article

The Therapeutic Effect of Beta-Aminobutyric Acid (βABA) on Hypercortisolism

Saja Aied Mohammed[1], Mohammed Abbas Jasim[2]
[1,2] College of Education for Women, University of Anbar, Iraq.

ABSTRACT

Certainly, the primary action of Propylthiouracil (PTU) is to inhibit the production of thyroid hormones (T4, T3) by preventing iodine molecules from combining with the amino acid tyrosine and thus increasing the secretion of thyroid hormone (TSH). This study aimed to investigate the effect of beta-aminobutyric acid (βABA) on hypercortisolism caused by high TSH levels. We performed the experiment on 20 male Sprague-Dawley rats divided into four groups (A, B, C, D) in each group five rats, three groups (B, C, D) exposed to hypothyroidism with propylthiouracil (PTU) by intraperitoneal injection peritoneum for 10 days. After the symptoms of hypothyroidism appeared, groups, C and D were treated with βABA at a concentration of 100 and 200 mg/kg body weight, also by intraperitoneal injection twice a week for three weeks, while keeping groups A, and B as control groups. The level of TSH, ACTH, and Cortisol was measured. The results showed a significant increase ($P < 0.05$) in the level of TSH and an increase in the level of cortisol with a decrease in the level of ACTH in the hypothyroid group, While the groups that were injected with amino acid, showed a decrease in the level of TSH, Cortisol and an increase in the level of ACTH in both concentrations. We conclude from the current study that hypothyroidism leads to hypercortisolism and that βABA has a therapeutic effect on elevated levels of TSH and cortisol.

Keywords- Beta-amino butyric acid (βABA), propylthiouracil (PTU), ACTH, Cortisol, TSH.

INTRODUCTION

The hormone cortisol is synthesized and secreted by the adrenal cortex it is considered the most important glucocorticoid and constitutes 90% of it. It also helps to deal with stressful situations, but high levels of it lead to many disorders. Such as weight gain, high blood pressure, and sleep problems, contributing to diabetes, chronic fatigue syndrome, and neuroendocrine [1]. It also affects the heart and blood vessels through its effect on the autonomic nervous system. Several studies have confirmed an increased risk of cardiovascular diseases, such as acute coronary syndromes, arrhythmias, sudden cardiac death, and stroke with hypercortisolism [2]. High levels of cortisol affect the brain through cognitive impairment and lead to neurodegeneration and Alzheimer's disease [3].

With the development of chemistry and biology, non-proteinogenic amino acids have become an effective tool for developing peptide-based drugs [4].

Amino acids are of particular interest due to their ability to stimulate insulin secretion, reduce hyperglycemia, and regulate metabolic processes in diabetic patients [5]. Recently, the use of Beta amino butyric acid (βABA) has emerged on the animal side, as βABA has the ability to reduce inflammation and heal wounds, in addition to its role in stimulating autoimmunity and the production of IgM, Igg antibodies, and its resistance to s.aureus bacteria [6]. It was also found [7] that βABA has a therapeutic role for diabetes by lowering the level of glucose in the blood. As well as its effect on some physiological and biochemical aspects, so the current study aimed to find out its effect on hypercortisolism associated with hypothyroidism.

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Address for correspondence: Mohammed Abbas Jasim
College of Education for Women, University of Anbar, Iraq.
Email: mohammed.a.jasim@uoanbar.edu.iq

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Materials and Methods

Materials

βABA & PTU: Purchased from (Hyper chem, China) (TSH Catalog No: E-EL-R0976, ACTH Catalog No: E-EL-R0048, Cortisol Catalog No: E-OSEL-R0002) All were purchased from Elabscience laboratory biological / USA.

Laboratory Animals

In this experiment, we used 20 male Sprague-Dawley rats purchased from the animal house in the city of Tikrit at the age of (9-10) weeks, with weights ranging from 50 ± 200 g, all of them were in good health, and special fodder was used to feed the animals, and the appropriate living requirements were prepared for them, such as light and temperature.

Experience Design

The animals were divided into four groups (A, B, C, D,) and each group consisted of five animals three groups (B, C, D) were exposed to hypothyroidism using PTU by intraperitoneal injection for 10 days. After the symptoms of hypothyroidism appeared, groups, C and D were treated with βABA at a concentration of 100 and 200 mg/kg body weight, also by intraperitoneal injection twice a week for three weeks, while keeping groups A, and B as control groups.

Sample Collection

Blood samples were collected from animals by drawing blood directly from the heart after the end of the experiment.

Statistical analysis of test results

The results were statistically analyzed using one-way ANOVA using the SPSS statistical program (Ver. 22), and the arithmetic means and standard error were also calculated.

Results

Thyroid stimulating hormone (TSH)

Statistical analysis showed in (Fig. 2) a significant increase in the level of TSH in the group of hypothyroid animals B (32.6 ± 1.585) compared to the control group A (19.6 ± 0.270). While a significant decrease in the level of TSH in the groups treated with βABA at both concentrations C (13.1±1.700) and D (20.3 ± 3.515).

Adrenocorticotropic hormone (ACTH)

Our results shown in (Fig. 2) showed a significant decrease in the level of ACTH in group B (39.25 ± 7.950) with hypothyroidism and groups C (100.25 ± 3.150), D (60.10 ± 2.600) and treated with βABA at both concentrations when compared with group A (237.9 ± 7.400).

Cortisol hormone

The results shown in (Fig. 3) showed a significant increase in the level of cortisol hypothyroidism in patients group B (27.500 ± 2.500) and group D (13.00± 2.300) affected and treated with βABA amino acid at a concentration of 200 mg/kg when compared with the rest of the groups, and no significant differences were recorded between group C (6.400 ± 1.100) infected and treated with βABA at a concentration of 100 mg/kg when compared with the control group A (3.640± 0.520).

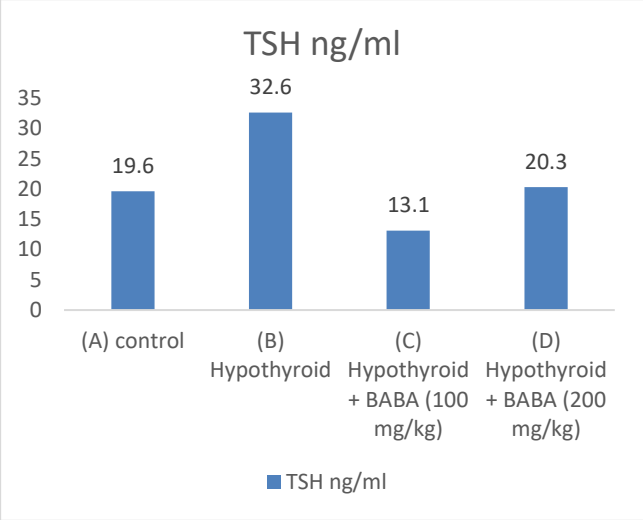

Figure 1: Effect of βABA on TSH level

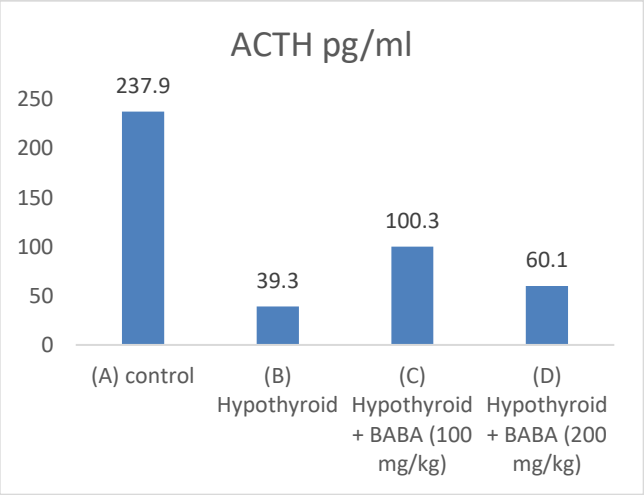

Figure 2: Effect of ßABA on ACTH level

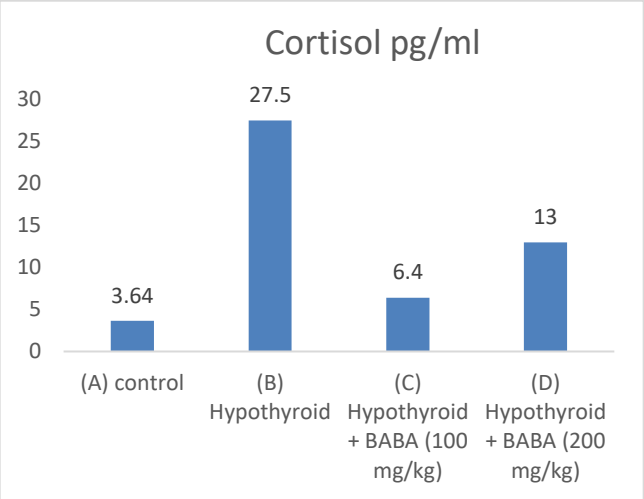

Figure 3: Effect of ßABA on Cortisol level

Discussion

The reason for the elevated TSH level in the group of hypothyroid rats is due to the effect of PTU, which also causes an increase in the level of Thyrotrophin - releasing hormone secreted by the hypothalamus and stimulates the release of TSH hormone from the anterior lobe of the pituitary gland and because the levels of the latter correlate closely with the levels of FT4, FT3 is an inverse relationship in an attempt to coordinate hormonal by a feedback mechanism, which is necessary to maintain body homeostasis, and these results are consistent with the results of [8, 9]. As for the effect of BABA, the results of the current study according to the studies based on GABA will be interpreted as similar to it since there are no previous studies on the topic of our current study findings. It was found that BABA reduced TSH levels in hypothyroid rats treated with it, and this result is consistent with [10].

Regarding the level of adrenal hormones, the reason for the low ACTH level in the group of hypothyroid rats is that hypothyroidism affects the level of adrenal gland hormones and this finding is consistent with [11]. When the stress of the body increases due to hypothyroidism, the hypothalamic-pituitary-adrenal (HPA) axis stimulates the secretion of the hormone ACTH, which increases the secretion of the hormone cortisol, but when the increase in the level of cortisol becomes excessive, the secretion of ACTH stops and its level decreases to reduce the increase in the level of cortisol, about the effect of βABA on the level of ACTH in infected and treated groups, this result is consistent with [12] in the ability of GABA to reduce the secretion of this hormone,

We also found regarding the level of cortisol the increase in the level of cortisol in a group of rats with hypothyroidism is associated with an increase in TSH, and this result is consistent with [13] in a study conducted to assess the state of the thyroid gland in stressed rats and with [14] that some levels of the adrenal gland rise in hypothyroidism, This confirms that disorders occurring in the thyroid gland (hypothyroidism) would affect the levels of adrenal gland hormones and cortisol levels, and this could lead to a chronic state of adrenal fatigue. These two glands work together to enhance the body's functions. As for the decrease in cortisol level in the affected groups treated with βABA, this result is consistent with [12] as GABA limits cortisol secretion and relieves stress.

Conclusion

We have found that hypercortisolism is associated with hypothyroidism, as when the body is stressed due to hypothyroidism, the hypothalamic-pituitary-adrenal (HPA) axis stimulates the secretion of adrenocorticotropic hormone (ACTH) and thus increases the secretion of cortisol, but when the increase in the level of cortisol becomes excessive, the secretion of ACTH stops, and its level decreases to reduce the increase in the level of cortisol, This confirms that disorders occurring in the thyroid gland (hypothyroidism) would affect the levels of adrenal gland hormones and cortisol levels, and this could lead to a chronic state of adrenal fatigue, We also found that beta-aminobutyric acid has a therapeutic effect on reducing the levels of TSH, ACTH, and cortisol.

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Statement of Animal Ethics

We declare that animals received appropriate treatment upon a study that was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the University of Anbar (Date.22/6/2022/ No. 86).

Author Contributions

Mohammed A. Jasim contributed to the study conception and design. Material preparation, data collection and analysis were performed by Saja Aied Mohammed and Mohammed. A. Jasim. The first draft of the manuscript was written by Saja Aied Mohammed and corrected by Mohammed. A. Jasim.

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