

## Hypothyroidism Increases Body Weight, Absolute and Relative Weight of Pituitary Gland in Male Albino Rats

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### ABSTRACT

**Objective:** To evaluate the increase in body weight, absolute and relative weight of pituitary gland in experimental hypothyroid male albino rat.

**Design:** An experimental animal study.

**Place:** Anatomy Department, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi.

**Methods:** Thirty adult albino rats were selected for the study and divided into two groups. Group A served as control group and received injection normal saline 1 cc intraperitoneally daily for six weeks. Group B was treated group and received carbimazole in a dose of 6µg/gm body weight intraperitoneally daily for eight weeks. Animals were weighed at the commencement and at the completion of treatment. Absolute weights of pituitary glands were recorded after the animals were sacrificed. Relative weights of pituitary glands were also calculated. The results were compared with control and correlated with the previous studies.

**Results:** Final body weight of animals were increased significantly ( $P<0.001$ ) in treated group (B) as compared to control group (A). Absolute weight of pituitary gland was significantly increased ( $P<0.001$ ) in group B as compared to group A. Relative weight of pituitary gland was significantly increased ( $P<0.001$ ) in group B as compared to group A.

**Conclusion:** There is increase in body weight of animals by the effect of carbimazole. Enlargement of pituitary gland due to its hyperplasia results in increase in the absolute weight. The increase in generalized body weight results in increase in relative weight of the organ.

**Key words:** Pituitary gland, hyperthyroidism, hypothyroidism, thyroid hormones, absolute weight, relative weight, albino rats.

### INTRODUCTION

Most patients with hyperthyroidism, Grave's disease and toxic nodular goiter report weight loss. The restoration of body weight is an obvious sign of normalization of thyroid function after antithyroid therapy. It is mostly observed that there is excessive weight gain in some patients after successful treatment with antithyroid drugs for their hyperthyroidism.<sup>1</sup> This study was done to determine the extent of weight gain after treatment with carbimazole, an antithyroid drug. Primary hypothyroidism or underactivity of the thyroid gland is common.<sup>2</sup> Thyroid hormone serves as one of the major regulators of resting energy metabolism. States of thyroid hormone excess lead to an increased metabolic rate and frequently presents with weight

loss.<sup>3</sup> Thyroid hormones are involved in metabolic regulation and affect body weight and body mass index (BMI). One might therefore expect to see equivalent weight gain in hypothyroidism as a result of a decreased metabolic rate.<sup>4</sup> Studies of hyperthyroid patients have demonstrated significant and sustained weight gain after initiation of treatment. Weight loss is frequently found in hyperthyroidism and weight gain is observed when hyperthyroidism is treated by giving antithyroid drugs like carbimazole.<sup>5</sup> Antithyroid drugs are widely used in the therapy of hyperthyroidism. The antithyroid drugs which are used include carbimazole, propylthiouracil and methimazole.<sup>6</sup>

Carbimazole is a prodrug given by oral route and is a thioamide type of antithyroid drug. After absorption, it is converted to methimazole. Carbimazole inhibits synthesis and iodination of thyroglobulin and coupling reaction.<sup>7</sup> Hypothyroidism may be primary or secondary. Primary, in which problem lies in thyroid gland and secondary in which failure in the secretion of thyroid-stimulating hormone (TSH) from the pituitary gland or failure in the secretion of thyrotrophin-releasing hormone (TRH) from the hypothalamus. Primary hypothyroidism may be clinical or subclinical. Clinical

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where free T4 is low and TSH is high. The incidence of clinical hypothyroidism is <1% in men and 0.5-1.9% in women and the incidence of subclinical hypothyroidism is 0.7-5.7% in men and 3-13.6% in women.<sup>8</sup> Individuals treated for hyperthyroidism gain body weight whatever treatment is used, but patients treated for primary hypothyroidism will not lose an appreciable amount of weight.<sup>9</sup> Persons with thyrotoxicosis decrease weight despite increased appetite and food intake, and weight is increased again after the treatment of hyperthyroidism. This weight regain is because of decrease in metabolic rate due to the decreased concentrations of thyroid hormone in blood.<sup>10</sup> Many individuals lose weight during acute catabolic stage of hyperthyroidism. Such Individuals should be given information about the risk of weight gain after the treatment with antithyroid drugs.<sup>11</sup> Both hypothyroidism and hyperthyroidism are widely seem to be associated with alterations in weight and BMI. Hyperthyroidism causes significant weight loss in some patients due to increased basal metabolic rate.<sup>4</sup> Many hypothyroid patients complain of slowness and decreased physical activity.<sup>12</sup> Relative weight of the organ depends on the body weight and absolute weight of the organ. Animal having higher body weight and high absolute weight also has high relative weight.

## MATERIALS AND METHODS

This study was performed in Department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Post Graduate Medical Centre (JPMC), Karachi. Thirty adult male albino rats of wistar strain weighing between 190-252 grams were selected for this study. Animals were put under observation for assessment to see their health and general condition, on the basis of weight changes.

The animals were divided randomly into two groups, A and B. Each group was comprised of fifteen animals, and was further divided into three sub groups, based on period of treatment i.e two, four and six weeks.

Group-A: A1, A2, A3

Group-B: B1, B2, B3

Group A animals were normal control, received 1c.c normal saline injection subcutaneously daily for their respective period of time. Group B rats received injection carbimazole (Neomercazole), used as an anti-thyroid agent in a dose of 6 µgms / gm body weight intraperitoneally daily for two, four and six weeks. Animals were weighed with the help of triple beam balance at the start and then at the end of of treatment. When the treatment was completed, animals were anaesthetized with ether. The animals were decapitated, pituitary fossae were exposed by removing the skull bones, and pituitary glands were dissected out, examined

for their gross appearance, weighed and fixed. Absolute weights of pituitary glands were recorded with the help of Sartorius electrobalance.

The relative weight of pituitary gland of a subgroup was calculated with the help of formula,

$$\frac{\text{The relative weight of pituitary gland} = \text{Mean weight of pituitary glands (mgs)}}{\text{Mean final weight of the animals (gms)}} \times 100$$

**Statistical Analysis:** The SPSS version 16.0 was used after entry of data. Quantitative variables i.e, weight of animals, weight of pituitary glands (absolute weight) and relative weight were analysed and mean  $\pm$  standard deviation were computed. P values were calculated by applying independent sample-t test.

## OBSERVATIONS AND RESULTS

The present study was aimed to observe the changes in body weight of animals and absolute and relative weight of pituitary gland both in carbimazole treated and control group of male albino rats. These observations and results on body weight and weight of the pituitary glands were recorded and compared with the control rats and with other studies. The animals from the control group (A) and the experimental group (B) remained alive throughout the study period. The effects of carbimazole on the general condition and behavior of the animals, body weight and weight of the pituitary glands were noted. Animals in group A were active and healthy, while those treated with carbimazole (group-B) appeared slow, ill looking, had sluggish behavior, decreased response to external stimuli and appeared bigger in size.

**Observation on Body Weight:** Animals were studied before the start of the treatment and at the time of sacrifice i.e at the end of second, fourth and sixth week. The changes in animal's weights in both groups at different time periods were recorded which were found significantly increased in treated group than in the control group.

The mean value of initial body weight (g) in group-A1 was 220.6  $\pm$  13.145, in group-A2 was 204.4  $\pm$  18.582, while in group-A3 was 205.2  $\pm$  20.167, and they were sacrificed at two four and six weeks respectively, The mean final weight was 243.0  $\pm$  11.640 in A1, 254.2  $\pm$  14.132 in A2 and 274.4  $\pm$  12.219 in A3 as shown in Table-1.

There was gradual increase in weight gain in control group-A. The initial body weight in group-A increased after 2, 4 and 6 weeks. In group-B1 the mean initial weight was 227.6  $\pm$  10.644, 214.8  $\pm$  13.989 in group-B2 and 214.4  $\pm$  11.845 in group-B3, and they were

**Table – 1 Mean\* Body Weight (G) of Male Rats in Different Groups at Variable Time Period**

Groups	Subgroups	Body Weights (G)			
		Initial Weights	Final Weights at Variable Time Interval		
			2nd Week	4th Week	6th Week
A (n=15)	A1 (n=5)	220.6 ±13.1	243.0 ±11.6	--	--
	A2 (n=5)	204.4 ±18.5	--	254.2 ±14.1	--
	A3 (n=5)	205.2 ±20.1	--	--	274.4 ± 12.2
B (n=15)	B1 (n=5)	227.6 ±10.6	288.6. ± 06.8	--	--
	B2 (n=5)	214.8 ±13.9	--	296.2 ± 07.7	--
	B3 (n=5)	214.4 ±11.8	--	--	310.4 ± 09.2

\*Mean ±Standard Deviation (SD) P value = 0.05 means statistically significant

**Table – 2: Mean\* Absolute Weight of Pituitary Gland (mg) of Animals in Different Groups at Variable Time Period**

Groups	No. of Subjects	Weight of Pituitary Gland (mg)		
		Durations		
		2 weeks( A1)	4 weeks ( A2)	6 weeks( A3)
Control (A)	n= 15	3.3 ± 0.2 N=5	3.1 ± 0.6 N=5	3.3 ± 0.2 N=5
Carbimazole treated group (B)	n=15	2 weeks ( B1)	4 weeks( B2)	6 weeks( B3)
		4.9 ± 0.2 N=5	4.9 ± 0.1 N=5	5.0 ± 0.3 N=5

\*Mean ± Standard Deviation (SD)P value = 0.05 means statistically significant

**Table – 3: Mean\*Relative Weights (mg) /100 grams of body weight) of Pituitary Glands of Animals in Different Groups at Variable Time Intervals**

Groups	No. of Subjects	2 weeks	4 weeks	6 weeks
Control (A)	n= 15	1.4 ± 0.1	1.3 ± 0.2	1.4 ± 0.1
Carbimazole treated group (B)	n= 15	1.7 ± 0.1	1.6 ± 0.1	1.5 ± 0.1

Mean ± Standard Deviation (SD)

**Table – 4: Mean\* Final Body Weight (G), Mean \*Absolute Weight, and Mean\* Relative Weight of Pituitary Gland (mg) of Animals in Different Groups at Variable Time Period**

Groups	Final Body Weight	Absolute weight	Relative Weight
Control (A) N=15	257.20± 17.869	3.253± 0.4172	1.3906±0.18827
Carbimazole treated group (B)N=15	302.73± 14.330	4.967± 0.2320	1.5646± 0.5520
P-Value	0.0001	0.0001	0.0001

Mean ± Standard Deviation (SD)

sacrificed at two four and six weeks respectively. The mean final weight was 288.6 ± 06.804 in B1, 296.20 ± 07.791 in group-B2, and 310.4 ± 09.236 in group-B3, as shown in Table-1.

The final body weights of animals in group B were increased significantly as compared to group A, at 2, 4 and 6 weeks.(P<0.001)

**Observations on Weight of Pituitary Gland:** The mean absolute weights (mg) of pituitary gland of different groups were changed at variable time intervals. In control group the mean weight of pituitary in A1 was 3.36 ± 0.207, A2 was 3.10 ± 0.682, and in A3 was 3.30 ± 0.235. They were sacrificed at 2, 4 and 6 weeks respectively, as shown in Table-2.

In carbimazole treated group (B) the mean weights of pituitary gland in B1, B2 and B3 were 4.94 ± 0.207, 4.96 ± 0.182 and 5.0 ± 0.332 and they were sacrificed at 2, 4 and 6 weeks respectively.

The increase in mean weight of the pituitary gland was noted in group-B as compared to the control. So when we compare group-A with B, increase in weight of pituitary gland was highly significant at two, four and six weeks period (P<0.001), as shown in Table-2.

The mean relative weights of pituitary gland were calculated at different time intervals in different groups as shown by table -3 The mean values of relative weights of pituitary glands in group B were increased significantly (P< 0.001), as compared to group A.

## DISCUSSION

Increase in weight is observed in individuals with treatment of hyperthyroidism. This study was aimed to observe the changes in the body weight of male albino rats which were made hypothyroid by injection of carbimazole as an anti-thyroid drug. There is increase in body weight of animals by the effect of carbimazole. The carbimazole decreases thyroid hormone level in blood and increased TSH release from pituitary gland which results in increase in the absolute weight of pituitary gland. Enlargement of pituitary gland due to its hyperplasia, leads to increase in its absolute weight. The increase in absolute pituitary weight and generalized body weight results in increase of relative weight of organ. Absolute and relative weights of pituitary glands were measured in both carbimazole treated and control groups of these animals. Increase in weight following treatment of hyperthyroidism with carbimazole is primarily due to decreased blood levels of thyroid hormones and lowered metabolic rate associated with these hormones. Lowered metabolic rate-results in gain in weight without increased appetite and food intake. The results of our study show that many animals increase considerably in weight as a final outcome of treatment of hyperthyroidism by giving carbimazole. Our study matches with the study of J Brunova<sup>1</sup> which shows that most patients with hyperthyroidism report weight loss. The restoration of body weight is an obvious sign of normalization after therapy. The large increase in weight gain was following treatment for hyperthyroidism. The main factors contributing to excessive weight gain were poor control of thyroid function and need for replacement therapy.<sup>1</sup> It is known that weight loss in hyperthyroidism is due to decrease in adipose tissue, and reduction in muscle and bone mass. Excessive weight gain following treatment with antithyroid drugs is mainly due to increase in muscle and bone mass.<sup>5</sup>

This study correlates with the study of Caroline S Fox<sup>13</sup> who states that the thyroid dysfunction is well recognized as a cause of weight changes. As weight loss is a frequent manifestation of hyperthyroidism, such patients when treated adequately gain nearly 4kg/year. Conversely weight gain is observed in hypothyroid patients and treatment with thyroid hormone results in modest weight loss.

Patients with hypothyroidism lose weight when treated and patients with hyperthyroidism gain weight when treated with carbimazole. Thyroid function may be an important determinant of body weight.

In hypothyroid patients receiving long term treatment with thyroid hormones, there was a strong association between increase in serum TSH concentration and decrease in resting energy expenditure which could result in significant weight gain over time. Low energy expenditure is associated with subsequent weight gain.

## CONCLUSION

This study concludes a large increase in the body and pituitary gland weight following treatment with carbimazole. Enlargement of pituitary gland results in increase in absolute weight. The increase in generalized body weight results in increase of relative weight of organ. The main factors contributing to excessive weight gain are assumed to be poor control of thyroid function and need for replacement therapy.

## REFERENCES

- 1 Brunova J, Bruna J, Joubert G, Koning M. Weight gain in patients after therapy for hyperthyroidism. *South African Medical Journal*. 2008;93(7):529.
- 2 Allahabadia A, Razvi S, Abraham P, Franklyn J. Editorial: Diagnosis and treatment of primary hypothyroidism. *BMJ*. 2009;338:b7253
- 3 Silva JE. The thermogenic effect of thyroid hormone and its clinical implications. *Annals of internal medicine*. 2003; 139(3):205-13.
- 4 Crocker MK, Kaplowitz P. Treatment of paediatric hyperthyroidism but not hypothyroidism has a significant effect on weight. *Clinical endocrinol* 2010; 73(6):752- 9.
- 5 Dale J, Daykin J, Holder R, Sheppard M, Franklyn J. Weight gain following treatment of hyperthyroidism. *Clinical endocrinology*. 2001;55(2):233-9.
- 6 Abraham P, Avenell A, McGeoch SC, Clark LF, Bevan JS. Antithyroid drug regimen for treating Graves' hyperthyroidism. *Cochrane Database Syst Rev*. 2010;1.
- 7 Bagchi C, Sinha DP, Tripathi SK. A suspected case of carbimazole-associated torsades de pointes. *Indian Journal of Pharmacology*. 2010;42(1):53.
- 8 Kostoglou-Athanassiou I, Ntalles K. Hypothyroidism-new aspects of an old disease. *Hippokratia*. 2010; 14(2):82.
- 9 Pears J, Jung R, Gunn A. Long-term weight changes in treated hyperthyroid and hypothyroid patients. *Scottish medical journal*. 1990;35(6):180-2.
- 10 Abid M, Billington CJ, Nuttall FQ. Thyroid function and energy intake during weight gain following treatment of hyperthyroidism. *Journal of the American College of Nutrition*. 1999;18(2):189-93.
- 11 Jansson S, Berg G, Lindstedt G, Michanek A, Nystrom E. Overweight--a common problem among women treated for hyperthyroidism. *Postgraduate medical journal*. 1993; 69(808): 107-11.
- 12 Bravernma LE, Utiger RD 2009 Introduction to hypothyroidism. *The thyroid: a fundamental and clinical text*. 9th ed. Philadelphia:Lippincott, Williams & Wilkins; 679-700.
- 13 Fox CS, Pencina MJ, D'Agostino RB, Murabito JM, Seely EW, Pearce EN, et al. Relations of thyroid function to body weight: cross-sectional and longitudinal observations in a community-based sample. *Archives of Internal Medicine*. 2008;168(6):587-92.

