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RESEARCH PAPER

THE EFFECT OF STRESS ON GLUCOSE METABOLISM AND GROWTH PERFORMANCE IN SPRAGUE DAWLEY RATS

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ABSTRACT

This study determines the dosage and duration dependent effect of cortisol-induced stress on glucose metabolism and growth performance. To achieve this objective, 35 Wistar rats, divided into group A as control, B as low-dose test (40mg/kg/bw), C as moderate-dose test (80mg/kg/bw), and D as high-dose test (160mg/kg/bw). The test groups were further divided into subgroups I and II, denoting the durations of the test-experiment (short term - 4 days and long term -8 days) respectively. In the course of the experiment, weight changes were monitored and blood samples were obtained for blood glucose analysis. The result showed that there was a significant dose/duration dependent weight loss ($p<0.05$) in all the test groups. However, in test group C and D, a non-significant dose/duration dependent increase in blood glucose levels was observed. Our findings suggest therefore, that increasing stress may lead to weight loss while ironically increasing blood glucose level; possibly by simultaneous induction of gluconeogenesis.

Keywords: Stress, Hydrocortisone, Glucose Metabolism, Overweight, Obesity.

INTRODUCTION

Cortisol is released in response to stress, sparing available glucose for the brain, generating new energy from stored reserves, and diverting energy away from low-priority activities such as the immune system in order to survive immediate threats or prepare for the exertion of rising to a new day (Scott, 2011). However, prolonged cortisol secretion (which may be due to chronic stress or the excessive secretion seen in Cushing's syndrome) results in significant physiological changes (Scott, 2011).

Cortisol, also known formally as hydrocortisone, is a steroid hormone, specifically a glucocorticoid hormone produced by the zona fasciculata of the adrenal gland (Scott, 2011); the second of three layers comprising the adrenal cortex. The cortex is the outer "bark" of each adrenal gland, situated on top of the kidneys. The release of cortisol is controlled by the hypothalamus, a part of the brain. It is released in response to stress and a low level of blood glucocorticoids. Its primary functions are to increase blood sugar through gluconeogenesis, suppress the immune system, and aid in fat, protein and carbohydrate metabolism (Hoehn and Marieb, 2010).

Clinical and experimental excesses of cortisol (Greminger et al., 1982; Connell et al., 1986) are respectively associated with increases in blood pressure and profound alteration of intermediary metabolism, resulting in characteristic obesity, insulin resistance, and changes in lipid metabolism.

Cortisol in high concentration is known to elicit many metabolic events (Eric et al., 2001). It has also been reported to play a more than permissive role when its plasma concentration does increase during stress. Its secretion which may be due to chronic stress has been said to affect the initiation of some chronic diseases like Rheumatoid Arthritis and idiopathic Arthritis (Akhigbe, 2007). This study investigates the effect of cortisol on blood glucose level and growth performance indicated by body mass using Wistar rats.

METHODS

Experimental Animals: Adult Wistar rats (35) of comparable weights (170 – 225 mg) were used for the study. They were purchased from the animal farm of Anthonio Research Centre, Anthonio Services Nigeria, Ekpoma, Edo State, Nigeria. They were fed with growers mash (produced by Grand Cereals Ltd, a subsidiary of UAO Nigeria PLC, Jos, Plateau State) which was purchased from an open shop in Ekpoma, Edo State Nigeria.

Animal Grouping: The animals were grouped into four groups (A – D); 5 rats per group. While group A served as the control, B, C and D formed the experimental group. The entire animals (Group A to D) received growers mash plus water given *ad libitum* during the acclimatization period.

Drug Administration: A randomized double-blind placebo-controlled comparison of 3 fixed intramuscular dosages of cortisol (40 mg/d, 80 mg/d and 160 mg/d) were prepared as described by (Newcomer et al., 2006) who used Low-dose (40 mg/d) treatment approximated glucocorticoids output during mild stress, while high-dose (160 mg/d) treatment approximated glucocorticoids output during maximal stress, spanning a range of glucocorticoids secretion relevant to physiological stress on animals.

The drug (Hydrocortisone Sodium Succinate BP 100mg) was mixed with sterilized water for injections BP 10ml (manufactured by VIFOR PHARMA PVT LTD, KSEZ KANDLA. The ratio of mixture was 1:1; that is 100mg of Hydrocortisone to 100ml of sterilized water.

After a period of two (2) weeks acclimatization, the animals were weighed before the experiment proper. The drugs were then administered via intramuscular route. Each member of the group was administered intramuscular cortisol as follows:

Group B_1 (Test I) 40 mg/d for four days.
Group B_2 (Test II) 40 mg/d for eight days.
Group C_1 (Test III) 80 mg/d for four days.
Group C_2 (Test IV) 80 mg/d for eight days.
Group D_1 (Test V) 160 mg/d for four days.
Group D_2 (Test VI) 160 mg/d for eight days.

Samples Collection: On the fifth day the rats in group A, B1, C1 and D1 were weighed, blood sugar level was determined and blood samples obtained with the aid of syringe and kept in EDTA anticoagulant fortified bottles. The experiment was repeated on the ninth day on groups B_2, C_2 and D_2.

Statistical analysis: The one-way analysis of variance (ANOVA) was employed in the data analysis using SPSS version 17. Results were presented as Mean ±SD at a level of significance $p \leq 0.05$.

RESULTS

Table 1 is a representation of the observed weight changes noted in the control and experimental rats during the experimental period. The animals in the control group showed no significant change in weight. The experimental groups that received the drug for four days (C1 and D1) and eight days (B2, C2 and D2) had a decrease in weight at the end of the experimental except for group B1 where weight gain was noted.

Table 2 is a representation of the observations on Blood Glucose levels (mg/dl) in the control and experimental groups. The mean blood glucose level (mg/dl) was observed to be highest in group D_2 (134.40±6.12) and lowest in group B_1 (100.00±6.12). The blood glucose level in group D_2 was significantly increased as compared to the control and group D_1 (same dose but different duration of drug administration) (see table 2).

Table 1 is a representation of the mean body weight changes recorded during the course of the experiment.

	Group A	Group B		Group C		Group D	
		1	2	1	2	1	2
Wt before exp (gm)	200.00 ±0.00	170.00 ±20.91	170.00 ±20.91	210.00 ±13.69	210.00 ±13.69	215.00 ±13.69	215.00 ±13.69
Wt after exp (gm)	200.00 ±0.00	195.00 ±11.18	160.00 ±22.36	205.00 ±11.18	170.00 ±11.18	210.00 ±13.69	165.00 ±22.36
Δ (gm) in wt	0.00.00 ±0.00	25.00* ±9.73	-10.00* ±1.45	-5.00* ±2.51	-40.00* ±2.51	-5.00* ±0.00	-50.00* ±8.67

All values are expressed as mean ± standard deviation. Means in a row with different asterisks (*) are significantly different at the p>0.05 level. Wt = Weight, Δ = difference (Wt after Exp – Wt after Accl).

Table 2: Presentation of observed blood glucose level in the experiment

	Group A Control	GROUP B		GROUP C		GROUP D	
		1	2	1	2	1	2
Glucose level(mg/dl)	109.00 ±7.11	100.00 ±6.12	101.80 ±8.67	116.00 ±14.50	113.80 ±18.49	121.20 ±10.13	134.40* ±23.90

Values are expressed as mean ± standard deviation. Means in a row with different asterisks (*) are significantly different at the p>0.05 level.

DISCUSSION

The observed dosage dependent feeding pattern of the test groups in this study aligns with the findings by Barton et al. (1987) that chronic cortisol administration causes both loss of appetite and aggressive feeding behavior in fish, which might explain the loss of weight among individuals engaging in regular stressful activities.

However, the observation that cortisol induced weight loss while ironically increasing blood glucose level, contradicts the report by Sandberg (2008) that high blood sugar or glucose level correlates with being overweight and rapid weight gain. Even the fact that high insulin levels trigger fat storage in the body following high blood sugar, implies that weight loss is more difficult when the glucose level is high (Sandberg et al., 2005).

Interestingly, the control of glucose and ketone body metabolism is integrated by a variety of hormones. The actions of insulin –a major anabolic hormone, is antagonized by rapidly acting catabolic hormones like glucagon and catecholamines, while others like thyroid hormones, growth hormone and cortisol, have more delayed effects (Johnston et al., 1982). Cortisol in particular, acts via the mechanism that induces the release of fatty acids from triacylglycerol stores and breakdown of muscle proteins; counters insulin by encouraging higher blood sugar while stimulating gluconeogenesis; promotes gluconeogenesis by increasing the cellular concentration of pyruvate carboxylase in the liver tissue; and triggers the expression of enzymes critical for gluconeogenesis (Michael, 2011).

It is obvious therefore, that the role of cortisol in mobilizing glucose in response to fright/flight/fight is a homeostatic response that depends on its potential to induce gluconeogenesis and glycogen synthesis, but our finding suggests that cortisol simultaneously trigger mechanisms that have negative influence on body weight and in a manner that possibly maintains physiological balance.

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AUTHOR(S) CONTRIBUTION

All the authors contributed towards the completion of this study and the presentation of this manuscript.