



Acute stress, salivary cortisol and calcium ions, in patients undergoing dental extraction procedure

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Abstract

Stress is well approved to be co-related to the dental extraction procedure, and linked to the increase in cortisol levels in patients undergoing dental treatments. Bone affected vastly by exposure to cortisol and that is mainly due to scavenging of minerals (calcium and phosphorus) from the bone by cortisol to be consumed as a fuel and energy source in the process of gluconeogenesis; hence, alter the density of bone and can cause substantial deterioration in bone quality and quantity. Cortisol can be influential on the function of both the osteoblasts and the osteoclasts and that will demonstrate significant changes on bone as well. This research investigated the relation between the levels of cortisol and calcium ions with the degree of stress before and after routine dental extraction.

Fifty two participants were included in this study, all met the inclusion and exclusion criteria designated for the research; they were subdivided into 2 groups, first group was admitted to salivary cortisol evaluation, and salivary calcium ions were achieved for the second group.

The collected data represent a significant increase in both salivary cortisol and salivary calcium ions in the post – dental extraction group when compared to the pre-extraction group. The evaluated salivary cortisol with mean of 4.589 ± 0.819 mmol/L for pre- extraction while, in the post-extraction the mean was 5.364 ± 1.017 mmol/L with a significant changes. The salivary calcium ions mean were 5.66 ± 0.985 mmol/L, while for the post-extraction mean was 6.380 ± 1.161 mmol/L with a significant changes .

The findings of this research gave an insight that stress plays an essential role in altering both salivary calcium ions and cortisol levels in the post-extraction period, as both increased significantly.

Key words: Stress, dental stress, salivary cortisol, salivary calcium.

Introduction

Stress can have profound effects on human physiology. Human attempts to explain major concepts of stress using a stimulus-response prototype, broadly on a psychobiological sensory operation system.

Cortisol is the main a glucocorticoid hormone synthesized from the zona fasciculata of the adrenal

cortex. Cortisol functions as a regulator for body mechanisms during stressful situations, its effect on increasing blood glucose level, reduction in immune response, and affects the body proteins and lipids ⁽¹⁾.

Bone formation and the relation to cortisol had been widely investigated and it has been noticed that the

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mechanisms of healing and formation reduced in relation to the increase in cortisol ratio; Chyun et al. tested the inhibitory effect of cortisol on bone formation and they proved that bone development is considerably decreased when the ratio of cortisol increased above normal levels ⁽²⁾. Many Researches have been focusing on the mechanisms by which cortisol inhibits the formation of bone and remineralisation process; decline in osteoblasts function, reduction of the re-uptake of calcium and phosphorus ions into the bone, and bone mineral resorption by the removal of the minerals components of bone, were all linked to the increased levels of cortisol, hence, the reduction in bone density ^(3, 4).

Dental extraction usually associated with stress. Many individuals are correlated to the predicted increase levels of cortisol which in turn can have an effect on calcium metabolism and bone formation ⁽⁵⁾. These changes could relate between oral surgery, salivary cortisol, and calcium levels.

The main aim of this pilot study was to assume a model that co-relate between the salivary cortisol and salivary calcium ions levels induced by teeth extraction procedure in whole saliva due to stress.

Material and Methods

The study was conducted in the department of Oral surgery, Al Mustansiria dental college, after approval by the institutional ethics committee and informed consent was acquired from all the patients prior to the conduction of the research process.

Total of fifty two participants were included in this study; the age mean was (34.5 ± 7.3) , all met the inclusion and exclusion criteria designated for the research. The inclusion and exclusion criteria were tailored in dependency with the major elements

that may alter the cortisol and calcium levels within the body. The study inclusion criteria: patients 18-45 years old, healthy, non- smoker and/or alcohol drinker, and required single tooth extraction. Exclusion criteria: Patients with or had any systemic disease (endocrine and metabolic) or using any type of medication and supplementation that may have an influence on the Hypothalamus Pituitary Axis (HPA) or may alter the calcium levels ^(6, 7, 8) were excluded; Furthermore, long term unemployed patients were excluded from the research as that may have an influence on the body cortisol levels ⁽⁹⁾. Pain, stress, and anxiety all are subjective attitudes and they have no direct methods for their measurement, hence the utilization of the Visual Analogue Scale (VAS) and the Hospital Anxiety and Depression Scale (HAD) as our measurement instruments. Any patient who scored more than 7 on the visual analogue scale (VAS) in the immediate post extraction period was excluded from this study ⁽¹⁰⁾. The participants were subjected to Hospital anxiety and depression scale (HAD); to ensure that the levels of cortisol are not affected by external influence of anxiety and depression which may alter the levels of cortisol ⁽¹¹⁾.

The collected patients' samples were divided into two main groups, first group dedicated to measure the cortisol levels while, second group was allocated as the calcium ions measurement group ; both groups were further subdivided into two sub-groups to measure the pre and post dental extraction effect of stress. The sample collection procedure based on chewing a cotton roll to stimulate salivary secretion (we avoided the use of citrus acid based salivary stimulants such as lemon because they have the potential to change salivary cortisol concentration which maybe reflected on our sample accuracy) ⁽¹²⁾. The

patients were asked to wash their mouth thoroughly prior to collection of saliva to remove food debris to ensure purity of saliva⁽¹³⁾. In order to control for the circadian rhythm of cortisol, all the procedures were preformed between 9 am and 11 am. The samples of saliva were collected at the same time frame of the day to avoid any changes in the circadian rhythms of both calcium and cortisol which may alter the standardized protocol of the research^(14, 15).

The samples were collected and sent for analysis and interpretation, which had been carried out in the clinical chemistry laboratories, college of dentistry, Al- Mustansiria University.

The analysis employed assay that employs the competitive inhibition enzyme immunoassay technique using Cortisol ELISA kit – (Accubind: Monobind) USA. Immunoassay was used to measure an anti-antibody specific to the antibody of cortisol has been pre-coated onto a microplate. Enzyme immunoassay requires essential reagents to produce efficient results. The calcium ions analysis was achieved using spectrophotometer kit, Biomegrb, Tunisia. Statistical analysis was performed using SPSS statistical software (version 22). ANOVA and t-test were applied to obtain the significance and test the hypothesis. Correlation between the examined groups was conducted depending on Person correlation test.

Results

The statistical evaluations of salivary calcium levels before and after extraction were listed in table one. The statistic evaluations of salivary cortisol level were listed in table two. The summarized data within the tables show that the pre and post extraction statistical values of both the calcium ions and cortisol dramatically changed.

Salivary cortisol and calcium ions showed significant changes in relation to dental extraction procedure; the results according to the p-value were significant (Table 1, Table 2). Figures one and two describe the means of the calcium ions and cortisol. The post-extraction means went up sharply in both of them. Positive person correlations between the expected and observed results were obtained; the plots showed data distribution in relation to the mean and the standard deviation. Figures 4, 6, 8, and 10 demonstrated the medians of the results and data distribution.

The calcium ions concentrations were significantly changed in the post extraction period with a mean of 6.38 ± 1.161 , when compared to the pre extraction concentrations which were demonstrated with a mean of 5.66 ± 0.985 ; table-1 give a comprehensive statistical analysis for the salivary calcium ions. The significant changes in salivary cortisol which are demonstrated in table-2 revealed that the post extraction period had a higher cortisol concentration in saliva with a mean of 5.364 ± 1.017 when compared to the pre extraction levels which were demonstrated with a mean of 4.589 ± 0.819 .

Discussion

According to the World Health Organization stress is the second most frequent health problem⁽¹⁶⁾. It is widely accepted that psychological stress can produce effects in a variety of physiological systems that are similar to those produced by physical challenges due to activation of two stress response systems. These systems are the sympathetic or autonomic system and the hypothalamus-pituitary-adrenal axis (HPA axis)⁽¹⁷⁾. Situations involving pain, anxiety and acute tissue injury which in turn enhance the secretion of cortisol.

Increase the activity of the HPA axis boost's these problems and included an alarmingly high incidence of cardiovascular disease, ulcers, and bony problems. The healing potential of bone, whether in a fracture or fusion model, is influenced by a variety of biochemical, biomechanical, cellular, hormonal, and pathological mechanisms ⁽¹⁾. Many Studies reported that dental operation confirms a wide variety of stress-related physical and emotional problems.

Numerous acute stressful experiences are not inherently very harmful, yet are associated with great pain and anxiety. The characteristics and experiences that the person brings to the situation are more important than any objective characteristics of the experience itself in determining how aversive the experience will be ⁽¹⁸⁾. Dental procedures can affect neuroendocrine axis; hence, the increase of cortisol secretion which is associated with anxiety and stress due the dental stimuli ⁽¹⁹⁾.

There is consistent evidence from a substantial number of studies that long-term exposure of the osteoblast to glucocorticoids results in decreased cell proliferation and reduced protein synthesis, the long term exposure will reduce osteoblasts function by decrease the expression of cyclin-dependent kinases and it will leave an effect on the genes that promote osteoblasts formation and functions ^(20,21). Osteoclast function can transformed by long term exposure to cortisol and glucocorticoids, different stages of these cells life cycle can be altered by this exposure and that will lead to promotion of cells production from the bone marrow, which will reduce the bone quality and quantity ^(22,23). There is greater agreement that circulating concentrations of parathyroid hormone are increased in patients with glucocorticoid excess and Hyperparathyroidism has been

demonstrated with acute infusions of glucocorticoids ^(3, 24, 25). Chiodini et al. pointed out; that patients with Cushing's syndrome, a condition of hypercortisolism, have reduced bone formation, lower bone density and an increased incidence of osteoporosis and fractures ⁽²⁶⁾.

The result of the current study predicted increasing both salivary cortisol and calcium concentration with stress. The relation between cortisol and bone is well established, cortisol exhibits its effect on bone mainly by affecting the calcium levels and metabolism; however, this relation is not linked yet to dental procedures, especially to dental extraction; although, few studies pointed out that long term exposure to cortisol can have an effect on the periodontal health condition, and it can responsible for bone resorption ^(27, 28).

The evaluated correlation values were positive before extraction with observed same behavior after extraction. These changes could be attributed to stress effect of extraction procedure.

The correlation between dental extraction and the stress accompanying the procedure is well demarcated, and linked to the increase in cortisol levels ⁽⁵⁾ this study demonstrated three major components which are stress, cortisol, and calcium levels, in relation to the dental extraction procedure; and the interrelation with each other.

The cortisol and calcium ions levels were following the same pattern as stress and it is very clear from the results that the significant increase in salivary cortisol is accompanied by a substantial increase in salivary calcium ions in the post-extraction period (Fig.1, Fig.2)..

Further research is recommended because changes in salivary calcium ions and salivary cortisol levels can be associated with bone healing and other potential pathological conditions which

necessitate additional work for confirmation.

In summary, the study findings suggested that endogenous cortisol within the normal range is negatively associated with increased calcium ions; however, both cortisol and calcium ions can be connected to the stressful event of dental extraction.

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Table-1: Statistical Analysis for calcium ions collected from saliva

Function	Group one (before extraction)		Group two (after extraction)
N0. of samples	26		26
Mean ± SD	5.66±0.985		6.38±1.161
Variance	0.97		1.34
Range	3.3		4.7
95% Confidence interval for mean	Lower Bound	5.27	5.91
	Upper Bound	6.06	6.84
Statistical Correlation	1. 0		0.76
P≤ 0.05 between the groups	0.001		

Table-2: Statistical analysis parameters for the cortisol in saliva

Function	Group one (before extraction)		Group two (after extraction)
N0. of samples	26		26
Mean ± SD	4.589± 0.819		5.364 ± 1.017
Variance	0.671		1.036
Range	3.30		3.70
STD. , Error of mean	0.154		0.192
95% Confidence interval for mean	Lower Bound	4.27	4.96
	Upper Bound	4.90	5.75
Statistical correlation	1.0		0.438
P≤ 0.05 between the groups	0.02		

Figure 1. The comparison between the pre and post extraction means of the salivary cortisol.

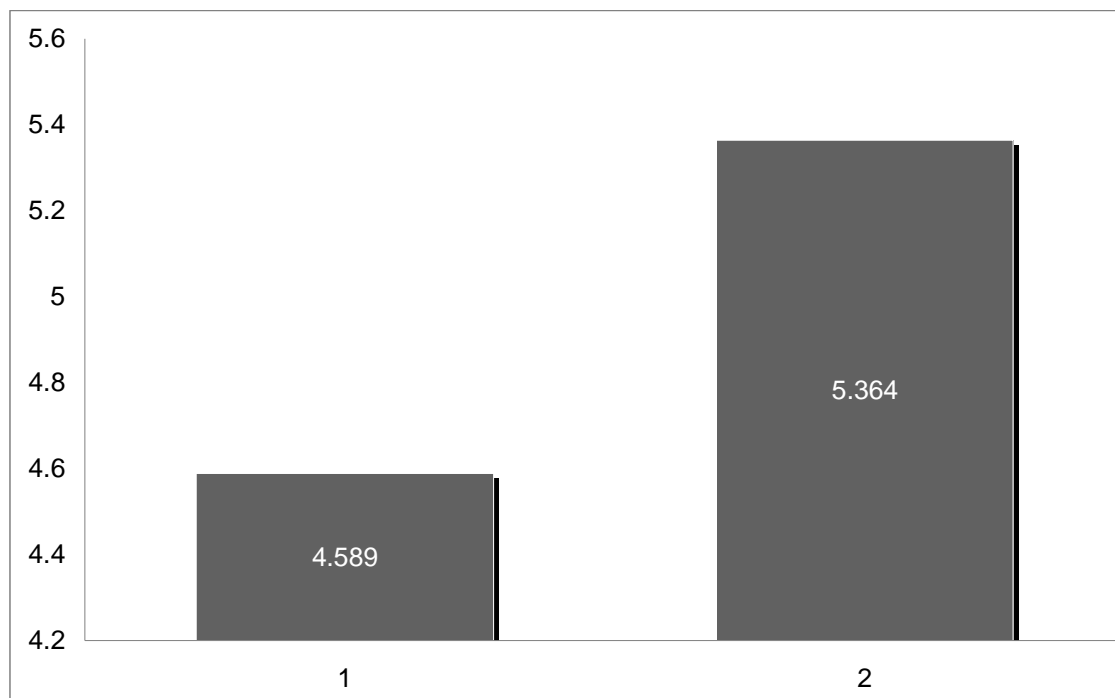


Figure 2. The comparison between pre and post extraction means of the salivary calcium ions.

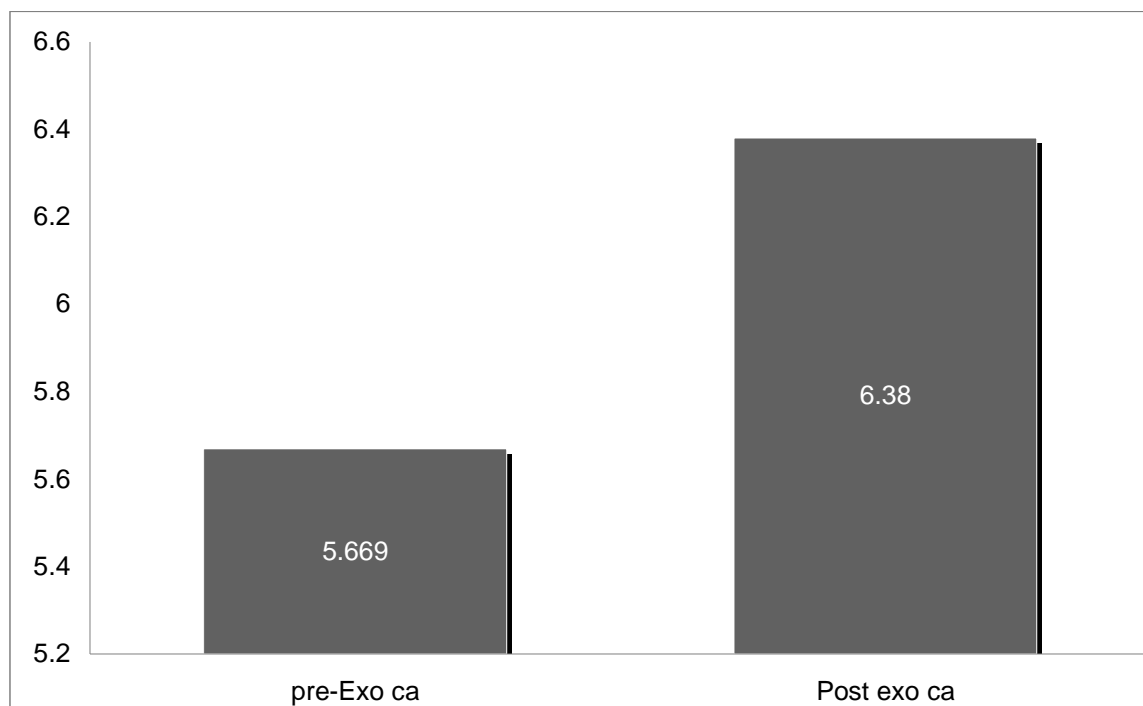


Figure 3. The plot of normal probability expected probability distribution for salivary calcium.

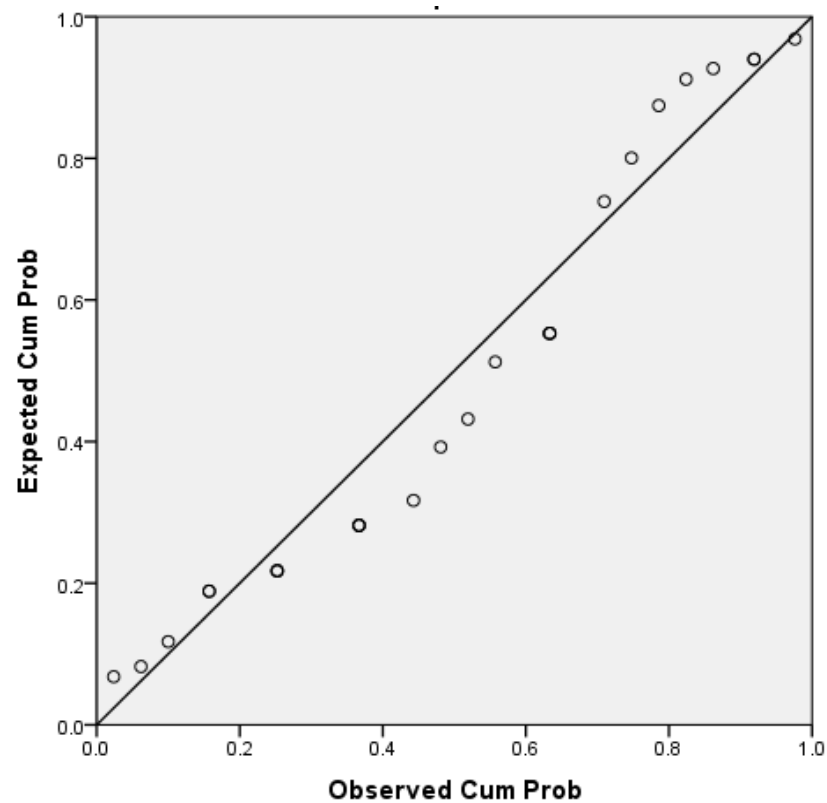


Figure 4. Pre-extraction calcium box-and-whisker plot

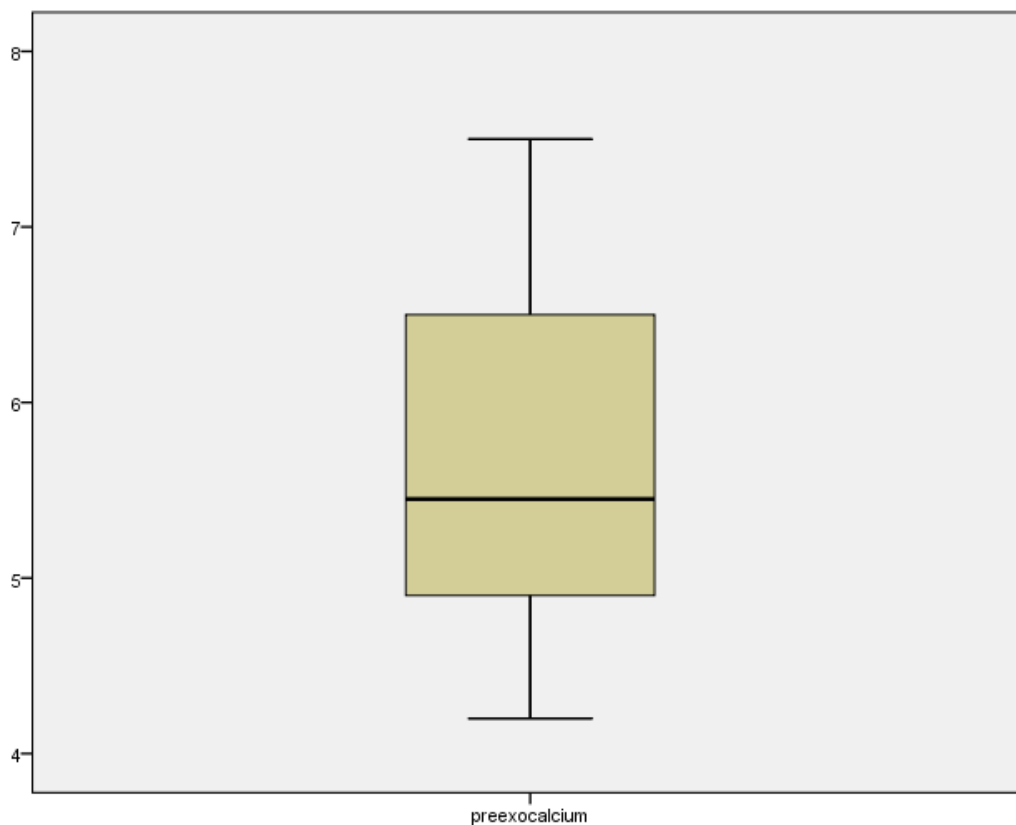


Figure 5. post extraction calcium normal probability plot.

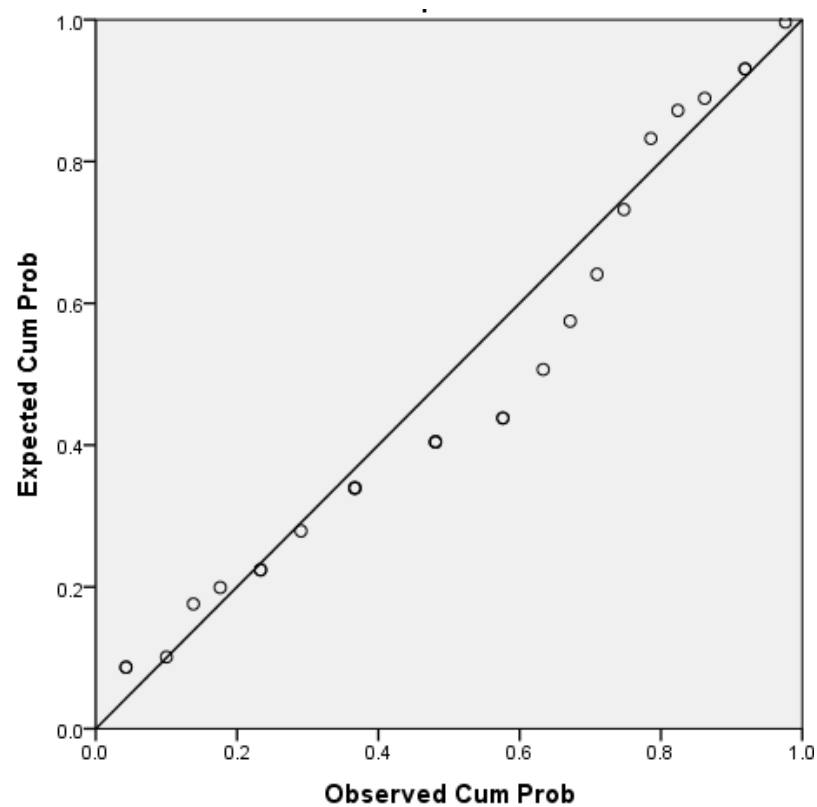


Figure 6. Post extraction calcium box-and-whisker plot

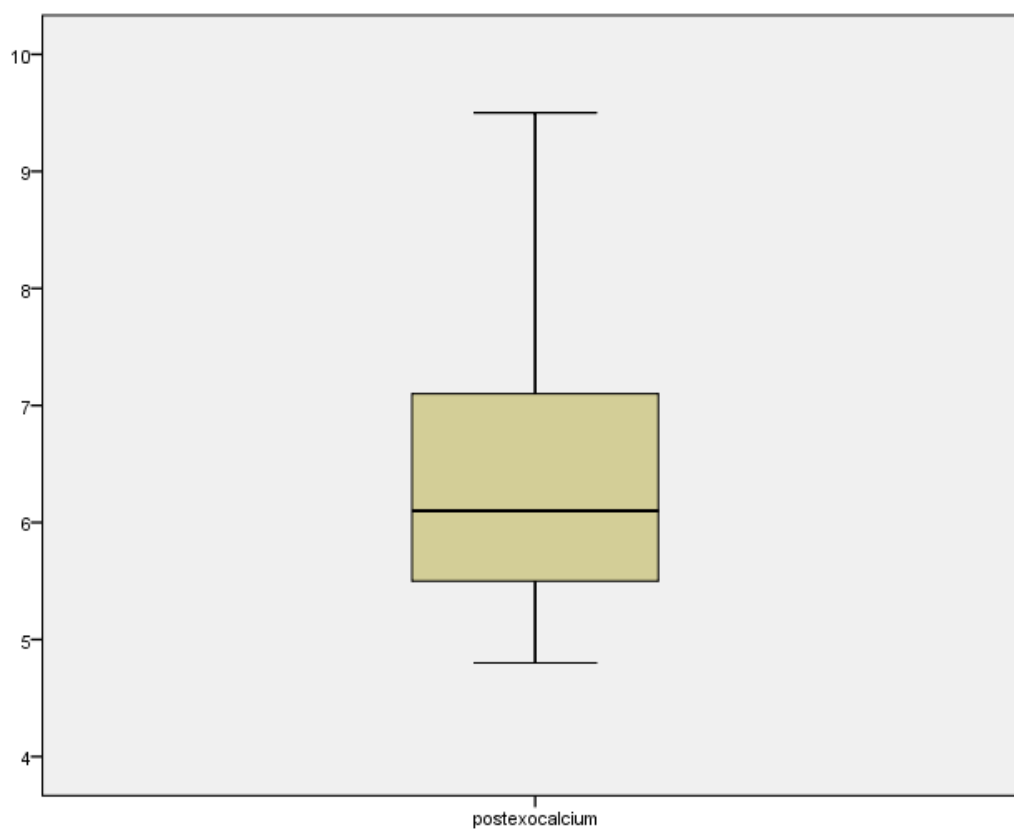


Figure 7. Normal probability plot for pre-extraction cortisol

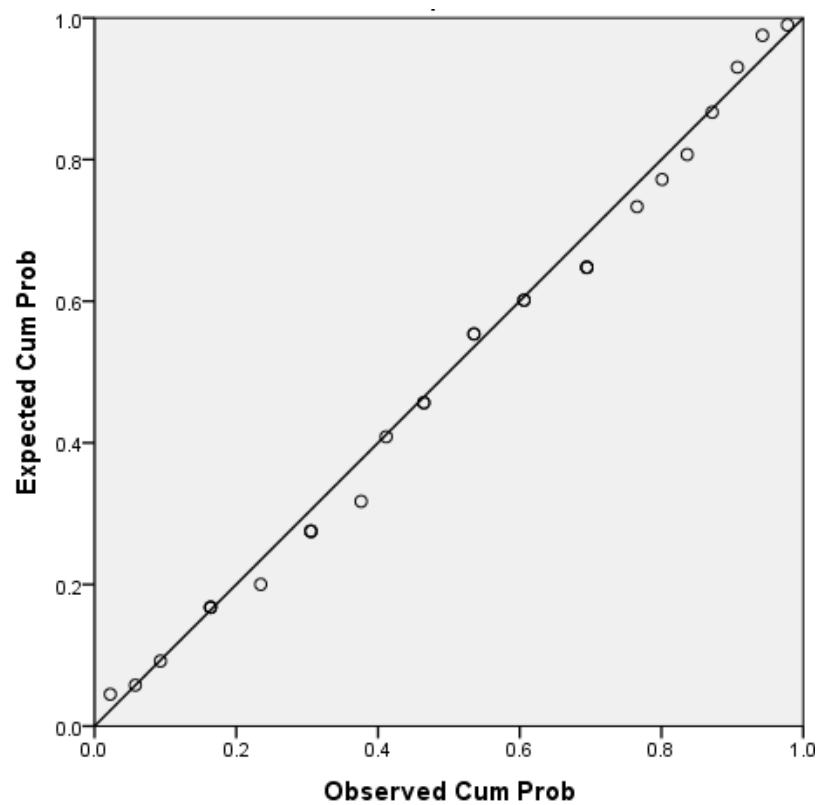


Figure 8. Pre-extraction cortisol box-and-whisker plot

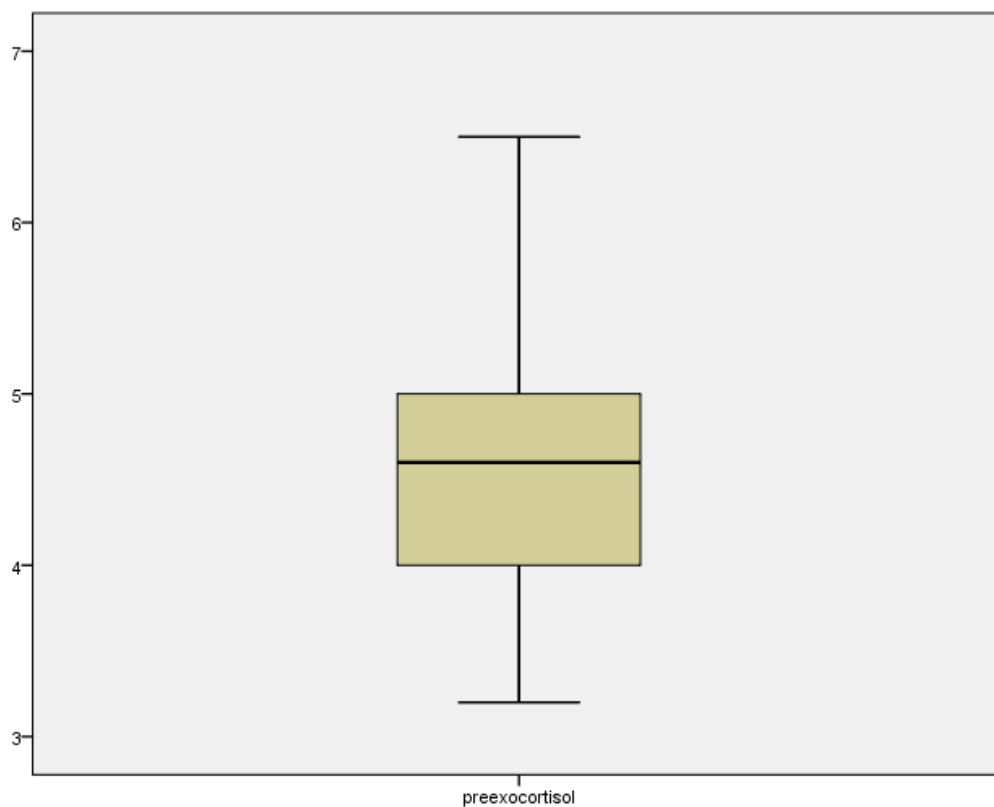


Figure 9 . The plot of normal probability expected probability distribution for salivary cortisol

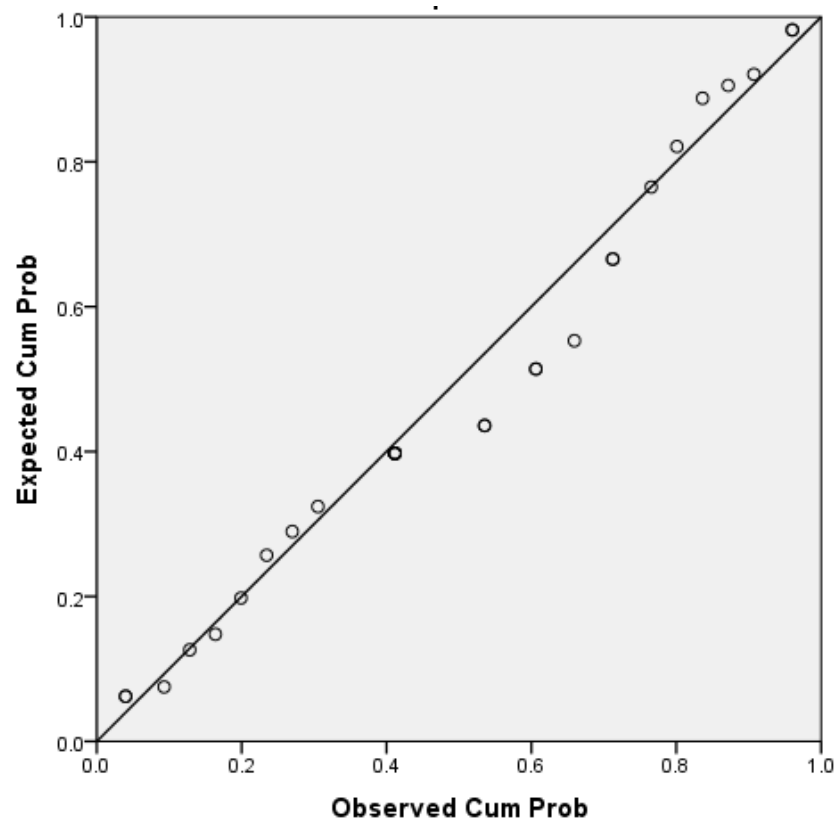


Figure 10. Post-extraction cortisol box-and-whisker plot

