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THE AUSPICIOUS EFFECTS OF FASTING ON SUGAR-REGULATING HORMONES

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Abstract

Objectives (Background):The purpose of this study is to categorize the baseline of the sugar-regulating hormones in pre-fasting and diabetic humans.Methods:This study has involved 30 normal subjects and 26 diabetic patients for investigating the effect of Ramadan fasting on their glucose regulating hormones. By taking pre-fasting, fasting, and post-fasting samples of the same subjects, the effect of fasting on the glucose regulating hormones was investigated. Results:Significant effects of fasting were observed on all the hormones by some being more affected than the others. Additionally, fasting appears to affect some hormones in different ways between the normal and diabetic subjects. It also appears that the regulation of these hormones is more control in the normal subjects than the diabetics resulting in tight control of the glucose within the normal range during fasting in normal subjects. Conclusion:Compared to the normal, diabetics showed improved regulation of their glucose after fasting. This may indicate that fasting does improve the regulation of glucose and possibly of the glucose regulating hormones.

Keywords: Diabetic patients, Fasting, Ramadan, Sugar-regulating hormones

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Introduction

Duration of voluntary abstinence after food and drink can be practiced subsequently by individuals globally. Changed concentration in fasting schedules can be evidenced by a plethora of popular press publications and diet recommendations [1]. Though, scientific indication for the healthiness during intermittent fasting in humans can be often inferred from animal studies, which is usually created on experimental data on religious fasting, specifically during Ramadan, or can be consequent from observational studies with modest sample sizes [2].

Glucose stability in movement can be firmly sustained in standard range by dynamic regulation from glucose creation and glucose usage within peripheral tissues, the liver, muscle, fat, and kidney [3]. Insulin is the main controller of glucose balance as it lowers postprandial plasma glucose by growing glucose interest and usage from peripheral tissues, and decreasing gluconeogenesis and glycogenolysis. Patterson and Sears [3] stated that counterregulatory hormones compared to insulin action such as glucagon and epinephrine, avoid hypoglycemia by growing gluconeogenesis and glycogenolysis, and lessening glucose uptake and ingesting from peripheral tissues in the period of fasting.

Several studies concerning intermittent fasting in animal models and volunteers have addressed significant effects including glucose homeostasis and enhanced insulin sensitivity [4-6]; enhanced performance and metabolic efficiency throughout exercise, elevated life expectancy and alertness [7-11]. On the contrary, a number of studies have reported adverse events as an outcome of intermittent fasting. Hypoglycaemia, ketoacidosis, dehydration, thrombosis, and hypotension are exhibited from diabetic individuals undertaking intermittent fasting [6, 12]. A significant elevation in blood pressure and total cholesterol was shown in middle-aged men [13]. Elevated plasma concentrations have also been reported in different studies following daily fasting for one month, which recommend changed circadian rhythms [14-20]. Intermittent fasting may lead to the deterioration of glucose tolerance in non-obese women and cause reduced energy expenditure in young women [21, 22].

The purpose of this study is to categorize the baseline of the sugar-regulating hormones in pre-fasting and diabetic humans. The indication for the well-being during fasting in humans can

be often induced from animal studies particularly rats, based on observational data on religious fasting (specially Ramadan), or derivative from investigational studies with modest sample sizes.

Methods

Blood samples were collected from 26 Type II diabetic patients attending the Diabetic Clinic at King Abdul-Aziz University Hospital just before Ramadan. These are the Pre- Ramadan samples. The samples were processed similarly as described below:

NormalAdults

Blood samples were collected from 30 non-diabetic normal subjects just before Ramadan. Fasting blood samples were collected from both normal and diabetic patients at mid-day (10^{th}-15“) Ramadan in plain (red-top) Vacutainertubes. The specimens were allowed to clot for 10-15minutes. Thetubeswerethenspunat10,000rpminacold(l0°C)centrifugefor10minutes. Theserawerethenseparatedintonewlabeledtubesandstoredat-20°C.

Post-RamadanSamples

After Ramadan, fasting blood samples were collected from the same subjects at 8 am during the middle of the month of (10^{th}-15^{th}) Shawwal for normal volunteers and up to the end of Dhu‘l-Qi‘dah for the diabetic patients. Blood samples were collected in plain (redtop) vacutainer tubes. The specimens were allowed to clot for 10-15 minutes. The tubes were then spun at 10,000 rpm in acold (10°C) centrifuge for 10 minutes. The sera were then separated into new labeled tubes and stored at -20 °C until analysis.

Statistical Analysis

Data obtained from the various measurements were organized and entered into a spread-sheet program (Microsoft EXCEL) where further mathematical, simple descriptive statistical (mean, standard deviation and standard error of the mean) and graphical treatment of the data were carried out. Statistical analysis of the data included F-distribution, parted and unpaired Student's I- tests, correlation tests and graphical presentations of correlations were carrying out using the statistical package program SPSS.

Results

The following are tabulated and graphical results for the normal and diabetic subjects involved in this study. The results are those, which were measured for blood samples collected before (Pre), during, and after (Post) Ramadan periods. As mentioned above, the number of volunteers dropped from the initial 34 normal to 26 normal and 26 diabetics to 21 diabetics on Ramadan and 22 normal and 20 diabetics after Ramadan (Table 1). The Ramadan results showed an increase, decrease or no change from those of the pre-Ramadan values for the same subjects (Tables 2-3).

Table 1: The effect of fasting on the levels of glucose regulating hormones in healthy adults

Change	**Hormones & number of subjects**							
	INSULIN	**CORTISOL**	**E2**	**TESTO**	**PTH**	**TSH**	**T3**	**T4**
Increase	9	12	15	16	17	20	15	11
Decrease	17	14	11	10	9	6	111	5
No change	0	0	0	0	0	0	0	0

Table 2: Post-Ramadan results shows an increase, decrease or no change from those of the pre-Ramadan values for the same subjects

Change	**Hormones & number of subjects**							
	INSULIN	**CORTISOL**	**E2**	**TESTO**	**PTH**	**TSH**	**T3**	**T4**
Increase	12	13	15	11	17	11	19	16
Decrease	10	9	7	11	9	11	3	6
No change	0	0	0	0	0	0	0	0

Table 3: Post fasting levels of glucose, cholesterol, TG, HDL-Cholesterol, LDL-Cholesterol in healthy adults. The result shows an increase, decrease or no change from those of the pre-Ramadan values for the same subjects.

Glucose	**Cholesterol**	**TG**	**HDL-Cholesterol**	**LDL-Cholesterol**
15	11	6	12	14
7	10	15	10	8
0	1	1	0	0

Significant differences were observed for male population between testosterone ($p<0.01$), cortisol ($p<0.005$), and PTH ($p<0.01$) levels in diabetic and normal subjects. Apart from the obvious differences in glucose levels ($p<0.0001$), significant differences were also observed between cholesterol ($p<0.001$), triglycerides ($p<0.05$), and LDL-cholesterol ($p<0.001$). These differences in hormones and between the two groups were basic initial differences that were not controlled since the groups came with a random background of diet and lifestyle (Table 4).

Changes in cortisol were the major significant hormonal difference between the two groups, with higher cortisol values in fasting diabetics than normal subjects ($p<0.001$). With the obvious difference in glucose, Ramadan cholesterol, triglycerides and LDL-cholesterol values were significantly higher in diabetics than normal ($p<0.001$, $p<0.001$ & $p<0.05$ respectively). These differences in values when compared to the pre-Ramadan values may suggest that some type of control may begin to show in diabetics. Indeed, significant changes in TSH ($p<0.05$) values between pre-Ramadan and Ramadan as well as between Ramadan and post-Ramadan ($p<0.05$) values were observed in diabetics (Table 4).

Table 4: Correlation Statistics for pre-Ramadan and post-Ramadan samples

Samples	Male population	Female population
Testosterone (nmol/L) VS Estradiol (pmoI/L)	r=0.724 p<0.01 n=12	r= 0.621 p<0.01 n=12
Testosterone VS FT3	r=0.738, p< 0.05, n= 12	r=0 860, p<0.05, n =12
Testosterone VS HDL-Cholesterol	r= 0.753 p<0.01 n=12	r= 0.635 p<0.01 n=12

Several significant positive and negative correlations were observed between the hormones with each other on one side, the hormones, and the dependent analyses on another side. The varied spectrum of correlations suggested that there is an intricate and interdependent system of regulation between these and possibly other hormones and factors. It is important to realize that those hormones measured may not be the only ones involved in the universal balance of glucose and related analytes in the body. Additionally, those hormones, while they may be involved in the regulation of glucose directly or indirectly are only operatable. Certainly, they are involved in

several body functions, which in turn may be affected in one way or another by fasting (Table 5).

Table 5: Significant correlations in the diabetic subjects

	Correlation between	**Correlation Coefficient (r)**	**Significance**
Pre-Ramadan (N = 21)	Cholesterol & LDL-Cholesterol	0.783	P = 0.0001
Ramadan (N = 20)	FT3 & E2 PTH & E2	0.764	P<0.0001
		0.827	P<0.0001
Post-Ramadan (N= 20)	FT3 & E2	0.765	P<0.0001
	FT3 & Testosterone & E2	0.711	P<0.001
	Cholesterol &LDL-Cholesterol	0.743	P<0.001
		0.875	P<0.0001

Discussion

The fasting Ramadan results showed an increase in glucose in 23 out of 26 subjects (88.5%) when compared to the pre-Ramadan values. This increase is a clear reflection of the fact that glucose regulation, mainly by increasing gluconeogenesis has been well established in these individuals since the blood samples were collected at mid-day during the middle of Ramadan (days 15-17). Glucose regulating hormones were affected by fasting in that there seems to be a balance between them in the increase or decrease with the net effect of increasing glucose through gluconeogenesis. While insulin was decreased in 17 out of 26 individuals (65.4%), TSH, T3, testosterone, PTH, estradiol all were increased in various proportions in more subjects. T4 and cortisol were decreased in more subjects than those who showed an increase. On an individual basis, there appears to be various increase and decrease, in that regulation of glucose through altering hormone levels was a function of the individual and could be well-linked to various factors such as diet type, time of last meal, physical, physiological and psychological factors. Each normal subject has his unique system of regulation of glucose through fine-tuning of the various hormones.

The striking outcome from this study is the increase in testosterone levels in male subjects during Ramadan. The increase in this hormone will likely boost various body functions such as

improvement of stamina, improving muscle mass and activity, and similar manly traits. Since sexual abstinence during fasting, the hormonal functions of testosterone were redirected towards improving the manly characteristics. Testosterone (mainly in males) showed a significant increase during Ramadan when compared to the pre-Ramadan ($p<0.01$) values in diabetic subjects. Although value-wise when glucose is considered, no significant change was observed, nevertheless, there seems to be a slow adaptation on an individual basis, which became clearer after Ramadan [23-27]. The change in cortisol was the most significant difference between the normal and diabetics in the post-Ramadan period ($p<0.05$). In addition to the difference in glucose, the post- Ramadan values were significantly different for cholesterol ($p<0.02$) and LDL-cholesterol ($p<0.05$). Signs of better control appeared more clearly in the post-Ramadan values for diabetics. The triglycerides did not show a significant increase in diabetics over the normal subjects. On an individual basis, glucose values are lower in the post-Ramadan period than the Ramadan and pre-Ramadan values. T4 levels show a significant increase after Ramadan when compared to the pre-Ramadan values ($p< 0.01$) and noticeable but not significant increase when compared to the Ramadan value [23-27].

This; together with other alterations during Ramadan, is strong tools to improve the quality of human being life. It is also noticeable that during the Ramadan period there is a much tighter control on glucose to remain within a smaller range than the pre-Ramadan or post-Ramadan values. This tight control is a desirable target in all individuals especially diabetics. The unique regulation processes during Ramadan becomes more obvious when the post-Ramadan results were observed. T3 and estradiol were more markedly increased than in the Ramadan period. T4, insulin, and cortisol were increased in more individuals whereas testosterone and PTH were decreased in more individuals when compared to the pre-Ramadan values. TSH is only increased in half of the subjects. Fasting effects also showed a decrease in cholesterol and triglycerides in more individuals, whereas HDL-cholesterol was increased in more individuals. These findings were encouraging as fasting of Ramadan was quite effective in reducing the risk of heart disease and related problems [28, 29].

The major limitation encountered so far included subject compliance, especially the diabetic patient who initially shown some willingness to participate fully but they cannot keep their commitment. The workers exerted tremendous efforts to follow and convince these subjects to continue with the full study at least pre, during, and after Ramadan. This resulted in the rather

delayed analysis and data acquisition and interpretation, as the samples had to be collected first before analysis for the hormones and other analyses. This is because the hormone assays come in the form of too expensive kits of the specific number of tests that have to be carried out in one or two close dates.

Insulin would be acknowledged as a potent hormonal regulator of both glucose appearance and disappearance during the rotation. Next, diabetes would be observed as a mono-hormonal disorder categorized by absolute or relative insulin deficiency. Although it is explored that, insulin can be the only pillar of therapy for patients through insulin-deficient type 2 diabetes. This study is beneficial for the doctors, medics, researchers and patients who further wants to investigate and understand the formation of the base-line of the sugar-regulating hormones in pre-fasting normal and diabetic subjects. It further states the possible correlation between the various measured parameters in the normal and diabetic subjects during fasting. Sex variations in the correlations have also been observed in the diabetic subjects in the three periods, pre-Ramadan, Ramadan, and post-Ramadan.

Conclusion

In conclusion, the effects of fasting on the glucose regulating hormones showed very significant effects both on the human and animal models. Glucose concentration of all the subjects were clearly controlled in normal human subjects during fasting in Ramadan. The impact of fasting on sugar-hormones were quite evident. It can be marked that 65% of subjects have decreased the level of insulin during Ramadan. TSH levels, Testosterone, PTH, Estradiol, and Cortisol were also seen to be increased. Post-Ramadan values showed improved control of glucose and suggested that regular fasting introduce beneficial effects and may improve the quality of life for these patients. It turns up that stimulating and diverse sort of correlations can be found among the hormones and glucose, and extra analytes with the improvement of fasting.

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Declaration:

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Conflict of interest: The authors declare that there is no conflict of interests regarding the publication of this paper.

Ethical Approval: This project was approved by the College of Medicine and King Abdulaziz University Hospital and

Consent of Participate: The patients' and normal volunteers' consents were taken after the explaining of the purpose of the study to each participant before taking the samples.

Consent for Publication: I agree that the content of this manuscript will not be copyrighted, submitted, or published elsewhere (including the internet), and I also agree to transfer all copyrights to SN Comprehensive Clinical Medicine.

Authors' contributions:

Hamed Khojah was responsible for the overall running of the project. All participant contributed equally in running the samples, collecting and analyzing the data, and writing the manuscript draft.

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