RESEARCH ARTICLE

The effect of Ramadan fasting on serum osmolality in diabetic patients

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Abstract

Objective: To observe the changes of osmolarity levels due to fasting in Ramadan among type 2 diabetic patients.

Method: The observational study was conducted from May 16 to June 3, 2019, at the Istanbul Medeniyet University, Istanbul, Turkey, and comprised adult type 2 diabetic patients of either gender visiting the diabetes outpatient clinics during the holy month of Ramadan. Those fasting were placed in Group A, while those not fasting formed Group B. Anthropometric measurements and medications in use were recorded. Blood samples were taken in the morning and before the evening meal. Serum osmolality was calculated using serum levels of sodium, glucose and blood urea nitrogen. Data was analysed using SPSS 16.

Results: Of the 52 patients, 27(52%) were in Group A and 25(48%) were in Group B. Overall, there were 22(42%) females and 30(58%) males. The mean morning serum osmolalities of the two groups were not different (p>0.05). The mean evening serum osmolality was not significantly different than the mean morning osmolality in Group A (p=0.22). In Group B, the mean evening serum osmolality was significantly lower than the mean morning osmolality (p=0.004). No significant difference was found between mean morning and evening serum osmolalities of those taking sodium-glucose cotransporter 2 (p>0.05).

Conclusion: There was no biochemical sign of dehydration with Ramadan fasting in type 2 diabetes mellitus patients.

Clinical Trial Number: [NCT04392570] Link: https://clinicaltrials.gov/

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Introduction

Diabetes mellitus (DM) is a significant public health problem that has an increasing prevalence with a high risk of mortality and morbidity.[1] People with DM should have their diet and treatment adjusted.

There are approximately 1.5 billion Muslims in the world, and the proportion of Muslims with DM is 4.6%, and it is estimated that more than 50 million people with DM fast during the month of Ramadan.[2,3]

People who fast during Ramadan abstain from behaviours, such as eating and drinking from sunrise (sahur) to sunset (iftar) for a month. The International Diabetes Federation (IDF) recommends that patients with diabetes who want to fast during Ramadan be evaluated by their doctors 1-2 months before Ramadan, and their risk scores should be calculated.[4] Patients at high risk are advised not to fast during Ramadan.[5] Dehydration during Ramadan, which coincides with hot summer days in some years, is an important problem. In their study investigating whether serum osmolality, an important indicator of dehydration, increases in Ramadan, Dikme et al. compared serum osmolalities of 62 fasting and 62 non-fasting patients admitted to the emergency department, and did not find any osmolality difference between the two groups.[6] In another study that examined the effects of regular exercise and fasting in Ramadan on osmolality in fasting female individuals who were healthy, regular exercise in while fasting in Ramadan led to some changes in the serum osmolality index, electrolytes and water.[7] No study was found to have investigated serum osmolality differences and risk of dehydration in fasting and non-fasting DM patients. The current study was planned to fill the gap by determining the risk of dehydration in DM patients based on serum osmolality differences likely to occur with Ramadan fasting.

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Patients and Methods

The observational study was conducted from May 16 to June 3, 2019, at the Istanbul Medeniyet University, Istanbul, Turkey. The study was registered as a clinical trial (NCT04392570. Those included using random sampling technique were adult type 2 DM (T2DM) patients of either gender visiting the diabetes outpatient clinics during Ramadan. Those fasting were placed in Group A, while those not fasting formed Group B. Those having

mental/cognitive problems, psychiatric diagnosis, life-threatening disease, type 1 DM (T2DM), and pregnant women with gestational DM (GDM) were excluded.

At the time of admission, anthropometric measurements and medications under use were recorded. The participants' body mass index (BMI) and waist circumference (WC) were calculated by an attending nurse. After the weight (kg) and height (cm) of the participants were measured with an electronic scale, BMI was calculated using the standard formula.

Blood samples were collected twice; in morning and before the evening meal. Serum osmolarities were calculated using serum levels of sodium, glucose and blood urea nitrogen (BUN). All serum samples that were collected were processed for routine biochemical parameters on the day of sample collection. Laboratory parameters, including fasting blood glucose (FBG) and glycated haemoglobin (HbA1c), were measured in a clinical laboratory of a teaching hospital in Istanbul. The serum osmolalities were calculated using the formula:

Sosm=(2×serum [Na mmol/L])+([glucose mg/dL])/18+ [blood urea nitrogen mg/dL]/2.8.[8]

Patients with evening osmolalities >300mOsm/kg and morning and evening osmolality difference >5 were accepted as at risk of dehydration.[9]

The sample size was calculated G*Power version 3-1, with power of 0.95 according to the post-hoc analysis with effect size 0.5 and *p*-value 0.05.[10]

The participants were informed in line with the Declaration of Helsinki[11] and consent was obtained before data collection.

Data was analysed using SPSS 16. Shapiro-Wilk test was used to check data normality. Descriptive statistics were reported as frequencies and percentages for categorical data, and as means and standard deviations for continuous data. The DM-related characteristics of the fasting and non-fasting individuals were evaluated using Spearman's Rank Correlation Coefficient, Mann-Whitney U Test and Wilcoxon Signed-Rank Test. P<0.05 was considered to be statistically significant.

Results

Of the 52 patients, 27(52%) were in Group A and 25(48%) were in Group B. Overall, there were 22(42%) females and 30(58%) males. The mean morning serum urea, sodium and osmolalitiy of the two groups were not different ($p>0.05$), but evening values were significantly different (Table 1).

Table-1: Socio-demographic, anthropometric and blood value results of fasting and non-fasting individuals.

Variables	Fasting (n=27) Median (25-75 percentiles)	Non-fasting (n=25) Median (25-75 percentiles)	*p*-value
Age (years)	54 (47-60)	56 (48.5-63.5)	0.486
Gender (F\M)	7\20	15\10	0.013*
BMI	30.47 (25.81-34.54)	27.74 (25.57-32.09)	0.533
Waist circumference (cm)	105 (94-113)	100 (91-114)	0.509
Diabetes Duration \ year	6 (5-9)	6 (4-9)	0.455
HbA1c (% (mmol / mol))	8.3 (7.8-8.8)	8.8 (7.25-9.15)	0.368
Glucose in Morning (Mg/dl)	154 (137-171)	147 (116.5-184.5)	0.707
Glucose in Evening (Mg/dl)	138 (121-147)	145 (112-201.5)	0.694
Potassium in Morning (mEq/L)	4.3 (4.1-4.8)	4.6 (4.2-4.85)	0.162
Potassium in Evening (mEq/L)	4.5 (4.2-4.7)	4.4 (4.2-4.6)	0.279
Sodium in Morning (mEq/L)	139 (138-141)	139 (138-141.5)	0.439
Sodium in Evening (mEq/L)	140 (139-142)	138 (133-139)	0.001*
Urea in Morning (mEq/L)	36 (30-39)	32 (25-38.5)	0.079
Urea in Evening (mEq/L)	36 (32-41)	32 (27-36)	0.018*
Osmolality in Morning	299.95 (296.6-302.36)	298.48 (295.87-303.51)	0.539
Osmolality in Evening	299.69 (298.1-304.92)	295.75 (285.05-300.24)	0.02*

BMI: Body mass index. HbA1c: Glycated haemoglobin. *p*-value was evaluated on a <0.05 significance level. *p-value < 0.05

Table-2: Evaluation of osmolality in the morning and evening by groups.

Groups		Morning Osmolality	Evening Osmolality	*p*-value
Fasting	Mean ±SD	299±5.34 (280-308)	301±5.53 (294-315)	Z: -1.225 [a]0.220
Non-fasting	Mean ±SD	299±4.77 (290-308)	292±11.57 (259-306)	Z:-2.919 [a]0.004*
Fasting & Non-fasting	*p*-value	Z:-0.614 [b]0.539	Z:-3.150 [b]0.002*	

[a]=Mann-Whitney U Test; [b]=Wilcoxon Signed-Rank Test; *=$p<0.05$; SD=Standard Deviation.

Table-3: Evaluation of morning and evening osmolalities of those using SGLT-2.

			Morning Osmolality	Evening Osmolality	Test value *p* Z
SGLT-2	User	Fasting (n=10)	300.31±3.12 (296-306)	301.70±4.76 (294-309)	Z:-0.866 [a]0.386
		Non-fasting (n= 8)	298,87±4.62 (293-305)	289.56±12.70 (265-306)	Z:-1.820 [a]0.069
	Non-user	Fasting (n=17)	299.09±6.35 (280-308)	301.56±6.08 (295-315)	Z:-0.639 [a]0.523
		Non-fasting (n=17)	299.24±4.97 (290-308)	293.21±11.21 (259-303)	Z:-2.107 [a]0.035*

[a]=Wilcoxon Signed-Rank Test; *=$p<0.05$; SGLT-2=Sodium-glucose cotransporter 2.

The mean evening serum osmolality was not significantly different than the mean morning osmolality in Group A ($p=0.22$). In Group B, the mean evening serum osmolality was significantly lower than the mean morning osmolality ($p=0.004$) (Table 2).

Table-4: Correlation analysis of morning and evening osmolarity differences of fasting and non-fasting individuals.

		n	r	*p*-value
Fasting individuals'	osmolality in morning osmolality in evening	27	0.429	0.025
Non-fasting individuals'	osmolality in morning osmolality in evening	25	0.482	0.015

*=Spearman. Correlation is significant at the 0.05 level (2-tailed).

No significant difference was found between mean morning and evening serum osmolalities of those taking sodium-glucose cotransporter 2 (SGLT-2) (Table 3).

In terms of the relationship between FBG and osmolality in Group A, there was a significant and moderate relationship between the morning and evening osmolality values (p=0.025, r=0.429). In Group B, this relationship was significant and moderate (p=0.015, r=0.482) (Table 4). Dehydration was observed in 7(26%) patients in Group A and 1(4%) patient in Group B.

Discussion

Fasting is a religious practice performed by Muslims in the ninth month of the Islamic calendar. The duration of the month varies between 29 and 30 days. The average fasting time between sunrise and sunset varies between 11 and 18 hours. Since this study, which was carried out in Istanbul, Turkey, coincided with the summer months, the duration of fasting varied between 16 and 17 hours. Due to the prolonged period and weather intensity, the risk of developing dehydration needed to be considered. Patients with DM represent a risk group.[12,13] There was no difference between the morning and evening osmolalities of the fasting patients. The morning osmolality of the non-fasting patients was lower than their evening osmolality. With the worry of weakness and thirst, fasting patients may abstain from being exposed to sunlight and from activities that require energy, and it is thought that dehydration might be prevented this way.

Although evening osmolality was found to be lower in the fasting patients than the non-fasting patients, this was not due to the fact that the fasting patients had become more dehydrated/hyperosmolar than in the morning, but it was because the non-fasting patients had a lower osmolarity than they had in the morning.

In fact, fasting in a hot season with an average seasonal air temperature of 25-27^{o}C and under conditions that include 16-17 hours of hunger and thirst may cause a relative increase in dehydration/plasma osmolality. However, the fact that the patients in this sample were generally sedentary, having no heavy outdoor activities, could have been effective in keeping their osmolality unchanged. Besides, those who agreed to participate in the study were perhaps more conscious, and, therefore, a selection bias may have occurred.

SGLT-2 inhibitors are increasingly used in the treatment of T2DM. However, there is limited evidence for the use of SGLT-2 inhibitors during fasting in Ramadan.[14-16] In fasting patients who use SGLT-2 inhibitors, the risk of dehydration is expected to increase even more due to diuresis and glucosuria, resulting from these drugs. However, in the current study, no change was found in the fasting and non-fasting patients in this regard. There was no significant increase in the evening osmolalities of the fasting patients. The fact that the non-fasting patients had lower evening osmolalities in the group of non-users of SGLT-2 suggested that the patients may have taken measures against dehydration. It should be noted that these patients were those who were followed up at the diabetes clinic, meaning that they were a relatively more educated group about the risks of diabetes and the drugs they used, and, therefore, they were careful in terms of measures against the risk of dehydration in this regard. It is clear that care should be taken in diabetic patients and in patients using diuretics/SGLT-2 in terms of dehydration, and training regarding the necessity of providing adequate hydration should be provided pre- and post-Ramadan.

In a prospective cohort study, it was reported that the use of SGLT-2 inhibitors during Ramadan in T2DM patients who received a fixed dose of SGLT-2 inhibitors before Ramadan did not increase the risk of ketonemia, hypoglycaemia and dehydration compared to patients who did not use SGLT-2 inhibitors. In the same study, the necessity of a careful pre-Ramadan assessment and training, including hydration recommendations, was emphasised for all diabetic patients who prefer fasting.[17]

High blood glucose may lead to osmotic diuresis, and, thus, an increase in plasma osmolarity. However, in the current study, there was no correlation between the pre-prandial blood glucose levels and osmolality in the morning and the evening. In the current study, no inferences were made about the number and function of nephrons. It will be useful to look at these values in addition to serum osmolarity in future studies.

The current study has its limitations as the sample only had T2DM patients who did not use insulin, and it was a random sample study; not a population study. Additionally, the daily activities of the patients and their environments (indoor, air-conditioned environment, etc.) were unknown. There was a limited number of cases in the study which was conducted at a single centre. Also, urine osmolarity of the patients could not be measured.

Besides, patients came to the hospital twice on the same day to have a blood test in the morning and in the evening may have had other daily routine activities curtailed. This may have caused the risk of dehydration to be underestimated. As an alternative methodology, urine osmolality might have been used.

However, all these issues reduced the margin of error likely to arise from these differences in both fasting and non-fasting patients. The similarity of the patients' osmolalities in the morning and evening enabled them to start under similar conditions, and, thus, it made the evening osmolality changes more reliable. Besides, the similarity of the patients in terms of age and anthropometric measurements was one of the strengths of the study.

Conclusion

There was no biochemical sign of dehydration with Ramadan fasting in T2DM patients.

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Conflict of interest: None.

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