

## Original Article

# Can Epileptic Patients on Carbamazepine Safely Fast Ramadan?

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### Abstract

**Objective:** To study the effect of fasting during Ramadan on the epileptic state of well-controlled epileptic patients taking the same protective doses of carbamazepine (CBZ) as they did before Ramadan.

**Study design:** A case series study including 40 epileptic patients in Mosul, Ninevah Province, Iraq, before Ramadan 1420 AH, which began December 9, 1999 CE. The patients were taking carbamazepine three times daily, and their epilepsy was well controlled. During Ramadan fasting, the same total daily amount of carbamazepine was administered, twice daily rather than three times daily. A blood sample was taken from each patient 10 days before fasting Ramadan and two samples on the 15th day of Ramadan, one at 9 a.m. (4 hours after the morning dose) and the second at 4 p.m. (1 hour prior to second dose). Serum CBZ concentration was measured by gas liquid chromatography, glucose was measured by glucose oxidase method, and sodium and potassium were measured by flame emission photometry.

**Results:** Statistical comparison between the means of CBZ concentration before Ramadan (control) and those of sample 1 ( $p > 0.1$ ) and sample 2 ( $p > 0.5$ ) during fasting in Ramadan showed no significant statistical differences. Also, there were no significant statistical differences between samples 1 and 2 during Ramadan ( $p > 0.1$ ). The values of glucose, sodium, and potassium remained within their normal ranges during Ramadan.

**Conclusion:** The present study showed that epileptic patients taking continuous prophylactic doses of CBZ two times daily can safely fast Ramadan safely.

**Keywords:** Epilepsy, fasting, carbamazepine, Ramadan.

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### Introduction

Ramadan is the 9th month of the Islamic lunar calendar. A lunar month is either 29 or 30 days. During Ramadan, adult Muslims are required to refrain from food, beverages, or oral drugs, as well as from sexual intercourse, between dawn and sunset. Ramadan can occur in any of the four seasons,

and the length of day varies with the distance from the equator. Accordingly, the time spent fasting varies generally from 11 to 18 hours a day.<sup>1</sup> Sick people whose health could be harmed by fasting are excused. However, they should make up for missed days of obligatory fasting after convalescence. If standard medical knowledge supports the conclusion that the illness is permanent, the person is required to feed the poor as a substitute for fasting.<sup>2</sup>

The fasting Muslim abstains from food and drink during the day, the time of activity and energy expenditure, but he or she is allowed to eat and drink at night, the time of relaxation and energy conservation. Inversion of food rhythm in Ramadan may be responsible for some of the metabolic changes reported in different studies during Ramadan,<sup>3-5</sup> which may have an effect on different bodily functions.

A large number of epileptic patients wish to fast Ramadan, but they are afraid of the effect of fasting on their epileptic state. Many metabolic changes may trigger seizures in those with a low seizure threshold.<sup>6</sup> These changes include hypoglycemia, hypocalcemia, hyponatremia, uremia, and disorders of amino acid and vitamin metabolism.

Many pharmacological agents have been used to control epileptic seizures. In many cases carbamazepine (CBZ) is one of the major antiepileptic drugs used in the treatment of epilepsy both in children and adults.<sup>7</sup> Epileptic seizures are well-controlled when the serum concentration of the drug is within a therapeutic effective range.<sup>8</sup>

The efficacy of CBZ in relation to the serum concentration of CBZ has been well-studied.<sup>9-14</sup> To our knowledge none of these studies deals with the effect of CBZ in relation to its serum concentration in protecting fasting epileptic patients from any metabolic changes that may occur during fasting. For this reason we decided to study the effect of fasting during Ramadan on the epileptic state of a number of well-controlled epileptic patients taking the same protective doses of CBZ during Ramadan as before.

### Patients and Methods

Forty epileptic patients in Mosul, Ninevah Province, Iraq, participated in the study. They were receiving CBZ therapy because of generalized tonic/clonic epilepsy. The patient group consisted of

23 women and 17 men. Participants' ages ranged from 16 to 47 years. The mean value of doses given was  $602.5 \pm 176.6$  mg daily. The duration of treatment ranged from 1 to 23 years.

Before Ramadan 1420, which began December 9, 1999, the patients took CBZ (Tegretol tablets 200 mg, ordinary tablets, manufactured by Ciba-Geigy) three times daily, and their epilepsy was well-controlled. The patients fasted during Ramadan, and the same total amount of CBZ was administered in two daily doses instead of three. One dose was administered at 5 a.m., before the beginning of the fast at dawn, and the second dose was administered at 5 p.m., after the end of the fast at sunset.

Blood samples (7 cc) were taken from each patient 10 days before the beginning of Ramadan. Two samples were taken on the 15th day of Ramadan, one at 9 a.m. (4 hours after the morning dose) and the second at 4 p.m. (1 hour prior to second dose). Serum CBZ concentration was measured by gas liquid chromatography using the method described by Thoma et al.<sup>15</sup> Glucose was measured by glucose oxidase method. Sodium and potassium were measured by flame emission photometry.<sup>16</sup>

Paired t-test was used to compare serum CBZ concentration of the control, sample 1 and sample 2. It also was used to compare serum glucose, potassium and sodium of sample 1 and 2. All values were expressed as mean  $\pm$  SD, and a value of  $\leq 0.05$  was considered statistically significant.

### Results

Table 1 shows the results of serum CBZ concentrations measurements in the 40 patients. The control measurement was taken before Ramadan. The second (sample 1) and third (sample 2) measurements were taken during Ramadan. Statistical comparison between the means of CBZ concentration before Ramadan (control) and those of sample 1 ( $p > 0.1$ ) and sample 2 ( $p > 0.5$ ) during fasting in Ramadan showed no significant statistical differences. Also, there were no significant statistical differences between samples 1 and 2 during Ramadan ( $p > 0.1$ ).

The values of glucose, sodium, and potassium remained within their normal ranges during Ramadan (Table 2). No statistically significant differences were found between the means of the two samples ( $p > 0.5$ ).

## Discussion

The patients in the present study have generalized tonic or clonic epilepsy, which was well controlled before fasting by therapy with CBZ administered in three daily doses. In Ramadan the same patients fasted, and the same total dose of CBZ was administered in a twice-daily regimen instead of three divided doses. All the patients remained seizure-free during fasting. No changes occurred in the epileptic state of the patients as a result of fasting and a modification in the frequency of daily drug administration.

The control of epilepsy by antiepileptic drugs depends on the blood level of the drug;<sup>17</sup> therefore, the antiepileptic concentration is regarded as a better guide for clinical management than physician assessment.<sup>18</sup> Control of epilepsy by an antiepileptic drug is obtained at a therapeutic concentration of the drug, which is called therapeutic range.<sup>8</sup> In the present study, three samples of blood were taken from each patient, one before fasting and two during Ramadan fasting. Measurement of serum CBZ concentration in the three samples was within the therapeutic range of CBZ (4-12 µg/ml),<sup>19</sup> and the means of the three samples showed no significant statistical differences. This means that the reduction of the frequency of administration of CBZ caused no fluctuation in the serum concentration of the drug, which may have affected the controlled epileptic state of the patients. It has been reported as a general principle of antiepileptic drug therapy that stable plasma concentration is desirable,<sup>20</sup> and fluctuation of serum levels during chronic treatment may be inconvenient because antiepileptic drugs usually act reversibly. In other words, their effect does not outlast their presence at the receptor sites or in the serum.

The therapeutic range of the drug is usually attained when a steady state of the drug blood level is reached. The time to reach the steady state is a function of the half-life of the drug,<sup>21</sup> which in the case of CBZ is about 16 hours.<sup>22</sup> Therapy with CBZ can be achieved with twice-daily administration of the drug because of its long half-life and because CBZ produces an active metabolite,<sup>23</sup> which may contribute to the maintenance of the therapeutic action of the drug.

Slow release preparations for CBZ have been made, which are not used in the present study

**Table 1. Serum carbamazepine concentrations (µg/ml). The control sample was taken 10 days before Ramadan. On the 15th day of Ramadan, sample 1 was drawn at 9 a.m., and sample 2 was drawn at 4 p.m.**

	Before Ramadan	Fasting patients	
	Control (40 patients)	Sample 1 (40 patients)	Sample 2 (40 patients)
Range	4.0-10.2	3.9-11.0	4.2-10.5
Mean	6.9±1.7	6.7±2.0	7.0±1.8

because they were not available. These preparations have been compared with the regular CBZ preparations in a number of studies. These studies showed that the slow release preparations gave lower trough levels, lower serum levels of CBZ<sup>10,11</sup> epoxide, and less diurnal fluctuation in serum levels than the conventional forms of CBZ. At the same time the steady state levels did not differ significantly in the two forms of CBZ preparations.<sup>24</sup>

In this study, the fasting patients remained seizure-free. In addition, the present study showed that the values of glucose, sodium, and potassium remained within their normal ranges.<sup>25</sup> It was found that hypoglycemia is one of the reversible causes of seizures.<sup>26</sup> Only a few studies have shown the effect of Ramadan fasting on serum glucose. One study showed a slight decrease in serum glucose in the first days of Ramadan, followed by normalization by the 20th day, and a slight rise by the 29th day.<sup>27</sup> Other studies have shown a mild increase<sup>28,29</sup> or variation in serum glucose concentration.<sup>30,31</sup> Hyponatremia is another metabolic abnormality that may cause seizures.<sup>32</sup> Alhazmi et al.<sup>3</sup> showed that Ramadan fasting does not cause significant alterations in serum sodium, and potassium. Also, in the present study, serum CBZ concentration remained within therapeutic range, which controlled the epileptic fit and protected the patient from any seizure attack that may be caused by any metabolic changes that may occur because of fasting. After Ramadan, the same patients continued taking two daily doses of CBZ for a month. They remained seizure-free.

As noted in the introduction, the length of time

**Table 2. Serum sodium, potassium and glucose concentrations during Ramadan (40 patients).**

Substance	Blood concentration	
	Range	Mean
Serum glucose (mg/100ml)		
Sample 1	70-110	87.1±10.5
Sample 2	71-110	83.3±10.8
Serum sodium (meq/L)		
Sample 1	134-148	140.4±3.2
Sample 2	135-148	140.2±3.4
Serum potassium (meq/L)		
Sample 1	3.5-4.9	4.2±0.5
Sample 2	3.5-5	4.1±0.5

of a Muslim's fast varies. The patients in this study fasted for approximately 11.5 hours. We think carbamazepine's long half-life and resulting drug concentration in the blood would allow the epileptic patient to fast safely even when the length of the day increases.

In conclusion, the present study showed that epileptic patients taking two daily doses of CBZ can safely fast Ramadan.

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