

An observational study of trigeminal neuralgia patients taking carbamazepine during the fasting month of Ramadan

Ajura Abdul Jalil, MCLinDent(Mal)¹, Shin-Hin Lau, FDSRCS(Eng)¹, Nur Suffia Sulaiman, MPH(Mal)²

¹Stomatology Unit, Cancer Research Centre (CaRC), Institute for Medical Research Centre (IMR), Kuala Lumpur,

²Cardiovascular, Diabetes & Nutrition Research Centre (CDNRC), Institute for Medical Research (IMR), Kuala Lumpur

ABSTRACT

Introduction: Trigeminal neuralgia is an agonising orofacial pain affecting unilaterally the distribution of the trigeminal nerve and it usually occurs in the middle and older age groups. Carbamazepine which is an anti-neuralgic as well as an anti-convulsant medication is the first line drug for treatment of trigeminal neuralgia. It is commonly taken as one tablet (200 mg) three times a day.

Materials and Methods: This is an observational study carried out from April to September 2014 to determine how Muslim patients on carbamazepine treatment for trigeminal neuralgia cope with their neuralgic pain. The pattern of how the medication was taken during the fasting month of Ramadan was also observed.

Results: A total of 29 patients participated in this study and 27(93%) observed the fast. Ten of them adjusted the carbamazepine dose from three times pre-Ramadan to twice daily during the fasting month. Three patients continued fasting despite feeling the pain during the daytime while five patients had their pain under control with the newly adjusted dose.

Conclusion: Medical professionals should advise trigeminal neuralgia patients on how to take and adjust their carbamazepine dose during the fasting month.

KEY WORDS:

Trigeminal neuralgia, carbamazepine, fasting month

INTRODUCTION

Trigeminal neuralgia is an unbearable agonising pain affecting the orofacial region. It is defined as a sudden, severe, brief, intermittent, stabbing, shock-like pain affecting unilaterally the distribution of the fifth cranial nerve, the trigeminal nerve. It is elicited by touching, talking, washing the face or eating of which a 'trigger zone' will be activated and the pain then radiates to the distribution of one or more branches of the trigeminal nerve. Carbamazepine is the first line drug for treatment of trigeminal neuralgia. It is an anti-convulsant and anti-neuralgic drug. Carbamazepine is initially prescribed at a lower dose as little as 100 mg two to three times a day. Later, the dosage is slowly increased by 100

mg every other day until adequate pain relief is established or until intolerable side effects prevent further upward titration. Typical maintenance doses range from 300 to 800 mg/day divided into two to three daily doses.¹ Therapeutic drug monitoring is essential for optimizing and individualizing carbamazepine therapy. However, carbamazepine has many side effects which include nausea, dizziness and rash as an allergic reaction. A few patients cannot tolerate the initial side effects and have to bear the pain. However, these side effects will usually improve in the following weeks. Adequate dosage is important to balance out between the pain control and side effects.

Ramadan, the ninth month in the Islamic calendar is a month of obligatory daily fasting for the Muslims. During the whole holy month of Ramadan, Muslims refrain from drinking and eating, including taking oral medications from dawn to sunset. However travellers, the sick or pregnant, nursing and menstruating women are excused from observing the fast. *Iftar* is the meal taken after sunset (breaking of the fast) and *Sahur* is the meal consumed before dawn or Fajr prayer. Patients on medications usually adjust their dosage during the day time. Hence, the aim of this study was to observe the pattern of carbamazepine dose intake among Muslim patients with trigeminal neuralgia during the fasting month and how these patients coped with their neuralgic pain.

MATERIALS AND METHODS

This observational study was carried out among patients who attended the Oral Medicine Clinic, Hospital Kuala Lumpur for treatment and management of trigeminal neuralgia. The authors (AAJ, S-HL) were clinicians who managed the patients in this study at the Oral Medicine clinic. All trigeminal neuralgia patients were reviewed every three months. Muslim patients who attended the clinic from April to September 2014 and who were treated with Carbamazepine were included in this study. All other trigeminal neuralgia patients who are non-Muslims or who are not taking Carbamazepine were excluded from this study. The Ramadan month was from 29th June to 27th July 2014. The fasting duration was from approximately 5.30 am to 7.30 pm (14 hours) daily. Patients who agreed to participate in the study were interviewed twice by the oral

This article was accepted: 7 September 2016

Corresponding Author: Ajura Abdul Jalil, Oral Pathology & Oral Medicine Specialist, Institute for Medical Research, Stomatology Unit, Cancer Research Centre, Jalan Pahang, Kuala Lumpur, Kuala Lumpur 50588, Malaysia

Email: ajura_jalil@yahoo.com

Table I: Summary of Carbamazepine dose regimen changes of trigeminal neuralgia patients and pain control during fasting month

Carbamazepine dose regimen	Pain control		
	Good pain control	Bearable pain	Poor pain control
No dose adjustment (continued with once/twice daily dose) (n=18)	17 (94.4%)	1 (5.6%)	0 (0%) *(one patient did not fast due to stomach ache/ulcer)
Dose adjustment (adjusted from thrice daily to twice daily dose) (n=11)	6 (54.5%)	4 (36.4%)	1 (9.1%) (did not fast due to severe trigeminal neuralgia pain)

Table II: Practical points of management of trigeminal neuralgia (TGN)

1	TGN is diagnosed through clinical findings and by excluding other more common causes of orofacial pain.
2	TGN manifests as sharp, shooting, lancinating, shock like pain over the face or mouth. These attacks usually lasts from few seconds to a few minutes and can occur spontaneously or be triggered by certain activities.
3	The first line of treatment is carbamazepine in titrated dose. The initial starting dose is from 100mg tds. The maximum dose of carbamazepine is 1600mg/day after which alternative therapy should be considered.
4	Haematological investigation: full blood count (FBC), liver function test (LFT), renal profile (RP) should be conducted periodically.
5	If the nature of TGN pain is different or has changed, further investigations such as magnetic resonance imaging (MRI) should be carried out (Reference 4).

medicine specialist during their regular follow-up appointments. The first interview was conducted one to eight weeks prior to Ramadan month. The second interview was carried out one to two months after the Ramadan. In the first interview, demographic data of patients such as gender, age and race were collected. Past medical history, current medications and prescribed dosages for treatment of trigeminal neuralgia were noted. Patients were then advised by clinicians on how to adjust their carbamazepine dose during the fasting month, especially those taking the carbamazepine three or four times a day. They were advised to break their fast to take medication due to any neuralgic pain experienced. In the second interview, they were questioned if they were able to fast during Ramadan or if they had to break their fast due to intolerable pain. They were asked if any changes were made to the dosage or frequency of trigeminal neuralgia medication. Microsoft Excel Program was used to carry out a descriptive statistical analysis for demographic details such as age, gender, dosage regime and pain control.

RESULTS

A total of thirty Malay patients (male=11, female=19) were interviewed. Their ages ranged from 31 to 82 years old and the mean age was 52.77 years. In the current study, the patients described the neuralgic pain in their own words as either sharp, poking, knife-like, electric-shock or unbearable, extreme, intense pain. One patient was unable to continue fasting due to extreme neuralgic pain while another developed oral ulcers and stomach-ache during the fasting month (unrelated to drug use) and she could not continue fasting. Other patients could carry out their fast. Twenty-seven patients were taking carbamazepine alone, and two were taking a combination of both carbamazepine and dilantin sodium and one had to be put on dilantin sodium after developing allergic reactions towards carbamazepine and was excluded from the study.

Eighteen patients who had mild to moderate trigeminal neuralgia were advised that they did not have to adjust the dosage and frequency of once or twice daily Carbamazepine. For those taking it twice a day, they took one tablet each

during breaking the fast and *sahur*. Ten of them adjusted the carbamazepine dose from three times pre-Ramadan to twice daily during the fasting month, of which four patients continue fasting despite feeling the pain during the daytime while six patients had their pain under control with the newly adjusted dose. However, one patient could not decrease his dose due to intense pain and had to continue with the three-time dose including the daytime dose, and was not able to fast. One patient managed to take carbamazepine three times a day and was able to fast by taking a tablet during breaking of the fast which was around 7.30 in the evening, one tablet before going to bed at midnight and the third tablet at dawn during *sahur* which was around 5 a.m. In another patient, she was able to maintain her pre-Ramadan dose of 600 mg Carbamazepine by taking the medication 200 mg during *iftar* and 400 mg during *sahur*. Both patients found these regimes to be effective with no pain experienced during the daytime. Table I shows changes in dose regime and pain control of trigeminal neuralgia patients.

In this current study, patients taking combination of both carbamazepine and dilantin sodium are also included in the data analysis as we want to see if these patients needed to adjust their carbamazepine dosage or the need to change to other medications for trigeminal neuralgia. Dilantin sodium is not a problem for patients to take during Ramadan since the medication is usually taken once daily and patients can either take it after breaking the fast or during *sahur*. In our study, none of the patients who were on a combination of both carbamazepine and dilantin sodium had to adjust their timing of medications.

Fifteen of the patients were on medications for other various reasons such as hypertension, hypercholesterolemia and diabetes. These medications are usually taken once or twice daily. Therefore, they had no difficulty in taking these medications during fasting month.

DISCUSSION

There is a lack of published research studying the patterns of medication intake during the fasting month for patients with trigeminal neuralgia. From our literature search, this appears

to be the first observational study in this area. The decreased frequency of the carbamazepine from three to twice daily dosage has an effect on the neuralgic pain experienced by our patients. Although they felt the pain, it was bearable during the day. Most of the patients had no reservations to adjust the frequency of the carbamazepine intake, with a few persisting to take it as twice a day despite feeling the pain. Only one or two patients who were on thrice a day dosage pre-Ramadan had difficulty reducing it to twice daily. Instead of reducing the frequency, they maintained the thrice daily dosage by adjusting the timing of the carbamazepine from eight hourly to only five hourly. In Malaysia the fasting starts at about 5.30 am and ends around 7.30 pm for breaking fast (14-hour duration), which leaves around ten hours for patients to take their medications before the next day of fasting. If they took medication twice daily, the first dose (taken during *iftar*) would last for ten hours and the second dose (taken during *sahur*) for 14 hours. As for those patients taking medication three times a day, there will be a five-hour lapse between each dose (taken during *iftar*, at midnight and at *sahur*).

Carbamazepine is the drug of choice for the treatment of trigeminal neuralgia. Carbamazepine is absorbed slowly and almost completely from the gastrointestinal tract with peak serum concentrations achieved within two to eight hours.² Carbamazepine is poorly water soluble therefore presence of food with related gastric juices and bile improves its absorption. With a twice daily regimen, peak serum concentrations of carbamazepine can be as much as 80% higher while with a four times a day regimen the differences are only 40%.² In the current study, for patients taking the medications three times a day with a gap of five hours, the serum concentrations may not be fully achieved hence the pain is not well controlled.

In the present study, dilantin sodium was prescribed as a combination with carbamazepine in two patients with uncontrollable pain. In another patient, carbamazepine was initially prescribed to the patient, however dilantin sodium was prescribed instead when the patient developed rashes all over her body after taking two tablets of carbamazepine. Two of our patients in the current study did not fast. One patient complained of extreme pain when the dosage of the carbamazepine was reduced to twice daily, hence he had to take it three times a day including the daytime dose. In another patient, although the neuralgic pain was controlled, the patient did not fast as she complained of oral ulcers and stomach-ache during the entire fasting month. Most of them experienced neuralgic pain especially during talking and taking ablution (i.e. washing of the face before obligatory prayers) in the daytime of the fasting month. However, the pain was tolerable, therefore they continued their fast. Patients with moderate to severe trigeminal neuralgia requiring thrice daily dosage may experience variable pain control due to adjustment to twice daily dosage.

This study had several limitations. Initially, pain score was included as part of our interview in the current study. However, most of our patients could not understand the pain score well (universal pain assessment tool) even after thorough explanation. Instead of scoring the pain, they

described the nature of the pain (either as throbbing, electric-shock like pain, stabbing and severe unbearable pain). Therefore, it was decided not to include the pain score as part of the interview. In future, questions have to be asked in a different way so patients, especially the elderly can understand and comprehend the questions. We also recommend the design of the interview to be simpler, where questions asked are brief and straight forward. Closed questions instead of open-ended questions would elicit more focused answers from patients. As this is an observational study, no research on the pharmacokinetic of carbamazepine taken during fasting was undertaken. In future it is recommended that the serum concentration of carbamazepine and its effectiveness during Ramadan are studied.

Gabapentin, an anti-epileptic drug has now been widely used for a treatment option for trigeminal neuralgia with less side effects. Cheshire³ suggested that gabapentin can be effective as a first or second line treatment for trigeminal neuralgia. It has been shown that the effective daily dose of gabapentin ranged from 100 to 2400 mg, with a mean daily dose of 700 mg for those with complete or nearly complete relief.³ It is proposed that gabapentin be prescribed for patients who cannot tolerate neuropathic pain upon adjusting the dose of carbamazepine during the fasting month of Ramadan. Table II highlights some important practical points of management of trigeminal neuralgia.

CONCLUSION

This is the first observational study to determine the pattern of the carbamazepine intake for trigeminal neuralgia patients during the Muslim fasting month. Patients who were on twice daily medication dose mostly maintained this dose with good pain control. Some patients with thrice daily dosage had good pain control on twice daily dosage during the fasting month. Most carried on with their fasting with some bearing tolerable pain with adjusted dose. As Oral Medicine specialists or other medical professionals taking care of trigeminal neuralgia patients, advice and guidance should be given to patients as well as recommendations on how to take and adjust medications, especially carbamazepine during fasting month.

ACKNOWLEDGEMENTS

The authors thank the Director General of Health, Malaysia and Director of Institute for Medical Research, Kuala Lumpur for their permission to publish this study. Many thanks also to the patients for their cooperation in this study.

REFERENCES

1. Obermann M. Treatment options in trigeminal neuralgia. *Ther Adv Neurol Disord* 2010; 3(2): 107-15.
2. Zakrzewska JM, Patsalos PN. Drugs used in the management of trigeminal neuralgia. *Oral Surg Oral Med Oral Pathol* 1992; 74(4): 439-50.
3. Cheshire WP Jr. Defining the role of Gabapentin in the treatment of trigeminal neuralgia: A retrospective study. *J Pain* 2002; 3(2): 137-42.
4. Headache Classification Committee of the International Headache Society (IHS). *The International Classification of Headache Disorders: 2nd edition. Cephalalgia* 2004; 24: 1-160.