

Antipsychotic medication therapy during the holy month of Ramadan: a literature review

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ABSTRACT

Objectives: To review the antipsychotic medication therapy during the holy month of Ramadan. **Methods:** In this study, we performed an extensive search of 50 databases through the Saudi Digital Library search engine. We included meta-analysis, randomized controlled studies and observational studies published in English language in May 2017. The search terms included Ramadan, fasting, medication, therapy, type of disease, and medication based on therapeutic class. The search on antipsychotic and anti-epileptic medication list and switch from regular days to Ramadan days included comparative safety, efficacy and cost of type of medication for each disease and national or international evidence-based guidelines including those switching short half-life to long half-life drugs. All nonoral dosage form of medication will be excluded in this study. All medications should be documented in the Ministry of Health drug formulary. **Results:** A total of 710 studies were shortlisted after an extensive search with specific terms. Of those, 104 studies were duplicate studies; therefore only 606 studies were included for further evaluation. The evaluation revealed that 27 studies discussed about the antipsychotic medications and Ramadan. Of these, only five were appropriate for further revision. According to our results, most of the studies were observational studies and a few have conducted experimental design studies. Three studies have a shared or similar study design (i.e., reports). Among all the reports analyzed in this study, most of them used study design. On the contrary, three studies mentioned the utilization of a descriptive approach; however, none of the studies mentioned the exact type of descriptive analysis conducted. One study was a clinical review and another study mentioned the applicability of a randomized controlled trial. Based on this, the authors suggested switching the antipsychotic and anti-epileptic medication from regular days to Ramadan days. **Conclusion:** There are no randomized clinical trials in the literature to validate the switching of medication from regular to Ramadan days. A list of antipsychotic medications that can be used to switch during Ramadan is highly warranted. Further studies to validate the medication used to treat psychiatric conditions during the holy month of Ramadan is recommended.

Key words: Antipsychotic, Medication, Therapy, Ramadan, Review.

INTRODUCTION

The holy month of Ramadan is the ninth month in the Hijri calendar in which Muslims fast intermittently and refrain from eating, drinking and other habits such as smoking. A Muslim in Ramadan fasts from sunrise till sunset each day for up to 29 to 30 days. The fasting hours during the day can change from 11 to 18 h according to the lunar calendar; therefore, it is forwarded by 10 days each year.¹ The concept of fasting in this holy month is to understand and learn patience and self-control.² It enables a Muslim to be connected on a spiritual level and be more conscious religiously.²

According to the estimation, Muslims comprise 24% of the population worldwide (1.8 billion).³ As the majority of this population fasts, there are physiological characteristics that differ in terms of age, weight, sex, diet and physical activity.⁴ The impact of partial fasting on the body depends on the daily fasting time that can affect biomarkers. Moreover, medications, smoking and diet can cause have an effect as well.^{5,6} In previous studies, it has been concluded that fasting during Ramadan has led to significant weight loss and energy consumption.⁷ In contrast, it was demonstrated that fasting in Ramadan leads to weight gain

and an increase in the energy intake in another study.⁸ Therefore, there is no clear conclusion which determines the exact effect of Ramadan on body composition.

During Ramadan, Muslims consume approximately two meals per day. *Suhoor*, which is the predawn meal, in which Muslims have enough food and fluid intake to preserve their energy during the day as much as possible. The second meal, *Iftar*, is the evening meal in which a Muslim breaks the fast with dates.⁹ Meal planning and food consumption are critical for patients to adhere to in order to reschedule medication intake for chronic conditions between meals or during a meal.⁹ Taking oral formulations of a drug during fasting can contradict a fast. Patients have difficulty sustaining their dosage regimen by skipping doses during fasting. Consequently, specific strategies such as the use of long-acting formulations or twice daily dosing regimens for drugs given multiple times per day during other months, have been implemented to avoid breaking the fast. Furthermore, it has been shown that during Ramadan there is a better medication adherence by the patient than that of other months.⁵ The use of antipsychotic and antiepileptic drugs during Ramadan is strictly scheduled.¹⁰

The number of relapses of mood disturbances during Ramadan has been previously reported for bipolar patients. It has been demonstrated that the relapses for fasting patients were higher than that of nonfasting patients; this emphasizes the importance of following the medication regimen during Ramadan.¹¹ However, the correlation between fasting and a manic or depressive episode of bipolar remains unclear.¹¹ Another study determined the frequency of seizures during fasting. Previously it was assumed that fasting was considered as a treatment for epilepsy.¹² The mechanism in which fasting can cause anti-epileptic effects remains under investigation. However, animal trials have supported this claim.¹² Regardless as to whether fasting can have a positive outcome on mood or seizure frequency, the emphasis of patient adherence to medications during Ramadan should not be different from nonfasting days. Although physiological changes can occur differently during Ramadan days, antipsychotic and anti-epileptic medication levels and effects are being continuously studied. Therefore, in this study, we aimed to explore the review of fasting Ramadan and antipsychotic as well as anti-epileptic medications.

METHODS

In this study, we performed an extensive search on 50 databases through the Saudi Digital Library (SDL) search engine: Wiley Online Library, Web of Science, Springer Link, Taylor and Francis, Social Science Journal accessed via ProQuest, Science Journal accessed via ProQuest, Scopus, SciFinder, Science Direct, Sage Journal, Royal Society of Medicine, Royal Society of Chemistry, Psychology Journals accessed via ProQuest, Pharmaceutical News Index accessed via ProQuest, Patient Education accessed via MD Consult, Drug accessed via MD Consult, Oxford Journals accessed via Oxford University Press, Ovid Journals, Nursing and Allied Health Sources accessed via ProQuest, Nature Publisher Group, MEDLINE Index accessed via ProQuest, MEDLINE Complete accessed via EBSCO, Medical Evidence Matter accessed via ProQuest, IGI InfoSci Journals, Health Management accessed via ProQuest, Health and Medical Complete accessed via ProQuest, Global Health Database-CABI, Family Health accessed via ProQuest, Eric accessed via ProQuest and EBSCO, Emerald, DynaMed accessed via EBSCO, Directory of Open Access Journal (DOAJ), Current Content accessed via Web of Knowledge, Dentistry and Oral Science accessed via EBSCO, Clinical Key-Nursing, Clinical Key-Physician, CINAHL accessed via EBSCO, Central accessed via ProQuest, CBCA accessed via ProQuest, Canadian Science Publishing, Cambridge Journals accessed via Cambridge University, Britannica Academic, BMJ Journals, BMJ Clinical Evidence accessed via BMJ Best Practice, BMJ Best Practice, Biology Journals accessed via ProQuest, ACM Digital Library, Academic Search Ultimate accessed via EBSCO, Cochrane Library PubMed. In addition to Google Scholar searched a lone without SDL. We included meta-analysis, randomized controlled studies and observational studies in English language in May 2017. The search terms included Ramadan, fasting, medication, therapy, type of disease and medication based on therapeutic class. The antipsychotic and anti-epileptic medication list and switch from regular days to Ramadan days based on literature found the search, that's included comparative safety studies, efficacy studies and cost of type of medication for each disease studies and national or international evidence based guidelines of switching short half-life to long half-life.¹³⁻¹⁵ The list containing antipsychotic and anti-epileptic medication included drug name, general dosing and frequency of administration during regular and Ramadan days. All settings of patient care services such as inpatient, ambulatory care, or community services oral medication were included. All non-oral dosage form of medication were excluded from analysis. All medications should MOH drug formulary. The study location included Saudi Arabia as top the priority after Gulf or Middle Eastern countries; if this data was

not found, then all countries were included in the analysis. If studies evidence not existed; the suggested came from author's experiences.

RESULTS

A total of 710 studies were obtained after an extensive search with specific terms. Of those, 104 were duplicate studies and 606 were included for further evaluation. The evaluation revealed that 92 studies discussed about medications related to diabetes mellitus and Ramadan, 27 studies discussed about the psychiatric medications and Ramadan, 27 studies investigated medications related to gastrointestinal disorders and Ramadan, 30 studies discussed about the use of antibiotics and Ramadan, 30 studies discussed about the cardiovascular medications and Ramadan, 15 studies discussed about medicines for asthma and rheumatoid arthritis and Ramadan and 402 studies discussed about other diseases and Ramadan. Of those 30 studies, only 5 were appropriate for further evaluation. The authors retrieved and summarized a total of 5 studies. Five countries (Iraq, Kuwait, Morocco, Pakistan and Turkey) have conducted a study relative to antipsychotic and anti-epileptic drugs. According to our results, most of the studies were observational studies and a few had experimental design in it. Three studies shared similar study design (reports). Reports were the most used method amongst the studies. On the contrary, three studies have mentioned the utilization of a descriptive approach; however, none of those mentioned the exact type of descriptive analysis conducted. Only one study resorted to clinical reviews. Moreover, only one study has mentioned the applicability of a randomized controlled trial.

There was one controlled study with one medication switch from three doses to two doses; the results showed there was a difference in the clinical outcomes and the concentration of medication. One study discussed about the drug level during fasting without any difference in the Ramadan days.

Three studies showed positive and conclusive results and two studies showed negative and unfavorable outcomes. In contrast, one study showed both negative and positive results. The positive outcomes favored the use of medication (e.g., carbamazepine and lithium) during Ramadan, with the focus on the drug's efficacy and safety. Some studies, however, failed to mention the drugs involved despite having positive outcomes.

However, the remaining two studies with negative results highlighted multiple reasons such as misuse of drugs that could lead to drug-food interactions and even progression of disease without any misleading changes to the required regimen during Ramadan. Moreover, one study showed a mix of outcomes. Missed doses were the ultimate issue; however, the study has mentioned an alternative to the problem that could benefit patients using the drug in Ramadan such as using a long-acting formulation of the drug to avoid missed doses.

In addition to our findings, the studies involved have shared advantages and disadvantages and a few of the studies were vague in terms of their assets and drawbacks. One of the advantages is that the information regarding the type of drug used, dose and frequency were gathered from evidence-based guidelines and researches and have provided the appropriate dose needed for each drug during fasting. Although the studies have obvious advantages, one study had a unique advantage. This study that was conducted in Iraq has shown the aftermath of fasting on glucose levels in addition to the results regarding drug used. Most of the studies have failed to mention the type of drug involved such as those conducted in Turkey. Another adverse outcome that was common amongst the studies was the small sample size that was chosen (Table 1). Based on the previous literature the authors suggested switching the antipsychiatry and anti-epileptic medication from regular days to Ramadan days (Table 2).

Table 1: The selected studies conducted during the holy month of Ramadan.

No	Authors	Year of publication	No of participant	Study design (RCT, Observations, etc.)	Medications	Outcome results	Advantages
1	Assad, A ¹⁶	1986 Kuwait	49	Report 1 month	Multiple Psychiatric Drugs	31 psychiatric patients did not comply for their drug regimen during Ramadan while 18 did comply.	
2	Aadil, N et al. ¹⁷	2004 Morocco	NA	Clinical review	Carbamazepine, Diazepam, Lithium	Extensive misuse of prescribed drugs during Ramadan may lead to therapeutic failures and drug/food interactions	Provide accurate and standardized advice on the appropriate use of drugs during the holy month of Ramadan. incomplete descriptions of the therapeutic schemes observed before and during Ramadan,
3	Khattab, E et al. ¹⁸	2008 Iraq	40	Non-RCT 1-23 years	Carbamazepine	epileptic patients taking doses of CBZ from three to two times daily was safely fast Ramadan	Only a few studies have shown the effect of Ramadan fasting on serum glucose and this study was one of them
4	Gomceli, YB. et al. ¹⁹	2008 Turkey	114	Observation 1 year	NA	Inpatients with epilepsy there was an increase in seizure frequency if they changed their drug regimes. Change in drug intake patterns, decrease in sleep duration and/or sleep fragmentation, emotional stress and also tiredness, either separately or all together, influence the occurrence of seizures during Ramadan fasting	The drug involved were not mentioned throughout the study
5	Faroo, S et al. ²⁰	2010 Pakistan	62	descriptive study 1 month	Lithium	it can be safely prescribed without the undue fear of adverse side effects during Ramadan	small sample size

Table 2: Antipsychotic and anti-epileptic medication therapy during regular days switching to Drug therapy during the holy month of Ramadan.

No	Drug therapy during Regular days ²¹⁻²⁵			Drug therapy during Holy Ramadan			Registration ^{*26}
	Regular Days	Doses/ Day	Frequency Per day	Regular Days	Doses/Day	Frequency Per day	
1	Amitriptyline	50-150 mg	In 1 dose or divided doses	Amitriptyline	50-150 mg	In 1 dose	RSFDA , MOHDF
2	Amisulpride	400-800 mg	Divided in 2 divided doses	Amisulpride	400-800 mg	Divided in 2 divided doses	RSFDA , MOHDF
3	Aripiprazol	10-30 mg	In 1 dose	Aripiprazol	10-30 mg	In 1 dose	RSFDA , MOHDF
4	Citalopram	20-40 mg	In 1 dose	Citalopram	20-40 mg	In 1 dose	RSFDA , MOHDF
5	Clobazam	20-40 mg	In 1-2 divided doses	Clobazam	20-40 mg	In 1-2 divided doses	RSFDA
6	Clonazepan	1.5-8 mg	In 2-3 divided doses	Clonazepan Clobazam	1.5-8 mg 20-40 mg	In 2 divided doses In 1-2 divided doses	RSFDA , MOHDF
7	Duloxetine	60 mg	In 1 dose	Duloxetine	60 mg	In 1 dose	RSFDA, MOHDF

8	Escitalopram	10-20 mg	In 1 dose	Escitalopram	10-20 mg	In 1 dose	RSFDA, MOHDF
9	Fluoxetine Escitalopram	20-60 mg Maximum	In 1 dose	Fluoxetine Escitalopram	20-60 mg Maximum	In 1 dose	RSFDA, MOHDF
10	Lacosamide	200-400 mg	Divided in 2 doses	Lacosamide	200-400 mg	Divided in 2 doses	RSFDA
11	Lamotrigine	100-500 mg	Divided in 2 doses	Lamotrigine	100-500 mg	Divided in 2 doses	RSFDA, MOHDF
12	Levetiracetam	1000-3000 mg	Divided in 2 doses	Levetiracetam	1000-3000 mg	Divided in 2 doses	RSFDA, MOHDF
13	Olanzapine	10-20 mg	In 1 dose	Olanzapine	10-20 mg	In 1 dose	RSFDA, MOHDF
14	Oxcarbazepine	900-2400 mg	Divided in 2 doses	Oxcarbazepine	900-2400 mg	Divided in 2 doses	RSFDA, MOHDF
15	Paliperidone	6-12 mg	In 1 dose	Paliperidone	6-12 mg	In 1 dose	RSFDA, MOHDF
16	Paroxetine	10-20 mg	In 1 dose	Paroxetine	10-20 mg	In 1 dose	RSFDA, MOHDF
17	Pheynetion	300-400 mg (Blood Level 10-20 mcg/ml)	Divided in 1-3 doses	Pheynetion	300-400 mg (Blood Level 10-20 mcg/ml)	In 1 dose	RSFDA, MOHDF
18	Pregabalin	150-600 mg	Divided in 2-3 doses	Pregabalin	150-600 mg	Divided in 2 doses	RSFDA, MOHDF
19	Risperidone	4-8 mg	In 1 dose	Risperidone	4-8 mg	In 1 dose	RSFDA, MOHDF
20	Sertraline	25-100 mg	In 1 dose	Sertraline	25-100 mg	In 1 dose	RSFDA, MOHDF
21	Trandolapril	1 mg	In 1 dose	Trandolapril	1 mg	In 1 dose	RSFDA
22	Trifluoperazine	2-10 mg	2 times	Trifluoperazine	2-10 mg	2 times	RSFDA, MOHDF
23	Valporic Acid	1000-3000 mg (Blood Level 40-100 mcg/ml)	Divided in 2-3 doses	Valporic Acid	1000-3000 mg (Blood Level 40-100 mcg/ml)	Divided in 2doses	RSFDA, MOHDF
24	Venlafaxine	75 mg	Divided in 2-3 doses	Venlafaxine ER	37.5-75 mg	In 1 dose	RSFDA, MOHDF
25	Zonisamide	100-600 mg	In 1-2 dose	Zonisamide	100-400 mg	In 1-2 dose	RSFDA
26	Clomipramine	25-100mg	In 1 dose	Clomipramine	25-100mg	In 1 dose	RSFDA, MOHDF
27	Fluvoxamine Maleate	100-300mg	In 1 dose	Fluvoxamine Maleate	100-300mg	In 1 dose	RSFDA, MOHDF
28	Mirtazapine	15-30mg	In 1 dose	Mirtazapine	15-30mg	In 1 dose	RSFDA, MOHDF
29	*RSFDA: The Drug had been registered in Saudi Food and Drug Authority, MOHDF: The Drug is Ministry of Health Drug Formulary						

DISCUSSION

In the Middle East, the stigma of having a psychotic as well as the neurological disease remains an obstacle to date. For instance, a study that was conducted in Saudi Arabia showed that the level of understanding of the community towards epilepsy was limited.¹⁷ In Riyadh, Saudi Arabia, survey respondents were unaware of epilepsy.¹⁷ Moreover, a survey conducted in Jeddah, Saudi Arabia, have demonstrated a level of acceptance towards the disease but a massive misunderstanding of how the disease function.¹⁸ Public education and acceptance towards those disorders are vital to improving the field of research in terms of the medications used for those diseases, especially during Ramadan. Therefore, it is crucial to initiate multiple kinds of research surrounding this topic to enhance not only the public's awareness but to assess the appropriate usage of anti-psychotic/antiepileptic in a fasting state. Moreover, the study methodology for the studies collected was mostly reported and only one of the studies conducted nonrandomized a clinical trial with limited number of medications. It is essential to enroll patients in experimental randomized clinical studies in order to have a significant meaning concerning the use

of those medications in Ramadan and to reflect the study results to the general population and allow an area for improvement. In contrast, some of the studies have provided details regarding the drug, dose, frequency and use during Ramadan and others non mentioned. The authors suggested of drug list of antipsychotic and anti-epileptic and switch from regular days and Ramadan days. The limitations of the studies gathered were small sample sizes in the clinical trials, the use of reports predominantly, the limited number of studies available and the lack of mentioning the drugs used for specific studies.

CONCLUSION

In conclusion, this systematic review highlighted that the use of anti-psychotic and antiepileptic medications during Ramadan has not been extensively evaluated and studied by current literature. The drawbacks were that the methodology chosen was not reliable nor sufficient for this type of field, although one study had performed non-randomized a clinical trial; however, the sample sizes were small with limited number of medications. Furthermore, the number of studies was minimal and some

of the studies have not mentioned the drugs involved. We believe that there is a need for further examination through clinical trials in order to highlight the critical factors and switch therapy related to antipsychotic/antiepileptic medications during Ramadan.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

ABBREVIATIONS

MOH: Ministry of Health; **KSA:** Kingdom of Saudi Arabia; **USA:** United State of America; **SDL:** Saudi Digital Library.

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