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# MIGRAINE AND FASTING

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## ABSTRACT:

Migraine is considered as the second leading cause of disability worldwide, most commonly seen in young women. Skipping meals, dehydration and fasting are among many triggering factors which have been described in literature as a cause of increased frequency and severity of migraine attacks. The underlying pathophysiology, prevention and management of fasting induced migraine has been documented, however, there is a lack of randomized controlled trials for the same. This review article discusses these important aspects in the light of published literature and gives directions on future areas of research.

## KEYWORDS:

Fasting, Migraine, Headache, Ramadan, Intermittent fasting

## MIGRAINE; EPIDEMIOLOGY

Migraine is a neurovascular disorder that affects over one billion people worldwide.<sup>1</sup> A migraine attack typically lasts from 4 to 72 hours and may necessitate taking time off from employment as well as cause disability, health care utilization, and direct health costs.<sup>2</sup> It is responsible for more disability adjusted life years in young women than any other communicable or non-communicable disease.<sup>3</sup> According to a systematic review that comprised of 302 community-based studies involving 6,216,995 participants, the global prevalence was 11.6% which means at least 1 in 10 people suffer from migraine headaches all over the world.<sup>4</sup> A cross sectional nationwide prevalence survey conducted on primary headache disorders in the adult general population of Pakistan included 4223 participants. It revealed the prevalence of migraine to be 22.5% in Pakistan with a 3:2 female preponderance.<sup>5</sup>

## COMMON TRIGGERS:

Several factors can trigger migraines in susceptible individuals such as dietary factors, stress, hormonal changes, disturbed sleep pattern, change in routine, usage of tobacco, sensitivity to certain odors, strenuous exercise, exposure to sun, climate change, and high altitudes. The dietary factors include alcohol and caffeine withdrawal, consumption of chocolate, aspartame, monosodium glutamate, and tyramine-rich foods like cheese and red wine. In addition, skipped meals or fasting and insufficient water intake frequently

cause migraine as well.<sup>6</sup> Among the most quoted dietary triggers, fasting or skipped meals was significantly more common and has been reported in up to 85.3% of patients with migraines.<sup>7</sup>

## FASTING AND INTERMITTENT FASTING:

Fasting means abstinence from food or drink or both for health, ritualistic or religious reasons for a defined period of time. For instance, it is mandatory for Muslims to fast during the holy month of Ramadan for 29 or 30 days depending on the lunar calendar. Muslims refrain from any intake of food, water, beverages, oral medicine, and smoking from sunrise till sunset.<sup>8</sup> Among rare exemptions are people with ongoing illnesses that may be adversely affected by the fasting state. Intermittent fasting involves fasting every day for a fixed duration, for instance fasting for 14 to 16 hours would restrict the eating window to 8 to 10 hours. This form of time restricted feeding is currently one of the most popular health and fitness trends used worldwide to lose weight, improve health and simplify lifestyles. However, the duration and form of intermittent fasting may vary according to an individual's dietary requirement and health status.<sup>9</sup>

## PURPOSE OF THE STUDY:

Our review on migraine and fasting was planned to gauge the association of the two and help the clinical practitioners to pay attention to this concern. Various studies have come out worldwide however consolidation of their findings has not been adequately

achieved as yet. Despite being one of the most disabling conditions, migraine is an underdiagnosed neurological entity. There is no definitive cure however with timely diagnosis the widely available preventive and abortive measures can be prescribed to sustain quality of life.

#### **MATERIALS AND METHODS:**

We conducted an online literature search through the Medline database and Cochrane library (PubMed/Cochrane library) from January 2000 to January 2021. We used keyword terms such as: “migraine and fasting”, OR “headaches and fasting”, OR “fasting triggers migraine”, OR “migraine in Ramadan”. We included the articles that were carried out in adults i.e. above 18 years of age and published (or translated) in English. Our literature search revealed 476 articles in PubMed and eight reviews in the Cochrane library, giving a total of 489 articles. 460 out of 489 were excluded due to duplicate results, unrelated title/abstract, and inaccessible full articles. Eventually, a total of 29 full-text articles were included in this review.

#### **FASTING AND BRAIN HEALTH:**

The International Classification of Headache Disorders, 3rd edition, published in 2018, describes the headache attributed to fasting as: “A diffuse non-pulsating headache, usually mild to moderate, occurring during and caused by fasting for at least 8 hours. It is relieved after eating”.<sup>10</sup> The exact mechanism remains unclear, but intermittent fasting may in fact reduce neuro-inflammation, decreasing insulin resistance and release of ketone bodies that activates anti-inflammatory mechanisms and cellular pathways that induce autophagy.<sup>11</sup> However, during fasting state factors such as caffeine withdrawal, lack of sleep, hypoglycemia, and dehydration contribute appreciably to developing a headache.<sup>12</sup>

#### **EFFECT OF FASTING ON MIGRAINE PATIENTS:**

A cohort of 32 observant Muslim migraine sufferers asked to fill a migraine diary during the Ramadan month and the following month (control) showed  $9.4 \pm 4.3$  migraine days in average during Ramadan when compared with  $3.7 \pm 2.1$  migraine days in average during the latter ( $p < 0.001$ ).<sup>12</sup> Migraineurs may have an underlying impairment of glucose and insulin metabolism.<sup>13</sup> Therefore, makes them more vulnerable to fasting compared to persons without migraine.

Dalkara et al. proposed that insufficient supply of glycogen-derived glucose at the onset of intense synaptic activity may lead to an imbalance between the

excitatory and inhibitory terminals, causing collective depolarization of neurons and astrocytes in a network. This may be followed by activation of perivascular trigeminal afferents and neuronal pannexin1 channels and lead to an inflammatory cascade. Subject to spread of depolarization, fasting may trigger migraine headache preceded by an aura.<sup>14</sup>

Dehydration due to water deprivation during a prolonged fast can trigger migraines. Human brain composition is around 75-78 % water. In a state of water deprivation it begins to produce histamines which can cause pain and fatigue. When asked, a total of 34 out of 95 (35.7%) migraineurs agreed that dehydration could provoke their attacks.<sup>15</sup> A randomized controlled trial of 50 patients with primary headaches divided them in two groups. An extra 1.5 L of water intake was encouraged in one arm and then followed up after a period of three months. Drinking more water did not reduce the objective parameters of the monthly headache such as frequency and duration. However, 47% in the water group experienced improvement of their headache subjectively as a result of increased water intake, compared to 25% in the control group.<sup>16</sup>

#### **MEDICAL TREATMENT OF FASTING INDUCED MIGRAINE:**

Individuals who experience migraine due to fasting, should avoid the latter unless absolutely necessary. Pharmacologic treatment includes prophylactic drugs and symptomatic treatment. A study was carried out during Yom Kippur in 2004 in 105 patients. Rofecoxib, a Cox-2 inhibitor with a 17-hour half-life was given as a 50mg dose prior to the 25 hour ritual fast. The results showed that only 18.9 % developed a fasting headache in the treatment group as compared to 65.4% in the placebo group.<sup>17</sup> Similarly 90 mg of Etoricoxib, which has a half-life of 22 hours, when taken prior to a 15-hour ritual fast showed a decrease in the frequency and intensity of headache during the first 5 days of the month of Ramadan.<sup>18</sup> While Frovatriptan has been effectively used to prevent catamenial migraines because of its long half-life, studies have demonstrated its benefit in prevention of migraines for the same reason. When taken at the onset of a 20-hour fast in migraine patients, it showed that 36.4% of them developed headaches in the intervention group as compared to 52.9% in the placebo group.<sup>19</sup> Caffeine may be used in combination with an NSAID with a long plasma half-life in order to maintain a steady caffeine intake on fasting days to prevent caffeine withdrawal.<sup>20</sup> Valproic acid is used as prophylactic treatment of migraine and in intravenous form it has been effective as abortive treatment in status

migraine.<sup>21</sup> It has been proposed that post-hypoglycemic migraine may be ameliorated by prophylactic treatment with valproic acid as well.<sup>22</sup>

#### **NON-PHARMACOLOGICAL TREATMENT:**

While medication is the mainstay of treatment, cognitive behavioral therapy (CBT) is effective in reducing pain and psychological comorbidity in migraine patients. A systematic review revealed that some studies provide evidence in support of CBT and people experiencing headaches or migraines benefited from using techniques such as stress management, biofeedback and relaxation.<sup>23</sup> Physicians treating migraine patients should discuss possible exacerbation during fasting period. For instance before the month of Ramadan, counseling should be provided regarding the prevention of hypoglycemia, dehydration and caffeine withdrawal. Consumption of high quantities of water each night should be encouraged along with minimal use of caffeine during night time to avoid withdrawal and diuresis induced water depletion.<sup>12</sup>

#### **FASTING AND OTHER HEADACHES:**

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In addition to migraines, other primary headaches may also result from fasting especially in persons that are already prone to have headaches. A prospective study of 91 patients revealed that 32% of the patients developed tension-type headache while 9% presented with clinical features of migraines on the first day of Ramadan.<sup>24</sup> Orthostatic headache may also get precipitated during fasting due to acute metabolic changes and dehydration during fasting and secondary decrease of CSF volume. A relapse of headache due to spontaneous intracranial hypotension in a patient who was previously treated conservatively has been reported.<sup>25</sup>

#### **CONCLUSION:**

The association of migraine in fasting states is well-known, however, the vulnerable population must be identified and educated regarding appropriate life style modifications, behavioral and medical therapy in order to reduce disability in migraineurs, improve their quality of life and decrease disease burden overall. Well-designed epidemiological studies will further aid in developing appropriate preventive strategies at the level of patients and primary care physicians.

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**Lubna Jafri**; data collection and analysis, manuscript writing, manuscript review

**Mohammad Wasay**; concept, data analysis, manuscript review