

SPECIAL COMMUNICATION

Mini-Symposium: Ramadan Fasting and The Medical Patient: An Overview for Clinicians

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Abstract

The daytime fasting of Ramadan is observed annually by millions of adult Muslims all over the world. Some may have mild, moderate or severe medical conditions. They may seek advice on feasibility and safety of fasting and/or their management. Physicians ought to have a working knowledge about the religious rules of Ramadan fast and their medical implications. In this article we present a concise summary of the proceedings of a series of symposia. Their objectives were to review the effects of Ramadan fasting on the health of Muslim patients with various chronic medical conditions and to propose practical management strategies. An initial introductory Islamic perspective on fasting to set the scene for the following presentations. The religious rulings excluding patients with acute and chronic medical conditions from fasting were highlighted. The roles of the medical professional in guiding patients on best ways to make

informed decisions to fast and feast safely were stressed. Available evidence from published literature and clinical practice was reviewed and practical guidance covering the major body systems was given. Generally speaking, fasting in Ramadan is possible for most stable chronically ill patients under medical supervision. The effect of fasting on health issues should be explained to patients well ahead of starting the holy month. Counseling patients about their use of medications as well as their suitability to undertake the fast is a major step in health care for Muslim patients. Available observations cover a spectrum of chronic medical conditions affecting various body systems. These include renal, hematological cardiac, neurological, rheumatologic, gastroenterological, endocrine conditions and drug therapy during Ramadan. Changes in the parameters of clinical functions in healthy people and in non-renal patients were minimal, insignificant and remained within the normal range. Patients on hemodialysis could fast safely on non-dialysis days. Stable renal transplant recipients do not seem to sustain any risk from fasting after the first year. No evidence of increased risk of renal stones and colic was found during Ramadan. No consistent rise in cardiac events was observed during Ramadan. Hypertension needs special treatment manipulations. Headache and risk of seizures are two neurological conditions with relevance to fasting. These can be managed by simple medical measures. Peptic acid disease complications may increase by the long fasting, however treatment with peptic disease medications reduces the risks. Hematological conditions influenced by dehydration such as sickle disease are better managed by adequate hydration particularly under stressful circumstances. Rheumatological conditions can be managed by usual therapies during Ramadan. Diabetes received most attention from the medical profession for obvious reasons. Several expert statements were published. Where the risk of hypoglycemia or hyperglycemia is increased many would advise against fasting. Patients controlled by simple regimens with low risk of hypoglycemia may be able to fast safely. Changes in medication aim at adjusting the amount and timing of the drug administration to match calorie intake thus preventing hypoglycemia in the daytime and hyperglycemia after sunset. In conclusion, management of the medical patients during Ramadan represents a special challenge to patients alike. Taking on this challenge is an opportunity to test the cultural-competence of health services.

Key Words: Islam, Ramadan Fasting, Ethnic, Cultural-competence, Diabetes, Cardiac, Coronary Heart Disease,

Drug Therapy, Arthritis, Headache, Multiple Sclerosis, Stroke, Epilepsy, Peptic Ulceration, Inflammatory Bowel Disease, Sickle Cell Disease, Thalassemia

Introduction

The daytime fasting during the lunar month of Ramadan is observed annually by millions of adult Muslims all over the world (1). Some of these individuals may have mild, moderate or severe medical conditions. Though they may theoretically be exempted from fasting, some may not realize this or may not be able to apply the religious ruling on their case (2). Frequently, they choose to ask their medical practitioner certain questions pertaining to their ability to fast safely. Others may decide to observe the fasting on their own accord but they may seek advice on how to adjust their life style and medication to suit the fasting. Whatever the case, physicians ought to have an updated working knowledge about fasting religious rules and its medical implications (3, 4). In our attempt to promote culturally competent clinical practice, we have run a series of symposia just before the month of Ramadan over that last couple of years. The general aims were to increase awareness amongst physicians and other health care professional of the medical implications of Ramadan fasting. The stated educational objectives were firstly to review the effects of Ramadan fasting on the health of Muslim patients with various chronic medical conditions and secondly to propose practical management strategies for those who choose to fast.

In this article, we present a concise extract from the salient points discussed in these symposia. Speakers were asked to present a summary of evidence available in the published literature and reflect on common clinical practice with view to provide some practical guidance. A focus was specifically made on firstly when to advise patients not to fast and secondly how to amend their therapeutic regimens during the fasting periods if fasting was deemed safe. An introductory discussion of an Islamic perspective of fasting aims to put the subsequent sections in a cultural context. Chronic medical conditions affecting major organ systems were discussed. However, we must admit that this report will not be exhaustive in its details and liberal use will be made of reference to the more detailed published original work and reviews articles. It is hoped for this mini-symposium to be a useful quick reference guide for the practicing clinician. We chose to submit it to Ibnosina Journal of Medicine and Biomedical Sciences, being an open access online publication, to allow unrestricted maximal free dissemination (5). We accept that the selection

of the subjects may have been limited on this occasion by the volume of available literature and influenced by the local expertise. We trust that the Journal's editors would welcome correspondence that may provide different or complementing views. We will sincerely receive such comments and critiques with an open mind and we will be eager to hear from all those who share our interest in the medical aspects of Ramadan fasting.

Fasting In Health and Disease: An Islamic Perspective

Ramadan is the month in which Muslims are ordained to fast every year. Fasting is an act of worship; it represents the fourth pillar of Islam. It involves abstaining from all intakes and from sexual intercourse from Dawn till sunset. There are implications for such abstinence on the human body physiology both in health and disease state. The Islamic jurisprudence principles that govern mandating or excusing fasting is addressed briefly here.

Islamic doctrine on regulating fasting during health and illness

A fundamental Islamic doctrine states: **Hardship brings Ease**. Fasting that endangers health is not in accordance with Islamic jurisprudence. The Quran states exemption from fasting for the traveler: this provides the basis for "prophylactic" exemption from fasting in the state of health if it leads to illness or health deterioration. Current illness is another excuse from fasting as stated in the Quran; this is particularly relevant if fasting worsens one's illness or delays recovery (1). The role of the physician is to guide the patient throughout different states of health so as to be cognizant of the consequences of fasting on his overall wellbeing. In acute and curable illness, fasting days can be made up for after the acute illness is over. In chronic diseases, however, fasting days can be made up for in the disease free/ stable periods of chronic illness. In cognitively intact patients with incurable disease, one feeds a poor person for every day not fasted. In demented or cognitively impaired persons with incurable diseases, fasting is no longer an obligation.

Physician's role in caring for the patient required/able to fast

First, it is important to know whether fasting will cause or hasten death, morbidity (organ damage- delayed healing – risk of complications), or excessive pain or difficulty for the patient. Second, the physician needs to determine whether or not it is safe to fast in disease free/stable periods of chronic illness, or to interrupt disease stabilizing/modifying

therapies in chronic disease, and whether or not therapy schedule could be safely adjusted to allow safe fasting. Third, the verdict on whether a particular intervention breaks the fast or not relies heavily on a clear descriptive of the medical intervention; There is general consensus opinion by Islamic jurist related to all such interventions that clearly mimic taking food or drink by oral route, such as taking oral medications. There is a difference; however, in Islamic jurist's opinion related to other routes (ophthalmic, otic, rectal, intramuscular, intraurethral, intrathecal, intravenous, inhalation, etc). One other important medical decision is whether an intervention that breaks fasting be done or postponed? Such an intervention can be postponed if it is not urgent/ emergent and there isn't a safe and acceptable alternative (that does not break the fast).

Should the physician answer patient's religious questions on fasting?

The best practice is for the physician to describe the nature of intervention and allow for the patient to consult with his religious reference of the school of Islamic jurist he follows.

In conclusion, fasting is one of the great "Pillars of Islam" and tokens of submission to almighty Allah. Islamic doctrine regulates fasting in order to promote a goal targeted practice of worship; soul purification without undue physical hardship or suffering. The physician plays a vital role in promoting and facilitating safe practice of fasting and preservation of physical health. In a patient oriented health care system, this role should be performed with knowledge, professionalism, and mutual respect.

Ramadan Fasting and The Kidney

Fluid alteration in fasting healthy adults

Several studies documented the renal function during Ramadan. In summary, these showed that urinary volume, osmolality, pH, nitrogen, solute, and electrolyte excretion remain normal (6) Changes in serum urea and creatinine are usually small and not statistically significant (6,7). In prolonged fasting, serum uric acid increases to abnormal values (7). This is probably due to decreases in glomerular filtration rate (GFR) and uric acid clearance. In Islamic fasting, however, there is only a slight increase in uric acid (6,8) due to the nature of fasting, which is short-lasting and intermittent. Ramadan fasting does not cause significant alterations in serum sodium and potassium (9) In experimental prolonged fasting, urinary excretion of

25 meq potassium per day has been seen, however, serum potassium remains normal.

Ramadan fasting in patients with chronic kidney disease

In general, many benefits have been suggested for calorie restriction. It retards aging, increases mean and maximum life-spans, reduces age-associated diseases such as carcinogenesis, immunosenescence, memory function, oxidative stress, reduces blood pressure, body fat, serum triglycerides, serum cholesterol, fasting blood glucose and insulin, increases HDL, reduces neuronal degeneration in experimental models of Alzheimer's and Parkinson's diseases, delays spontaneous tumorigenesis in p53 deficient mice (sarcoma, lymphoma), reduces angiogenesis, increases apoptosis, and inhibits growth in the CT-2A mouse brain tumour model. The mechanisms unrelated to weight reduction, involve Leptin, serum Insulin-like growth factor 1 (IGF-1) etc. These may represent an adaptive metabolic response system to maximize survival during periods of food shortage (10,11).

The health concerns include the safety of fasting in patients with chronic kidney disease, haemodialysis, renal transplantation recipients and the effect on renal stone disease. These issues will be discussed here by reviewing the published work and concluding to the consensus/expert opinion on the practical management recommendations.

The safety of fasting in patients with chronic kidney disease

The effect on health and well being of the month-long intermittent fast and fluid restriction has been studied in various potentially vulnerable groups in addition to normal healthy individuals in many countries (12). The majority of the studies have found significant metabolic changes, but few health problems arising from the fast. A reduction in drug compliance was an inherent negative aspect of the fast. Common findings of the studies reviewed were increased irritability and incidences of headaches with sleep deprivation and lassitude prevalent. A small body mass loss is a frequent, but not universal, outcome of Ramadan. During the daylight hours of Ramadan fasting, practicing Muslims are undoubtedly dehydrating, but it is not clear whether they are chronically hypo hydrated during the month of Ramadan. No detrimental effects on health have as yet been directly attributed to negative water balance at the levels that may be produced during Ramadan.

A prospective study was performed on 15 predialysis chronic kidney disease (CKD) patients and six healthy volunteers as control (13). They were studied during two

phases: when the subjects were drinking and eating freely before the start of Ramadan, and a second phase toward the end of Ramadan. Glomerular filtration rate (GFR) using DTPA dynamic renal scan and tubular cell damage were estimated. The change in glomerular filtration rate was not different between the CKD and control groups. The urinary N-acetyl- β -D-glucosaminidase (NAG) percentage change was found to be significantly higher in the CKD patients compared to the control group. There was a significantly positive correlation between the NAG values and the change in the blood glucose level ($p=0.001$), hence diabetic CKD patients should be meticulously followed during Ramadan fasting. In conclusion, fasting Ramadan may have injurious effect on the renal tubules in CKD patients. Larger studies are recommended to determine the extent of tubular injury and renal function in CKD patients during Ramadan fasting.

Renal effects of NSAID in Ramadan

Alfaraj et al (14) evaluated the combined effect of Ramadan fasting and short-term use of different non-steroidal anti-inflammatory drugs (NSAIDs) on renal function in healthy volunteers. They assigned the study subjects to six different groups, five of whom took different NSAIDs and the sixth was a control group. Measurements of serum and urinary markers of renal function were taken before fasting, 10 days into fasting while using NSAIDs, and five days after stopping the use of NSAIDs. The results showed slight changes in serum and urine measurements during fasting while using NSAIDs. These changes, although were significant in some cases, were within the normal range and were noted in all the study groups including the control group. This suggests that short-term use of NSAIDs in healthy subjects during fasting is not particularly associated with any major adverse effects on the renal function.

Ramadan fasting in patients on chronic hemodialysis

Many physicians recommend that patients with hemodialysis may avail themselves to the exemption of chronic disease and pay the ransom instead of fasting. However, data is available from only a single study reported by Al-Khader et.al. (15). They examined 40 patients on hemodialysis for more than 6 months. They fasted on non-dialysis days only and blood samples obtained predialysis on non-fasting days. They noted increased interdialytic weight gain during Ramadan but no significant difference in mean arterial BP. Significant rise in predialysis K^+ concentration before Ramadan was also observed. However, there was no need for hospitalizations for pulmonary oedema and no

clinical adverse effects of hyperkalemia. Based on these observations, they recommended that fasting on non-dialysis days is probably safe and that dietary advice in fasting patients assumes increasing importance.

Ramadan fasting and renal transplantation

With the increase in the number of renal transplants performed in Islamic countries as well as improved quality of life, the question of the safety of fasting Ramadan is being asked more often (16,17). Transplant patients are at increased risk of adverse effects related to fasting due to their underlying illness and immunosuppressive medication (17). The major concern in these patients is that if dehydration and accumulation of metabolites may result in irreversible deterioration in renal function or facilitate rejection episodes via inducing changes in immune system. Several reports of varying sizes addressed these issues. Argani et al (18) studied 24 patients and found no significant increase in body weight, blood pressure, and renal function. They concluded that Ramadan fasting was not harmful to stable renal transplant patients with a 12-hour fasting pattern. They recommended that patients should be observed carefully during the fast. Einollahi et al (19) studied 19 fasting kidney transplant recipients and compared them with 20 matched recipients who did not fast. All patients had serum creatinine values below 1.5 mg/dL at entry to the study. No significant changes in serum creatinine concentrations during Ramadan were observed in either group suggesting safety of fasting Ramadan in recipients with stable renal function. The same group reported in another study of 41 Ramadan fasting kidney transplant recipients who were compared to matched controls that the mean of estimated glomerular filtration rate (GFR) did not significantly change after 30 days of fasting in either group (20). The authors concluded that for patients with GFR higher than 60 mL/min, Ramadan fasting did not cause impairment of allograft function. Abdulla et al (21) evaluated 17 renal transplant recipients with normal function and 6 with stable but impaired allograft function (plasma creatinine levels not exceeding 300 mmol/L). They also found no significant changes in any of the studied parameters during Ramadan. They concluded that Ramadan fasting did not cause any significant adverse effects on kidney transplant recipients with normal or impaired graft function. They too suggested that it is safe for those patients to fast during Ramadan after one year of renal transplantation. Ghalib et al (21) studied a group of 68 renal transplant recipients (35 fasting and 33 non-fasting controls) over 3 years. The mean GFR after the third

Ramadan did not differ significantly from that at baseline in the fasting group. Furthermore, no rejection episodes or renal function deterioration were observed during or soon after Ramadan. The largest study was reported by Said et al (23) involving 145 kidney transplant recipients (71 patients fasted during Ramadan and 74 did not). Renal function did not show any significant change between the two groups during Ramadan fasting. Cyclosporine toxicity was observed in two fasters, and acute rejection episodes occurred in other two, urinary tract infection occurred in two more. No graft or patient loss occurred in any of the groups. The authors concluded that fasting Ramadan by kidney transplant recipients with normal kidney function is safe. Finally, Boobes et al (24) studied 22 kidney transplant patients with stable kidney functions and voluntarily chose to fast Ramadan. Body weight, blood pressure, renal and metabolic biochemistry and cyclosporine levels remained stable after Ramadan fasting. The authors concluded that for it is safe for kidney transplant recipients of more than one year with stable graft function to fast Ramadan.

Based on these findings, the general belief among medical professionals in transplantation is to allow fasting when the transplanted kidney graft is functioning well for at least one year (16,17). In a recent analysis, the total number of transplant patients fasting during Ramadan studied in the reviewed articles was 213 patients. This may not be large enough to have a final conclusion. However, none of the studies found any significant adverse effects related to Ramadan type fasting. Two groups suggested preserving Ramadan fasting to patients without impaired allograft function; no evidence was presented in any of them to support this conclusion.

Renal stones and renal colic

The prevalence of renal colic in Ramadan was compared with other months of the lunar year (25). The records of 574 subjects who were admitted to two medical centers in Iran were reviewed. They included 398 males and 176 females. Twenty-seven males and 16 females were admitted in Ramadan and 371 males and 160 females in other months of the year. Colics were more common in June, July and November (68, 65 and 60 patients respectively). Forty-three subjects were admitted in Ramadan. The frequency in Ramadan was not significantly different from mean admission of the year (48 patients). There was also no significant difference between frequency of admissions in Ramadan and mean admission during cold half of the year (37 patients). Furthermore, the mean admissions in warm seasons (64 patients) were significantly higher

than Ramadan ($p < 0.001$). This data suggest that the lack of difference in the two groups indicates that higher temperature rather than fasting as a cause for renal colics.

In summary, changes of renal function during Ramadan fasting are minimal, insignificant and values remain in normal ranges. No consistently injurious pattern could be seen in patients with chronic renal impairment from fasting during Ramadan. Many patients on chronic haemodialysis could tolerate fasting on non-dialysis days well. Adverse effects in any patients with normal or impaired (but stable) renal allograft function were observed. Fasting in Ramadan is probably safe in stable renal transplant recipients

Care of Cardiac Patients During Ramadan

Cardiovascular diseases are becoming increasingly common. Eating and fasting states may directly and indirectly affect the risk factors for these diseases. There are two practical questions that face clinicians in this context. These are 1. Does Ramadan fasting produce a detrimental effect on heart patients? 2. How to manage common cardiac conditions during Ramadan?

Cardiac diseases in Ramadan: risks and concerns

Fasting may affect cardiac patients because of the limited time allowed for food intake and the heavy physical worship that is performed after a heavy meal, as well as the inability to take any medications. Common adult cardiac diseases to be considered in the present discussion are ischaemic heart disease, hypertensive heart disease and congestive heart failure. Several studies were published on these conditions as summarized below:

Ischaemic heart diseases during fasting

Several studies investigated whether Ramadan fasting has a negative effect on the incidence of presentation with acute coronary syndromes (ACS) such as acute myocardial infarction (AMI) and unstable angina (UA). Temizhan et al. evaluated retrospectively patients who were hospitalized at an emergency center (26). Throughout the years of the study the number of cases with acute coronary heart disease was significantly lower in Ramadan but the ratio of this population to all patients was not statistically significant between the periods. Al Suwaidi et al. used a database of all patients admitted to a cardiology department in Qatar where over 95% of Qatari adults regularly practise fasting (27). All patients presenting with ACS were identified. Periods corresponding to Ramadan in the calendar were

established. A total of 20856 patients were admitted of whom 8446 were Qataris. There was no significant difference in the incidence of acute myocardial infarction or unstable angina before, during or after Ramadan. A prospective investigation whether Ramadan fasting has any effect on patients with heart disease in 465 outpatients was performed in several medical centers in the Gulf region (28). Detailed assessments were performed before, during and after Ramadan. It was found that 91.2% of these patients could fast and only 6.7% felt worse while fasting. Of the studied subjects, 82.8% were compliant with cardiac medications and 68.8% were compliant with dietary instructions. Only 19 patients needed hospitalization during Ramadan for cardiac reasons. Furthermore, an attempt to determine if fasting has any effect on the circadian presentation of acute cardiac events. Patients (total 1019; 162 fasting) with acute coronary events were analysed by Al Suwaidi et al. (29). The relationship of time of presentation of initial symptoms with fasting was evaluated. Although, fasting patients were tended to present to the emergency department in the time periods between 5-6 AM and at 11 PM and were less likely to present in the time periods 1-2 PM and 5-6 PM, these differences were not statistically significant. However, fasting patients were less likely to have their symptoms start between 5 and 8 AM and more likely to have symptoms between 5 and 6 PM and between 3 and 4 AM ($P = 0.002$). Data from these studies suggest that the effects of fasting during Ramadan on stable patients with cardiac disease are minimal. Most patients with stable cardiac disease can fast safely. No increase in hospitalization was noted during Ramadan. Exogenous factors associated with fasting such as changes in food intake and/or sleep timings, affect the circadian rhythm do influence the timing of presentation of acute coronary events.

Congestive heart failure

Chamsi-Pasha and Ahmed (30) studied 86 fasting outpatients with heart disease Ramadan in Jeddah, KSA. Assessments were performed just before the start and on the last day of Ramadan. 62, 18 and 6 patients were in New York Heart Association (NYHA) Class I, II and III respectively. Seventy-four patients could fast during the entire month and 9 patients missed the fasting for up to 7 days. Al-Swuidi et al. (31) investigated whether Ramadan fasting has any effect on the number of hospitalization for congestive heart failure (CHF) in a geographically defined population using the data base described earlier. Patients were divided according to the time of presentation as before, during and after the month of Ramadan. The number

of hospitalization for CHF in various time periods was analyzed. Overall, 2160 Qatari patients were hospitalized for CHF. Hospitalizations for CHF were not significantly different in the months before, during and after Ramadan (182, 208 and 198 cases respectively). There were no significant changes in the NYHA Class ($p=0.12$) nor in any of the haematological or biochemical parameters during the fasting of Ramadan. These two studies demonstrate that the effects of fasting during Ramadan on stable patients with cardiac disease are minimal and that fasting is not associated with any significant increase of occurrence of CHF or excess need for hospitalization for CHF.

Hypertension and Its management in Ramadan

Many factors may theoretically influence ambulatory blood pressure during Ramadan. These include fasting-refeeding per se, sleep changes, changes in timing of intake of medication. Herbal et al. (32) studied the consequences of Ramadan fasting on variations of the blood pressure (BP) in the course of 24 hours. They selected 99 hypertensive patients and studied their BP profile. All these patients have an ambulatory blood pressure measurement (ABPM) before the fast and during Ramadan. No statistically significant difference was noted between these 2 periods neither for the systolic BP (SBP) nor for the diastolic BP (DBP), for the BP of 24 hours, and the diurnal and nocturnal periods. They observed that during the month of Ramadan the peak of the awakening is delayed by 2 hours and the nocturnal trough is delayed by 1 hour. Perck et al (33) investigated the effects of fasting on 17 treated hypertensive patients. A 24-hour BP monitoring was carried out twice: before Ramadan and during the last week of the month. All patients continued their medications, which were all administered once daily. They assessed 24-hour MBP as well as average awake and average sleep BP. There found no difference between the MBP before or during Ramadan. This was confirmed a more recently by study (34) in treated subjects with grade 2–3 hypertension using combination drug therapy. Twenty-four hours ambulatory blood pressure monitoring was performed during and after Ramadan. No statistically significant difference was found between 24h mean blood pressures in the two monitoring periods, except for a small rise before dawn while having a morning meal (34). These studies concluded that in patients with uncomplicated essential HTN, Ramadan fasting was well tolerated. The variations of BP are minimal and are probably related to the changes in sleep, activity, and eating patterns. Therefore treated hypertensive patients might be assured that, with continuation of prescribed medications,

fasting during Ramadan could be safely undertaken.

Based on these observations, the formal recommendations were made on management of hypertension during Ramadan by two professional bodies in the Arabian Gulf region (35, 36). They include that 1) Physician's advice and management should be individualized. 2) Patient education should emphasize the need to maintain compliance with non-pharmacological and pharmacological measures. 3) Diuretics are better avoided, especially in hot climates or to be administered in the early evening. 4) Patients are encouraged to seek medical advice before fasting in order to adjust their medications if needed. 5) A once daily dosage schedule with long acting preparations is recommended. 6) Patients with HTN should be advised to take a low salt, low fat diet. 7) Patients with difficult to control HTN, should be advised not to fast until their BP is reasonably controlled and 8) Patients with hypertensive emergencies should be treated appropriately regardless of fasting.

In conclusion, Ramadan fasting is safe in stable patients with heart disease. Most cardiac medications can be prescribed once or twice daily. The incidence of acute myocardial infarction is not increased during Ramadan. A fairly small group of patients with cardiac conditions should be advised to refrain from fasting during Ramadan. These include patients with acute cardiac illnesses, acute myocardial infarction and acute coronary syndromes. Patients with severe congestive heart failure and those with uncontrolled hypertension requiring multiple dosages during the daytime should be counselled against fasting. Patients with severe congestive heart failure requiring high doses of diuretics; especially if they are prescribed via IM or IV routes. Patients who experience exacerbation of their illness during fasting that require additional therapy or medical consultation. A general advice for hypertensive patients during Ramadan can be offered. Patients should consider reducing the doses of their diuretics and use them after Iftar. They should take the long acting medicines before Suhoor (eating before dawn). Avoid high salt intake or Liquorice drinks. Those with severe hypertension and are on multiple medications may not be able fast safely.

Neurological Disorders During Ramadan

Neurological conditions may be affected by fasting for different reasons. There are reports in the literature addressing effects on a few select conditions. These include headache (including migraine), epilepsy, risk of stroke, neurodegenerative diseases, and multiple sclerosis. Other conditions have been mentioned in the context of

Ramadan fasting.

Headache

In the international classification of headache, "Fasting Headache" is included in "headaches attributed to disorder of homeostasis" (37). Fasting headache is usually diffuse or located in the frontal region, and the pain is non-pulsating and of mild or moderate intensity. In most cases, the headache occurs after at least 16 h of fasting and resolves within 72 h after resumption of food intake. The likelihood of developing fasting headache increases directly with the duration of the fast. Headache sufferers have a higher risk of developing headache during fasting than people who do not usually suffer from headache. Hypoglycemia and caffeine withdrawal have been implicated as causative factors but the evidence for hypoglycemia as a causative factor is weak. In a random sample of hospital staff, a specially designed questionnaire was distributed to 150 fasting persons on the second day of Ramadan (38). Completed questionnaires were obtained from 116 subjects. Headaches were reported by 41% of those who fasted as compared to 8% of those who did not fast ($P=0.002$). The headache was of tension type in 78% of the cases. Headache frequency increased with the duration of fasting and affected mainly those prone to have headaches, especially tension type. The most important exogenous-associated factor was caffeine withdrawal. Factors such as lack of sleep, hypoglycemia, and dehydration may have been contributory in a small number of cases. Under different circumstances, the use of prophylactic COX2 inhibitors was suggested to end to the Yom Kippur headache observed by Jews. This was confirmed in two randomized placebo controlled double blind trials of 50 mgs of Rofecoxib (39) or 120 mgs of Etoricoxib (40) taken just before the start of fasting. Thus confirming that fasting headache can be prevented or attenuated by COX2 inhibitors. In conclusion, fasting headache can be reduced by a progressive reduction of caffeine consumption in the weeks preceding the month of Ramadan and/or taking a cup of strong coffee just before the start of the fast. Alternatively use of simple analgesics may be needed in high-risk patients.

Epilepsy and fasting

There is some evidence that epileptic patients are more prone to increased seizure frequency in the month of Ramadan. This may result from a complex interaction of multiple factors namely changes in timing of drug intake, alterations of biokinetics of antiepileptic drugs, sleep cycle disturbance and physical and emotional stress that is a part

of day long fasting. In one study (41), 114 known epileptic patients were included. They were followed up in epilepsy clinic in the 3 months following Ramadan (2004). All of them fasted during Ramadan. 38 patients had seizures during Ramadan and one of these patients developed status epilepticus during the fasting month. 29 patients (76.3%) of them reported changing their drug regimens according to the times of Iftar and Suhour. When the seizure frequency of these patients during Ramadan was compared to that in the previous year and last 3 months period just prior to Ramadan, a statistically significant increase was observed ($p<0.001$). However, in those who received monotherapy or polytherapy, no difference in the frequency of seizures during Ramadan was seen. Changing drug regimen seems to be the most important reason for the increase in seizure frequency during Ramadan. Even though the drug doses given to patients were the same as before Ramadan, there was an important increase in the risk of having seizures in the patients who changed their drug regimens when compared with those who did not change. During Ramadan, accurate distribution of drugs prescribed twice a day is difficult to achieve between iftar and suhour as the dosing time and time span between the doses are altered. These alterations could affect the drug's plasma concentration profile and, therefore, its efficacy and tolerance. In addition, drug-food interactions may result in reduced, delayed or increased systemic availability of a drug. Circadian rhythm has to be considered as an important factor that influences drug pharmacokinetics. In nine patients (23.7%) with a monotherapy of valproic acid (taken as single evening dose), seizure frequency increased even though no change was made to their drug regimen. In another study, Adil et al (42) assessed the pharmacokinetics of valproic acid in 12 healthy volunteers during fasting. A single oral dose of 800 mg was administered to the first group of subjects ($n=7$) in the evening and to the second group ($n=5$) in the early morning. Each group was submitted to three treatment phases: the first was carried out 3 weeks prior to Ramadan (PR), the second one at the end of the first week of Ramadan (R1) and the last at the end of the third week of Ramadan (R3). The study showed a significant influence of the alterations in life rhythm and administration schedule on the pharmacokinetic parameters of this drug. The decrease in the plasma elimination half-life was attributed to the reversal of the feeding rhythm and the alteration in the rest/activity cycle could modify the circadian evolution of physiological parameters that are required for hepatic metabolism such as hepatic enzymatic activity and hepatic blood flow. Evidence suggests that changing the timing

of medication increases the likely hood of seizure. Sleep fragmentation and sleeplessness are also important factors in seizure recurrence. Fat rich meals eaten during Ramadan also affect the bioavailability of medications.

Stroke and fasting

Akhan et al. (43) investigated whether stroke incidence differs during Ramadan compared to other months. All patients admitted from 1991-1995 were divided into those with stroke in Ramadan and those not in Ramadan. They found no statistically significant differences between the age and sex distribution of patients and the incidences of strokes in both groups. In another study by Omoululu et al. (44), patients hospitalized solely for ischemic stroke and intracerebral haemorrhage were evaluated retrospectively to study the effects of Ramadan on stroke. The ratio of these cases to other patients hospitalized in the neurology department was determined. The in-hospital clinical course and mortality rates of the patients with stroke were evaluated. Within the entire cohort, the most frequently encountered type of stroke was ischemic ($P < 0.05$). The proportions of hemorrhagic and ischemic strokes had no statistically significant differences between the periods before Ramadan, during Ramadan, and after Ramadan ($P > 0.05$). The ratio of hemorrhagic stroke decreased in hypertensive patients during Ramadan ($P < 0.05$). In diabetic patients, the ratio of ischemic stroke increased in the month of Ramadan significantly ($P < 0.05$). Although Ramadan fasting had an adverse effect on diabetic patients with ischemic stroke, there was no negative effect on hypertensive patient with hemorrhagic stroke or stroke frequency.

Cerebrovenous thrombosis during fasting

Saadarnia et al (45) determined whether fasting would affect the frequency of cerebral venous and sinus thrombosis compared to other months. All patients ($n=162$) with cerebral venous and sinus thrombosis admitted to three neurological centers from 2001 to 2006 in the Isfahan. Patients were divided into two groups according to the month of onset of cerebral venous and sinus thrombosis. The first group included patients with cerebral venous sinus thrombosis that occurred while fasting ($n=33$) and the second group was composed of patients with onset in other months, while not fasting ($n=129$). From 2001 to 2006, the mean number of patients' diagnosis during fasting month was 5.5 versus mean number of patients during all other non-fasting months that was 1.95. The analysis showed a significantly increased frequency of cerebral venous

sinus thrombosis events in Ramadan compared to other months ($p=0.000$). They concluded that fasting increases frequency of cerebral venous and sinus thrombosis. These findings are inconsistent with other reported studies on arterial stroke and need to be confirmed by other studies. It seems that healthy people have no problem with regard to cerebral venous and sinus thrombosis while fasting, but susceptible persons, such as those with hypercoagulable states and women who take oral contraceptive pills, may be at increased risk.

Multiple sclerosis

Muslim multiple sclerosis (MS) patients are concerned whether prolonged fasting might have an unfavourable impact on the course of their disease. A prospective study to determine the effects of prolonged intermittent fasting on the course of multiple sclerosis in a cohort of patients was recently reported (46). The cohort consisted of 40 adult multiple sclerosis patients who fasted during Ramadan and 40 patients who did not fast. Only patients with mild disability (using expanded disability status scale were included. All patients were followed for 6 months after Ramadan to assess their scored changes and to record the number of clinical relapses. At the end of the study, no significant changes in the scores or the frequency of clinical relapses were detected between the 2 groups ($p<0.05$). It was concluded that fasting had no short-term unfavourable effects on the disease course in MS patients with mild disability. However, larger studies of longer duration are needed to validate the results of this study.

Neurodegenerative conditions

Parkinson disease management can be tricky during fasting. The serum half life of most medication used in Parkinson's disease is less than 6 hours with the notable exception of Pramipexole and Selegiline. In the early stages of the disease, use of a dopamine agonist like pramipexole can be used twice daily. In more advanced disease, the need for more frequent drug administration prohibits fasting. As is true with Parkinson's disease, patients with early features of dementia like memory decline can be treated with drugs like Donepezil once daily. More advanced disease requires institution of multiple medications for management.

Miscellaneous conditions

Myasthenia Gravis requires frequent medication administration. Half life of Mestinon (Pyridostigmine) is less than 6 hours. Therefore patients with serious myasthenia gravis that require continuous treatment should break the

fast otherwise they will have a risk of crisis. Patients with essential tremors can be managed with Propranolol, extended release preparation or with Topiramate. The serum half lives of both medications fairly long.

Therefore, headaches and seizures are the main two neurological conditions that are known to get worse with fasting. For headaches, a tablet of an analgesic and a cup of coffee might suffice. For seizures, patient should be encouraged to sleep well and not to change the drug timing. Other conditions have to be treated on individual basis.

The Gastrointestinal Tract During Ramadan

Digestive system during fasting and Fed States

Under normal circumstances, fasting (not eating) is the normal state of feeding and the postprandial state is the temporary state. Overall, during fasting there is a reduction in the secretions and slowing in the GIT motility. The GIT motility at the proximal Gut (stomach + small intestine) in fasting has 4-5 postprandial phases till next meal. The migratory motor complex (MMC) incorporates 3 phases. A long non contracting 30 minutes (phase I). This is followed by an equally long phase II characterized by irregular sub maximal contractions in amplitude and frequency and culminating in a short phase II of regular periodicity every 70 – 90 min. The maximal contractions (frequency & amplitude) are rhythmic at a rate of 12/min. The increase the lower oesophageal tone, gall bladder tone and bile transit rate. In the fed state (post-prandial), the MMC cycle terminates abruptly and is replaced by submaximal irregular contractions < 12/min. The LES tone (resemble Phase II) and this phase lasts 4 – 5 hours. This is regulated by neuro-hormonal control involving the myenteric plexus and several hormones such as insulin, somatostatin, glucagon, secretin, motilin, gastrin, cholecystokmin, neurostarsin, NO. The interaction is very complex and not well understood. The colon does not participate in MMC and it has its independent periodic activity.

Effects of fasting on chronic GI diseases

Gastroesophageal reflux disease (GERD)

After Iftar, the lower esophageal sphincter (LES) pressure is decreased encouraging reflux and resulting in increased symptoms. Therefore, it is recommended that no contraindication to fasting in most cases. Diet should contain a lower fat content and the meals are made smaller in size. If erosive disease is evident by endoscopy, treatment should be given in the form of proton pump inhibitors (PPI's) at iftar and suhour. For non-erosive reflux disease

(NERD) or GERD diagnosed by symptoms only, a single daily dose of PPI should be adequate before Iftar.

Peptic ulcer disease (PUD)

Earlier reports suggested increased incidence of complication rate with Ramadan fasting (47-51). Recent reports following the wider usage of PPI's in patients with peptic disease suggest that equal healing and no complication with or without fasting Ramadan (52-54). In one report, increased perforations were observed after Ramadan.

Bowel diseases

During Ramadan, management of inflammatory bowel diseases namely Cohn's, disease and ulcerative colitis will depend on the phase of the disease. In active disease, fasting is not recommended and full nutrition support is needed with high dose medications. In patients with quiescent disease, the usual medications may adequately be divided taken between two to four times. Patients are less likely to come to any harm from fasting during this phase (55). It is most likely that fasting will be helpful for irritable bowel syndromes (56). No association was found with acute surgical conditions such as acute appendicitis (57).

Changes in liver function tests during Ramadan fasting

During fasting liver glycogen content is decreased by glycogenolysis as it is utilized to maintain blood glucose level. It is noteworthy that a normal liver stores up to 1200 Calories, which is enough to support blood glucose for 24 hours of fasting. Fasting hyperbilirubinemia represents a rise in the circulating unconjugated bilirubin. It occurs in healthy individuals but to a much higher extent in patients with Gilbert's disease. Serum bilirubin levels return to baseline at 12-24 hours after resumption of regular meals. Normocaloric lipid-free diet may produce a similar effect. The mechanism of fasting hyperbilirubinemia is multifactorial. Decreased hepatic clearance of bilirubin and enhanced heme catabolism has been incriminated. Lipolysis of adipose tissue with subsequent desquamation and release of bilirubin suggested by correlation of non-esterified fatty acids levels with bilirubin levels in fasting normal subjects. Reduced conjugation and decreased intestinal motility (by enhancing enterohepatic cycling) may also be contributing. During Ramadan serum bilirubin levels were shown rise after 10 days fasting in some studies but not in others (58). However, no significant changes in ALT, AST, protein, albumin in any of the studies in normal

people.

Effects of fasting on chronic liver disease

There are no data on chronic hepatitis B & C. There does not seem to be any contraindication for fasting. Patients who are therapy should continue on standard treatments such as Peginterferon, Ribavirin, Lamivudine, Adefovir, or Entecavir. Similarly, there are no reports on fasting for patients with autoimmune hepatitis. However, there should be no reason to refrain from fasting. Patients who are on treatments such as Prednisone, Azathioprine, Cellcept may safely continue to take them in the evening time.

On the other hand patients suffering from cirrhosis should be assessed individually, on the same lines discussed above; patients who are compensated may fast and continue on their usual medications and dietary modifications such as salt restriction whereas patients with decompensated cirrhosis should be advised against fasting. Though there are no available data on liver transplant patients during Ramadan, safety data from renal transplants discussed above may possibly be safely extrapolated to this situation. The care of post liver transplantation should be very carefully assessed and offered carefully tailored “individualized” management recommendation.

It is therefore recommended that most mild and stable GI conditions do not constitute a reasonable cause for avoiding fasting. Examples of these include stable inflammatory bowel disease, irritable bowel disease and stable chronic hepatitis. However, patients should be discouraged from fasting. It is not advisable to fast in the presence of active GI conditions like complicated peptic ulcer diseases, Crohn's disease, ulcerative colitis and de-compensated cirrhosis. It may not be advisable to fast immediately after liver transplantation but the decision for stable post-transplant patients should be taken on individual basis. It is generally recommended for patients who will fast to follow healthy dietary habits before starting Ramadan. This include avoidance of over-eating, eating low fat food, drinking plenty of water, and adjusting previous medications to once or twice daily regimes to meet the timing of Iftar & Suhoor as guided by their physician's advice.

Diabetes and Ramadan Fasting

Diabetes is a disorder of carbohydrate, lipid and protein metabolism. Diet and exercise are basic methods of controlling diabetes. Daytime fasting during Ramadan will predictably interfere with these endeavours. In addition, therapeutic agents employed in diabetes management could produce adverse events if not matched by balanced diet and

exercise. Patients are very keen on observing the fast by religious and social factors (59-61)

Risks and health concerns

Daytime hypoglycemia is due to lack of carbohydrate intake and/or lack of down ward adjustment of doses of insulin or oral hypoglycaemic agents. Evening Hyperglycaemia is due to excessive intake of food. In the daytime, hyperglycemia may be due to overzealous reduction or total omission of insulin dose at Suhoor time. Severe Hyperglycaemia with or without ketoacidosis may complicate inter-current illness. Dehydration may occur with risk of thrombosis (62,63).

Practical management recommendations

There are two questions that need to be answered. 1) When to advise against fasting? 2) What is the optimal therapeutic regimen? Patients with type 1 and type 2 diabetes who are allowed or choose to fast should be given specific information on fasting and recommendations on therapeutic changes. They should be warned against skipping meals, taking medication irregularly or nighttime gorging.

Who should be discouraged from fasting?

The advice in favour or against fasting is being addressed. There are widely accepted consensus criteria for advising against fasting based. An alternative approach proposed am more elaborate stratification system to categorize risk in patients with type 1 or type 2 diabetes who fast during Ramadan into very high, high, moderate and low (62,63) These are freely available as public domain and can be consulted on the internet. Because of the religious nature of the fast, the use of the terms “indicated” and “contraindicated” were deemed to be inappropriate (62,63). These are based on the practical translation of the Quran teaching that “Muslims should not put themselves at risk by fasting” (1). However, many diabetic subjects choose to fast and the physician should be sympathetic and sensitive to their convictions and try and work out a programme that will minimise the risk. The physician should stress the situation of severe or recurring hypoglycaemia or hyperglycaemia when patients MUST break the fast and make no further attempts to fast.

How to manage diabetes during Ramadan for those in whom fasting is deemed safe?

Life style modifications

Healthy life style practices should be re-enforced before and during Ramadan. Excessive gorging, or compensatory

overeating of carbohydrate and fatty foods, contributes to poor control and wide excursions in blood glucose and weight gain in those who are well-controlled patient (62-63). Therefore, patients should be encouraged to maintain their good dietary habits. Regular light to moderate exercise during Ramadan is safe in type 2 patients and may continue either in the morning or at night. It is probably prudent to avoid exercise in the final few hours of the fast when the risk of hypoglycaemia is maximal particularly in insulin-treated patients (62,63)

Modification of drug regimens

Type 2 diabetes

Patients with type 2 diabetes can be controlled by adhering to similar drug regimens to the pre-fasting period with the morning oral hypoglycaemic given at the break of the fast and the pre-dinner dose is usually reduced by 25–50% and given pre-Suhoor. Anecdotally, use of Nateglinides with Iftar may produce fewer excursions of blood glucoses after Iftar either as a replacement to sulphonylureas or new addition to metformin of Glitazones (62,63). Metformin could be given post-Iftar and Suhoor. Some patients may not tolerate the post-Suhoor dose because of the gastrointestinal side effects. If a slow-release preparation of metformin is available, the whole daily dose may be taken altogether after Iftar. Patients on insulin and sulphonylureas combination should take their basal insulin (Isophane, Glargine or Detimer) about 10 pm to 12 midnight and the oral hypoglycaemic agents taken at Iftar. Glitazones and incretin-based therapy may not need to be changed.

Type 1 diabetes

If a type 1 diabetic individual chooses to fast, then great care should be taken to monitor and adjust the dose of insulin accordingly.

Those on intensive insulin treatment should receive their long-acting basal insulin (such as Glargine and Detimer) at Iftar or at the usual time of 10 pm - 12 midnight (Isophane Insulin should be given as usual before bed). The dose of basal insulin needs to be adjusted according to blood glucose levels between mid-day and Iftar time. The short-acting insulin or rapid-acting insulin analogue are adjusted at Iftar and Suhoor times. The doses of these can be adjusted according to amount of food consumed; previous experiences and blood glucoses measured 2-3 hours after iftar (conveniently after Isha prayers). For assessment of the pre-Suhoor insulin doses, blood glucose can be measured between 11-12 mid day Patients on

conventional twice daily insulin regimens should take their usual morning dose before Iftar and their usual evening dose before Suhoor. However, the latter need to be adjusted so that the fast-acting component remains the same and the intermediate acting insulin is cut by 50% or omitted. Those on pre-mixed insulin such as 30/70 or 25/75 preparations should have their morning dose before the Iftar in the same or even greater dose. However the pre-Suhoor dose should be reduced or substituted with shorter acting insulin only. Insulin analogues have the advantage of being injected immediately before the meal. Patients on insulin pumps usually require reduction of the basal insulin rates with meal-oriented adjustment of the bolus insulin (64). On whatever regimen, individualized advice remains the corner stone for management with guidance and full support by physicians and diabetes educators (65).

Blood Disorders and Their Management During Ramadan

In normal healthy people, only minor changes occur in haematological parameters during fasting. In particular, no significant changes in haemoglobin and RBC indices and WBC are essentially unchanged. Mild increase may be observed in hematocrit possibly secondary to hemoconcentration. Platelet count remains normal but may increase mildly. Serum Iron and Total Iron Binding Capacity (TIBC) might be mildly depressed indicating no significant change in iron stores. No changes in clotting time or bleeding time (66-68).

Some of the haematological conditions, which might require special attention during Ramadan fasting will be discussed. In general, fasting in patients with chronic blood disorders is not associated with adverse outcome and it hardly requires special management measures apart from change in the administration schedule for patients on medical treatment. However, there are few clinical conditions that may bear some relevance to fasting and warn special attention. These include sickle cell disease, thalassemia, oral anticoagulation, chronic myeloproliferative disorders and chronic leukaemias.

Sickle cell anaemia

It is a hereditary haemoglobinopathy with some ethnic predilection relevant to the present discussion. There are reports of higher risk or increased incidence of vaso-occlusive crisis during Ramadan. In one study, 40 patients were followed up for 3 years. Significant increase was found in the number of crises (69). Among the clinical

consequence directly attributed to dehydration are the renal complications in patients with sickle cell trait when severely dehydrated producing a hypertonic environment in the renal medulla.

Thalassemia

It is also an inherited blood disorder of haemoglobin synthesis. Health maintenance during Ramadan is based on maintaining acceptable haemoglobin level during the fasting month. Most patients would only need one day for transfusion during Ramadan. Some patients might choose to have their blood transfusion after Iftar as inpatient (Unpublished Observations). Others prefer to re-fast this day after Ramadan. Patients have to adhere with Iron chelator regimen. Desferrioxamine is given by subcutaneous infusion over 8-12 hours. Alternatively oral iron chelator Deferasirox may be given as single daily dose on empty stomach. Management of any possible endocrine disorders such as diabetes or thyroid dysfunction or cardiac dysfunction should continue as outlined by the physician. Current therapy for Iron overload deferoxamine is the most common drug used for iron chelation. Because of its short half-life (20 minutes), it must be given by continuous infusion 8 to 12 hours/day, 5 to 7 days/week. Compliance is poor because of side effects and quality-of-life issues. Oral therapy remains to be highly desirable.

Chronic myeloproliferative disorders

These indicate clonal hematopoietic disorders including proliferation of one or more haematopoietic lineage. The median age at diagnosis is 60. Examples of this group include polycythemia vera/essential thrombocythemia/myelofibrosis. Impact of fasting on risk of complications/thrombosis under these circumstances is not well defined though mild increase in haematocrit is possible. Phlebotomy in stable patients is hardly needed during Ramadan. Hydroxyurea is well tolerated in general. Newly diagnosed polycythaemia vera should be phlebotomized without delay to haematocrit below 45.

Safety of warfarin therapy

An excellent study documenting the sum of thromboembolic as well as bleeding events, in patients using anticoagulation has shown equal events rate between fasting versus non fasting patients (70). Thus confirming safety of fasting for patients on anticoagulation. Warfarin should be taken at the same time every evening. Close INR monitoring is required. Effective patients' education should be able to prevent surprises. Care and attention should be

paid to dietary habits. In particular, patients should avoid sudden intake of foods rich in vitamin K than usual. This will predictably reduce Warfarin action.

Rheumatological Conditions During Ramadan Fasting

There are three aspects of Ramadan fasting that have some relevance to Rheumatologic conditions. These include the effect of fasting itself on the course of rheumatic diseases, the effect of rheumatic disorders on fasting and the relationship between Ramadan and intake of medication. The later aspect is discussed elsewhere within this mini-symposium.

Effect of fasting on Rheumatoid arthritis

When animals are put on low calorie diets there is an increase in their life spans of 15 days to 26 days. Studies that addressed these effects of fasting include studies on fasting and lacto-vegetarian diet on rheumatoid arthritis (71). Controlled trial of fasting and one-year vegetarian diet in rheumatoid arthritis (72) showed that beneficial effects were only transient for 4-5 days of fasting mainly on pain and swelling and no long term benefit was observed. The symptoms returns back within a week of resuming normal diet.

Fasting and inflammation

The changes in interleukin-6, C-reactive protein and other biochemical parameters during prolonged intermittent fasting were observed in 40 healthy volunteers of normal weight, aged 23-39 years, who fasted during Ramadan (73). They were compared with 28 healthy, age and BMI-matched volunteers who did not fast. Measurements were collected just before, during and after Ramadan. Serum IL-6, CRP, homocysteine, vitamin B12, folate, total cholesterol, Triglycerides, LDL and HDL levels were measured. IL-6, CRP and homocysteine levels were found to be significantly low during Ramadan in the fasting subjects when compared to basal values. Lower levels of such inflammatory markers indicate less inflammatory processes and possibly less arthritis and bursitis.

The effects of Ramadan fasting on neutrophil's respiratory burst and CIC was studied in 21 normal young fasting Muslim individuals using standardized chemiluminescence and poly ethylene glycol methods respectively. There were no significant changes of CL activity of circulating neutrophils and CIC levels comparing the results obtained before and after Ramadan. More over there was a good correlation between these two immunological parameters (74,75).

Effect of Rheumatoid arthritis on fasting of Ramadan

Active arthritis may interfere with their ADL due to active/chronic joints and muscles pain, fatigue, and tiredness. Other effects of this multisystem disorder may affect heart, GI or renal system. In addition, patients with rheumatoid disorder are prone to malnutrition. Chronic inflammation, increase production of cytokines, increase catabolic rate and protein break down. In addition, patients with RA usually have difficulty in preparing food secondary to pain and joints swelling. Long-term usage of medication may lead to PUD, gastritis, and folic acid deficiency.

Drug therapy and Ramadan-friendly prescribing

Fasting will, by definition, be interrupted by administration of medications during the fasting hours. Medications can cause significant nausea and vomiting and other side effects that can make fasting difficult. Dehydration can happen with diuretics use if fluid intake was not enough. Drugs pharmacokinetics can be altered by fasting and binging after breaking the fast. In one of the earliest studies, 81 patients were surveyed to determine alteration of their drugs regimen during Ramadan (76). Of these 42% patients adhered to their usual treatment, 58% changed their intake pattern, 35% stopped their treatments, 8% changed the administration schedule, and 4% took all the daily doses in one intake. In another survey of 325 outpatients in a Kuwaiti hospital, 64% changed their therapeutic scheme during the month of Ramadan and 18% took their daily medicines in a single intake (77). It is generally observed that patients often modify their drugs without seeking any medical advice by changing the timing, the number of doses, the time span between doses, and the total daily dosage (78). There are widely accepted Islamic teachings or (Fatwa) regarding various routes of medications' intake. Permissible routes of medications intake include: intravenous, intramuscular, per rectum, per vagina, topical, eye drops, sublingual, nasal, and inhaled medications (79).

Asthma and Chronic Obstructive Airway Disease (COPD)

In addition to the fact that many religious scholars have permitted using inhalers during fasting, it is very possible to obtain a good control on obstructive airways, so that the need for rescue inhalers during fasting hours is negligible. Using "Long acting beta 2 agonist + steroids" inhaler twice daily and titrating the dose up to achieve better Asthma / COPD control (80). Long acting anticholinergic inhaler "Tiotropium" can provide 24 hours bronchodilator effect.

For cases requiring systemic steroids, this can be given as once daily dosing with a meal "Iftar or Suhoor" depending on life style and waking hours during Ramadan. For Patients still using theophylline, a great caution to be taken because of its vulnerable pharmacokinetics with eating patterns during Ramadan. A single dose of long acting preparation to be given late night with enough time after Iftar and before Suhoor. Only if necessary a level can be monitored. Using Oxygen inhalation has been permitted in a consensus meeting of Islamic scholars and medical experts in Casablanca 1997 (79).

Antihypertensive Medications

Diuretics dosing has to be adjusted down during fasting and matched to fluid intake. Avoiding dehydration and electrolyte imbalance is often encountered with diuretics, particularly in cardiac patients where this can lead to serious cardiac dysrhythmias. Diuretics are not first choice as a new antihypertensive for a fasting patient. Monitor electrolytes, urea & creatinine more frequently. Dosing of ACE inhibitors or ARBs may have to be adjusted, given the potentially hypovolemic status. Almost all classes of antihypertensive drugs have once daily dosing which is highly recommended. This includes beta blockers, calcium channel blockers, ACE Inhibitors or Angiotensin-receptor blockers (ARBs), vasodilators & centrally acting antihypertensive drugs. Some are also available in patches lasting between 24-72 hours. Studies have shown that fasting does not interfere with BP control as measured by 24 H BP monitoring including Systolic, diastolic, mean, diurnal or nocturnal BP (35,36).

Arthritis

Using a single oral with or without topical anti-inflammatory medications as needed can replace the multiple oral dosing and provide relief during fasting.

Anti-epileptic drugs

Multiple case reports of seizures increased frequency have been attributed to missing medications. Therefore providing a long acting formulation or replacing by a single daily dose of anti-epileptic medication can avoid these unnecessary events. Closer monitoring of blood levels of antiepileptic might provide an added safety as discussed above.

Final Remarks

The daytime total fasting during holy month of Ramadan is a sacred obligation for all healthy Muslim adults. The

medical ramifications of this Ramadan fasting in patients with individuals with acute and chronic medical conditions have attracted increasing interest of physicians and biomedical scientists over the last 30 years as evidenced by the increasing original and review articles in the international and regional medical literature. Studies in normal healthy adults are of academic value in enabling us understand its implications in various disease conditions. On the other hand, studies in disease states are of particular clinical value in documenting the physiological, biochemical and clinical changes during the fasting month. These observations should enable physicians establish the safety or otherwise of observing the fasting in very specific clinical conditions. Thus providing an evidence-base for the medical opinion given to patients to inform their personal choice to fast or not to fast and enable and educating physicians on how to best manage patients who choose to fast.

Observing the fasting in Ramadan is possible for many chronically ill patients who are stable and are under medical supervision. The effect of fasting on health issues should be explained to patients well ahead of starting the holy month. Counselling patients about their use of medications as well as their suitability to undertake the fast is a major step in health care for Muslim patients. Detailed guidance is now internationally available for some conditions such as diabetes as a result of close cooperation between medical and "Fiqh" institutions. The literature is rich with studies on other aspects such as cardiology, gastroenterology and pharmacology. Other professional bodies should follow suit to provide some consensus opinions and practical guidance on clinical management. Our series of symposia and this very article is one such humble attempt. We welcome future collaboration with colleagues all over the world.

References

1. The Holy Quran. Sura 2: Verses 183-185.
2. Beshyah SA. Fasting During The Month of Ramadan for People with Diabetes: Medicine and Fiqh United at Last. *Ibnosina J Med BS* 2009;1:58-60.
3. Sulimani, RA. Ramadan fasting: Medical aspects in health and in disease. *Annals Saudi Medicine* 1991;2:637-41.
4. Azizi F. Research in Islamic fasting and health. *Annals Saudi Medicine* 2002;22:186-91.
5. Bagarsa O. *Ibnosina Journal of Medicine and Biomedical Sciences*. *Ibnosina J Med BS* 2009;1:1.
6. Cheah SH, Ch'ng SL, Hussein R, Ducan MT. Effects of fasting during Ramadan on urinary excretion in Malaysian Muslims. *Br J Nutr* 1990;63:329-37.
7. El-Hazmi MAF, Al-Faleh FZ, Al-Mofleh IB. Effect of Ramadan fasting on the values of hematological and biochemical parameters. *Saudi Med J* 1987;8:171-6.
8. Sliman NA, Khatib FA. Effect of fasting Ramadan on body weight and some blood constituents of healthy Muslims. *Nutr Rep Intern* 1988;38:1299-306.
9. Murphy R, Shipman KH. Hyperuricemia during total fasts. *Arch Intern Med* 1963;112:659-62.
10. Braverman E. The Benefits of Fasting. *Total Health* 1994;16:46.
11. Ramadan J. Does fasting during Ramadan alter body composition, blood constituents and physical performance? *Med Princ Pract* 2002;11;Suppl 2:41-6.
12. Leiper JB, Molla AM. Effects on health of fluid restriction during fasting in Ramadan. *European Journal of Clinical Nutrition* 2003;57 Suppl 2:S30-S38.
13. El-Wakil HS, Desoky I, Lotfy N, Adam AG. Fasting the month of Ramadan by Muslims: Could it be injurious to their kidneys?. *Saudi J Kidney Dis Transpl* 2007;18:349-54.
14. Al-Arfaj HF, Alballa SR, Alhaider AA, Huraib SO, Al-Arfaj A, Bamgboye E. Effect of short-term use of different non-steroidal anti-inflammatory drugs on renal function during fasting in Ramadan. *Saudi J Kidney Dis Transpl* 1995;6:9-14.
15. Al-Khader AA, Al-Hasani MK, Dhar JM, Al-Sulaiman M. Effects of diet during Ramadan on patients on chronic hemodialysis. *Saudi Med J* 1991;12:30-31.
16. Al-Khader, A.A. Ramadan fasting and renal transplantation. *Saudi J Kidney Dis Transpl* 1994;59:463-65.
17. Khedmat H, Taheri S. Ramadan fasting and transplantation: Current knowledge and what we still need to know. *Saudi J Kidney Dis Transpl* 2010;21:417-20.
18. Argani H, Mozaffari S, Rahnama B, Rahbani M, Rejaie M, Ghafari A. Evaluation of biochemical and immunologic changes in renal transplant recipients during Ramadan fasting. *Transplant Proc* 2003;35:2725-6.
19. Bernieh BO, Mohamed AO, Wafa AM. Ramadan

- fasting and renal transplant recipients: Clinical and biochemical effects. *Saudi J Kidney Dis Transpl* 1994;5:470-73.
20. Einollahi B, Lessan-Pezeshki M, Pourfarziani V, Aghdam B, Rouzbeh J, Ghadiani MH, Nemati E. Ramadan fasting in kidney transplant recipients with normal renal function and with mild-to-moderate renal dysfunction. *Journal International Urology and Nephrology* 2009;41:417-22.
 21. Abdalla AH, Shaheen FA, Rassoul Z, Owda AK, Popovich WF, Mousa DH, al-Hawas F, al-Sulaiman MH, al-Khader AA. Effect of Ramadan fasting on Muslim kidney transplant recipients. *Am J Nephrol* 1998;18:101-4.
 22. Ghalib M, Qureshi J, Tamim H, Ghamdi G, Flaiw A, Hejaili F, Taher S, Katheri A, Shaheen F, Al-Khader AA. Does repeated Ramadan fasting adversely affect kidney function in renal transplant patients? *Transplantation* 2008; 85:141-4.
 23. Said T, Nampoory MR, Haleem MA, Nair MP, Johnny KV, Samhan M, Al-Mousawi M. Ramadan fast in kidney transplant recipients: a prospective comparative study. *Transplant Proc* 2003;35:2614-6.
 24. Boobes Y, Bernieh B, Al Hakim MR. Fasting Ramadan in kidney transplant patients is safe. *Saudi J Kidney Dis Transpl* 2009;20:198-200.
 25. Basiri A, Moghaddam SM, Khoddam R, Nejad ST, Hakimi A. Monthly variations of urinary stone colic in Iran and its relationship to the fasting month of Ramadan. *J Pak Med Assoc* 2004;54:6-8.
 26. Temizhan A, Donderici O, Ouz D, Demirbas B. Is there any effect of Ramadan fasting on acute coronary heart disease events? *Int. J. Cardiol* 1999;70:149-53.
 27. Al Suwaidi, A Bener, A Suliman, R Hajar, A M Salam, M T Numan and H A Al Binali. A population based study of Ramadan fasting and acute coronary syndromes. *Heart* 2004;90:695-6.
 28. Al Suwaidi J, Zubaid M, Al-Mahmeed WA, Al-Rashdan I, Amin H, Bener A, Hadi HR, Helmy A, Hanifah M, Al-Binali HA. Impact of fasting in Ramadan in patients with cardiac disease. *Saudi Med J* 2005;26:1579-83.
 29. Al Suwaidi J, Bener A, Gehani AA, Behair S, Al Mohanadi D, Salam A, Al Binali HA. Does the circadian pattern for acute cardiac events presentation vary with fasting? *J Postgrad Med* 2006;52:30-3.
 30. Chamsi-Pasha H, Ahmed WH. The effect of fasting in Ramadan on patients with heart disease. *Saudi Med J* 2004;25:47-51.
 31. Al Suwaidi J, Bener A, Hajar HA, Numan MT. Does hospitalization for congestive heart failure occur more frequently in Ramadan: a population-based study (1991-2001). *Int J Cardiol* 2004;96:217-21.
 32. Habbal R, Azzouzi L, Adnan K, Tahiri A, Chraibi N. [Variations of blood pressure during the month of Ramadan] *Arch Mal Coeur Vaiss* 1998 Aug;91(8):995-8.
 33. Perk G, Ghanem J, Aamar S, Ben-Ishay D, Bursztyn M. The effect of the fast of Ramadan on ambulatory blood pressure in treated hypertensives. *J Hum Hypertension* 2001;15:723-5.
 34. Ural E, Kozdag G, Kilic T, Ural D, Şahin T, Çelebi O and Komsuoglu B. The effect of Ramadan fasting on ambulatory blood pressure in hypertensive patients using combination drug therapy. *Journal of Human Hypertension* 2008;22:208-10.
 35. Saudi Hypertension Management Group. Saudi hypertension management guidelines, 2007: Executive summary / Saudi Arabia, Saudi Hypertension Management Group – Riyadh, 2007. p 26-27.
 36. No authors. Hypertension During Ramadan and Hajj. In: *Guidelines For Management of Hypertension in Primary care Settings and Outpatient Clinics in the Kingdom of Bahrain.*, Ministry of Health, Health Promotion Council, Bahrain, 2008;p 35-36.
 37. Headache Classification Subcommittee of the International Headache Society. *The International Classification of Headache Disorders, 2nd Edition.* Cephalgia 2004, 24 (Suppl 1): 1-150.
 38. Awada A, Al Jumah M. The first of Ramadan headache. *Headache* 1999;39:490-3.
 39. Drescher MJ, Elstein Y. Prophylactic COX 2 inhibitor: an end to the Yom Kippur headache. *Headache* 2006;46:1487-91.
 40. Drescher MJ, Alpert EA, Zalut T, Torgovicky R, Wimpfheimer Z. Prophylactic Etoricoxib is effective in preventing Yom Kippur Headache: A placebo-controlled double-blind and randomized trial of prophylaxis for ritual fasting headache. *Headache* 2010;50:1328-34.
 41. Gomceli YB, Kutlu G, Cavdar L, Inan LE. Does the seizure frequency increase in Ramadan? *Seizure* 2008;17:671-6.

42. Adil N, Fassi-Fihri A, Houti I, Benaji B, Ouhakki M, Kotbi S, Diquet B, Hakkou F. Influence of Ramadan on the pharmacokinetics of a single oral dose of valproic acid administered at two different times. *Methods Find Exp Clin Pharmacol* 2000;22:109-14.
43. Akhan G, Kutluhan S, Koyuncuoglu HH. Is there any change of stroke incidence during Ramadan? *Acta Neurol Scan* 2000;101:259-61.
44. Omoululu SU, Temuzhan A, Ppepuncu E, Tandouan U, Zbakir P. Effects of Ramadan Fasting on Stroke. *Turk J Med Sci* 2003;33:237-41.
45. Saadatnia M, Zare M, Fatehi F, Ahmadi A. The effect of fasting on cerebral venous and dural sinus thrombosis. *Neurol Res* 2009;31:794-8.
46. Saadatnia M, Etemadifar M, Fatehi F, Ashtari F, Shaygannejad V, Chitsaz A and Maghazi HA. Short-term effects of prolonged fasting on multiple sclerosis. *Eur Neurol* 2009;61:230-32.
47. Leca A and Fortesa L. [Greater incidence of perforated peptic ulcers in the Ramadan period.] *Afr Fr Chir* 1954;12:577-8.
48. Vach B. [Perforation of gastroduodenal ulcer among the population of Tunis. Effect of the Ramadan on the frequency of perforations]. *Rozhl Chir* 1966;45:300-4.
49. Ozkan S, Durukan P, Akdur O, Vardar A, Torun E, Ikizceli I. Does Ramadan fasting increase acute upper gastrointestinal haemorrhage? *J Int Med Res* 2009;37:1988-93.
50. Donderici O, Temizhan A, Kucukbas T, Eskioglu E. Effect of Ramadan on peptic ulcer complications. *Scand J Gastroenterol* 1994;29:603-6.
51. Torab FC, Amer M, Abu-Zidan FM, Branicki FJ. Perforated peptic ulcer: different ethnic, climatic and fasting risk factors for morbidity in Al-Ain medical district, United Arab Emirates. *Asian J Surg* 2009;32(2):95-101.
52. Bener A, Derbala MF, Al-Kaabi S, Taryam LO, Al-Ameri MM, Al-Muraikhi NM, Al-Mansoor TM. Frequency of peptic ulcer disease during and after Ramadan in a United Arab Emirates hospital. *East Mediterr Health J* 2006;12:105-11.
53. Chong VH. Impact of Ramadan on upper gastrointestinal endoscopy referrals in Brunei Darussalam. *Singapore Med J* 2009;50(6):619-23.
54. Mehdi A, Ajmi S. [Effect of the observance of diurnal fast of Ramadan on duodenal ulcer healing with lansoprazole. Results of a prospective controlled study] *Gastroenterol Clin Biol* 1997;21:820-2.
55. Tavakkoli H, Haghani S, Emami MH, Adilipour H, Tavakkoli M, Tavakkoli M. Ramadan fasting and inflammatory bowel disease. *Indian J Gastroenterol* 2008;27:239-41.
56. Afifi ZE. Daily practices, study performance and health during the Ramadan fast. *J R Soc Health* 1997;117:231-5.
57. Sulu B, Gunerhan Y, Ozturk B, Arslan H. Is long-term hunger (Ramadan model) a risk factor for acute appendicitis? *Saudi Med J* 2010;31:59-63.
58. Roky R, Houti I, Moussamih S, Qotbi S, Aadil N. Physiological and chronobiological changes during Ramadan intermittent fasting. *Ann Nutr Metab* 2004;48(4):296-303.
59. Salti I, Benard E, Detournay B, Bianchi-Biscay M, Le Brigand C, Voinet C, et al. EPIDIAR study group, A population based study of diabetes and its characteristics during the fasting month of Ramadan in 13 countries: results of the epidemiology of diabetes and Ramadan 1422/2001 (EPIDIAR) study. *Diabetes Care* 2004;27:2306-11.
60. Beshyah SA, Benbarka MM and Khalil AB. The Practices and Outcomes of Diabetic Patients during Ramadan Fast: A Survey in a Specialist Clinic. *Ibnosina Journal of Medicine and Biomedical Sciences* 2009;1:16-19.
61. Elmehdawi RR, Mukhtad NA, Allaghi NA, and Elmajberi SJ. Fasting of Ramadan in peoples with diabetes in Benghazi, Libya: an exploratory study. *Libyan J Med* 2010;5: 5036.
62. Al-Arouj M, Bouguerra R, Buse J, Hafez S, Hassanein M, Ibrahim MA, et al. Recommendations for management of diabetes during Ramadan. *Diabetes Care* 2005;28: 2305-11.
63. Beshyah SA, Benbarka MM and Sherif IH. Practical management of diabetes during Ramadan fast. *Libyan J Med* 2007;2:185-9.
64. Benbarka MM, Khalil AB, Beshyah SA, Marjei S, Awad SA. Insulin pump therapy in Muslim patients with type 1 diabetes during Ramadan fasting: an observational report. *Diabetes Technol Ther* 2010;12: 287-90.
65. Beshyah SA. Diabetic patients and Ramadan fasting: What advice do they get and from whom. *Qatar Medical Journal* 2009;18:77-8.
66. Ramadan J. Does fasting during Ramadan alter

- body composition, blood constituents and physical performance? *Med Princ Pract* 2002;11 Suppl 2:41-6.
67. Dewanti L, Watanabe C, Sulistiawati and Ohtsuka R. Unexpected changes in blood pressure and hematological parameters among fasting and non fasting workers during Ramadan in Indonesia. *European J Clin Nutrition* 2006;60,877–81.
 68. Sarraf-Zadegan N Effect of fasting in Ramadan on Hematological values. *Annals Saudi Medicine* 2000;20:5-6.
 69. Johani K and Qureshi N. Incidence of Sickle cell crisis during Ramadan, *Middle East Journal Of Emergency Medicine* 2004; 4 Oral Abstract #4. (available at <http://www.hmc.org.qa>).
 70. Saour JN, Sick JO, Khan M, Mamo. Does Ramadan fasting complicate anticoagulant therapy. *Ann Saudi Med* 1989;9:538-40.
 71. Sköldstam L, Larsson L, Lindström FD. Effect of fasting and lactovegetarian diet on rheumatoid arthritis. *Scand J Rheumatol* 1979;8(4):249-55.
 72. Kjeldsen-Kragh J, Haugen M, Borchgrevink CF, Laerum E, Eek M, Mowinkel P, Hovi K, Førre O. Controlled trial of fasting and one-year vegetarian diet in rheumatoid arthritis. *Lancet* 1991;338:899-902.
 73. Aksungar FB, Topkaya AE, Akyildiz M. Interleukin-6, C-Reactive Protein and Biochemical Parameters during Prolonged Intermittent Fasting. *Ann Nutr Metab* 2007;51:88-95.
 74. Latifynia A, Vojgani M, Jafarieh H, Abofazeli T. Neutrophil Respiratory Burst (Innate Immunity) During Ramadan. *Journal of Biological Sciences* 2007;7:997-1000.
 75. Latifynia A, Vojgani M, Abofazeli T, Jafarieh H. Circulating immune complex during Ramadan. *J Ayub Med Coll Abbottabad* 2007;19:15-8.
 76. Aslam M and Assad A. Drug regimen and fasting during Ramadan. *Public Health* 1986;100:49-53.
 77. Aslam M, Healy MA. Compliance and drug therapy in fasting Muslim patients. *J Clin Hosp Pharm* 1986;11:321-5.
 78. Adil N, Houti IE, Moussamih S. Drug intake during Ramadan *Br. Med J* 2004;329:778-82.
 79. No author “An Islamic View of Certain Contemporary Medical Issues:”, The 9th Fiqh-Medical Seminar, Casablanca, Morocco, 8-11 Safar 1418 (14-17Jun 1997)
 80. Daghfous J, Beji M, Louzir B, Loueslati H, Lakhel M, Belkahia C. Fasting in Ramadan and asthmatics and sustained release theophylline. *Ann Saudi Med* 1994;14:523.