Glycaemic control in south Asian patients during feasting and fasting

In the UK, type 2 diabetes is at least four times more common in the south Asian community than the Caucasian population. The vast majority of south Asians in the UK are Muslims, Hindus or Sikhs. Fasting and feasting are an integral part of these faiths, so these patients expose themselves to an increased risk of hyperglycaemia and hypoglycaemia. This article provides advice on adjusting both oral medication and insulin during fasting.

Type 2 diabetes mellitus is characterized by hyperglycaemia secondary to insulin resistance, progressive decline in glucose-stimulated insulin secretion from pancreatic beta-cells and increased hepatic gluconeogenesis. In the UK, type 2 diabetes is at least four times more common in south Asians than in Caucasians (D'Costa et al, 2000). South Asians are also at higher risk of developing cardiovascular disease (Hamman et al, 2002) and nephropathy, and have a 40% higher mortality rate (Raleigh et al, 1997) despite a lower incidence of obesity, itself an important risk factor in the development of type 2 diabetes (Abate and Chandalia, 2001). Westernisation of lifestyle may play a role in the increased prevalence of type 2 diabetes in migrant Asian Indians, but epidemiological studies have shown that these factors alone are not sufficient to explain this trend (Abate and Chandalia, 2001).

One important factor contributing to this difference is increased insulin resistance in Indo-Asians. This may be explained by either environmental or genetic factors, or a combination of both (Abate and Chandalia, 2001; Das, 2006). Insulin resistance is a key feature of the metabolic syndrome (Hamman et al, 2002). Migration and urbanization have been linked with the development of type 2 diabetes in south Asians (Fall, 2001; Hamman et al, 2002; Sadikot et al, 2004). Social deprivation, unemployment and poverty combined with diabetogenic lifestyle factors may be aetiological factors in development of the metabolic syndrome (Williams and Pickup, 1992).

Aetiological factors in type 2 diabetes mellitus

Truncal obesity

In truncal obesity, fat is deposited subcutaneously and on intra-abdominal viscera. Lipolysis of this fat liberates large amounts of non-esterified fatty acids (Boden and Shulman, 2002), which increase gluconeogenesis in the liver and impair glucose uptake and use in muscle. Non-esterified fatty acids may also inhibit insulin secretion by B-cells (Boden and Shulman, 2002). Cytokines released by adipose tissue (Sell et al, 2006) and increased sympathetic drive (Modan and Halkin, 1991) may also play a role in insulin resistance.

Exercise

Low levels of physical exercise (Tuomilehto et al, 2001) and a sedentary lifestyle (Hu et al, 2003) are associated with the development of type 2 diabetes. Exercise increases insulin sensitivity and prevents obesity. Irrespective of other risk factors, physical exercise leads to a 25–60% risk reduction of developing type 2 diabetes (Tuomilehto et al, 2001). A meta-analysis has demonstrated that, when compared with the general population, south Asians participate in less physical activity and have lower levels of fitness (Fischbacher et al, 2004).

Genetics

Type 2 diabetes shows a clear familial preponderance, but does not exhibit typical Mendelian genetics. Siblings of type 2 diabetic patients have a 4-fold increased risk of developing the disease and offspring have a 3.5- or 4-fold increased risk depending on whether one or both parents are affected (Das, 2006). Several different gene loci have been mapped to identify loci for common type 2 diabetes susceptibility genes; among the best replicated regions is chromosome 1q21-q24, which was mapped independently in Utah Caucasians and in Pima Indians (Das, 2006). Other loci for type 2 diabetes have been reported on chromosomes 1q21, 2q, 3, 5, 11q, 12q and 20q (Das, 2006). Studies to map specific gene loci in Indians have so far been unsuccessful and are ongoing. Evidence also suggests a genetic basis for insulin resistance. Environmental factors in utero have been proposed as possible aetiological factors in the development of type 2 diabetes and the metabolic syndrome (Williams and Pickup, 1992).

Ethnic origin and religious festivals

The vast majority of south Asians in the UK are of Indian, Pakistani or Bangladeshi origin, and the predominant religions practised by these people include

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Islam, Hinduism and Sikhism. Fasting is an integral part of Islam and Hinduism and feasting during religious festivals is common to all of these religions.

For Muslims, fasting during the month of Ramadan is a must and typically they will wake in the early hours before sunrise and eat a small meal 'Seher'. They then abstain from food and drink during daylight hours, breaking the fast at sunset with the 'Iftar' meal. This usually comprises dates and water followed by a proper meal which, among the Asian community, is commonly a combination of high calorie foods including fried food, curries, rice and desserts. The Islamic calendar is lunar, hence Ramadan can fall in any season and the length of the fast varies vastly according to the number of daylight hours. Eid is the festival which marks the end of Ramadan and is traditionally celebrated with huge feasts. Children, the infirm (with acute or chronic illness), pregnant and menstruating women are exempt from the fast. Medication taken in any form invalidates the fast.

Diwali, or 'the festival of lights', is a 5-day festival celebrated by Hindus and Sikhs and symbolizes the victory of good over evil in Hindu folklore. Diwali is celebrated with long, elaborate feasts. Hindus commonly fast during some of the days and break the fast at sunset with food rich in sugar and carbohydrates. On their New Year's Day, a huge assortment of sweets is an absolute must and the day is spent feasting with family and friends.

Hindus, Muslims and Sikhs (who also celebrate the festival Vaisakhi in April) show great fervour when it comes to their religious festivals, considered to be a time of spiritual renewal and purification. Individuals strive and struggle in the pursuit of spiritual reward. Consequently, people are reluctant to miss the opportunity to fast, often irrespective of illness or physical state.

As Ramadan is the longest period over which fasting and feasting is practiced by the largest part of the south Asian population in the UK, i.e. the Muslims, this will now be discussed in more detail.

Table 1. Recommendations for fasting patients with type 2 diabetes mellitus

Medical assessment to risk stratify patients	Measure body mass index, blood pressure, glycated haemoglobin (HbA_{1c}), lipids, renal function and co-morbidities
Dietary advice	Slow energy release foods should be consumed before and after fasting (e.g. grains, wheat, semolina, beans, rice)
	High calorie foods (e.g. sugar-rich sweets, ghee) should be minimized if not avoided
	No more than three dates should be eaten when breaking the fast
Medication	Metformin – one-third of the daily dose before the start of the fast and two-thirds of the dose at the end of the fast
	Glitazones – the normal dose should be taken at the end of the fast
	Sulphonylureas – the morning and afternoon dose should be taken at the end of the fast and the evening dose before dawn
	Prandial regulators – take at the beginning of and on breaking the fast
	Combination therapy – adjust dose and take before and after fast
Type 1 diabetes and insulin-treated type 2 diabetes	Patients with poor glycaemic control (HbA_{1c} >10%) or those who are prone to ketoacidosis or hyperosmolar coma or hypoglycaemia should not fast
	If patients choose to fast their insulin doses should be adjusted after consultation with the diabetic team
	Shorter-acting insulin analogues are better during periods of fasting
Self management	Patients should be encouraged to self-manage their disease during periods of fasting
	Checking blood sugar does not break the fast
	Seek medical help when complications occur
Exercise	Patients with type 2 diabetes should be encouraged to exercise during fasting periods

Ramadan

Fasting during Ramadan is one of the five pillars of the Islamic faith, which all adult Muslims must perform. However, those who are unwell or for whom fasting may lead to harmful consequences, for example diabetic patients, are exempt (The Holy Koran, Al-Bakarah, 183–5). Despite this exemption a multinational study of 13 countries found that 43% of type 1 and 79% of type 2 Muslims with diabetes fasted for at least 15 days during Ramadan (Salti et al, 2004). Thus, during Ramadan many patients with diabetes will fast, a reality that physicians must recognize and address by providing guidance and advice to allow safe fasting (*Table 1*).

Guidelines

The relative benefits and harm of fasting have been studied and practical recommendations have been provided for patients and their physicians regarding fasting during Ramadan (Akbani et al, 2005). A working group for the American Diabetes Association produced guidance on clinical assessment and risk stratification of diabetic patients with regard to the potential risks of fasting during Ramadan (Al-Arouj et al, 2005). However, these consensus statements have limitations in day-to-day clinical practice, especially when Muslims are formed from diverse ethnic groups. Therefore the advice provided should take into account the cultural and behavioural characteristics and language of each ethnic group.

Evaluation for fasting

All diabetic patients who wish to observe Ramadan must undergo a medical assessment of physical wellbeing and overall control of glycaemia, blood pressure and lipids, as well as renal function. This allows their medical practitioner to risk stratify the patient and adjust their diet and daily drug regimen to be taken at Seher and Iftar meal times. Arguably, all patients with type 2 diabetes who are overweight (>20% above ideal weight or body mass index (BMI) >28 kg/m^2) should fast.

Dietary advice

Patients should be advised to eat slow energy release foods (e.g. grains, wheat, beans and rice) before and after

a daily period of fasting. Patients must try to minimize their intake of ghee (clarified butter) on chapattis, deep fried snacks (samosas, pakoras) and limit their intake of high fat, sugar rich sweets when breaking the fast. Dates are commonly consumed at Iftar and should be limited to a maximum of three. Patients who control their diabetes by diet and physical activity alone can fast safely.

Tailoring drug regimens

Metformin

Patients on metformin alone can fast safely as this has a very low risk of hypoglycaemia. They should, however, change the timing of their tablets during Ramadan so that they take one-third of the dose in the morning at Seher and two-thirds upon breaking the fast at Iftar.

Glitazones (rosiglitazone and pioglitazone)

Patients may continue to take glitazone tablets as normal, with food at Iftar. For those on combination treatments, such as Avandamet containing rosiglitazone and metformin, the dose should be adjusted to take half a tablet at Seher and one and a half tablets at Iftar.

Sulphonylureas

The morning and lunchtime dose of sulphonylureas should be taken at the end of the fast, and any evening dose should be taken before dawn. This has been shown to be safe and effective with glibenclamide (Belkhadir et al, 1993). A study compared 52 type 2 diabetic patients on either diet only, sulphonylurea (glimepiride or gliclazide once daily) or repaglinide during Ramadan. No change in body weight, fasting plasma glucose, fructosamine, glycated haemoglobin (HbA_{1c}) or total cholesterol were found (Sari et al, 2004). Triglyceride levels decreased in both groups on treatment, and high density lipoprotein cholesterol increased in patients on repaglinide only.

In an open-label, prospective, observational study from six countries (Algeria, Egypt, Indonesia, Jordan, Lebanon, and Malaysia), 100 newly diagnosed and 232 treated patients with type 2 diabetes were commenced on glimepiride once in the evening, and their metabolic control and incidence of hypoglycaemia were assessed before, at the end of, and 2 months after Ramadan (Glimepiride in Ramadan (GLIRA) Study Group, 2005). HbA_{1c} improved and was maintained in both newly diagnosed patients (9.2±1.7%, 7.7±1.2%, and 7.1±0.9%) and in previously treated patients (8.4±1.8%, 7.7±1.5%, and 7.3±1.3%) without any increase in the incidence of hypoglycaemia (Glimepiride in Ramadan (GLIRA) Study Group, 2005). Patients on a sulphonylurea who have a hypoglycaemic episode should be considered for a change to a regimen with the lowest risk of hypoglycaemia. The measured release formulation of gliclazide (Diamicron MR, Servier Laboratories, Slough) has been shown to have a lower (50%) rate of hypoglycaemia compared to glimepiride (Schernthaner et al, 2004).

Prandial regulators

Repaglinide or nateglanide may be useful for fasting because their short action allows them to be taken with Seher and Iftar. Their rapid onset and short duration of action facilitates better post-prandial control of hyperglycaemia with reduced risk of hypoglycaemia. This has been confirmed in a study of 235 Muslim patients with type 2 diabetes during Ramadan which showed that the number of hypoglycaemic episodes was significantly lower in patients taking repaglinide (2.8%) compared to those on glibenclamide (7.9%) (P=0.001). A significant reduction in serum fructosamine concentration was seen in the repaglinide group (-16.9±4.9 μmol/litre *vs* -3.8%, P<0.05) (Mafauzy, 2002), presumably a result of greater lowering of postprandial glucose.

Insulin

People with type 1 diabetes and poor glycaemic control (HbA_{1c} >10%), who are prone to ketoacidosis or hypoglycaemia, should be advised not to fast. It is vital that those who decide to fast understand not to stop taking insulin during Ramadan. Their insulin dose should be adjusted after consultation with their diabetes team. The dose of long-acting insulins (glargine or detemir) should be reduced by ~20% to reduce the risk of hypoglycaemia and should be given with the evening meal.

Insulin prandial analogues (Lispro, Eli Lilly, Basingstoke; and Novo-Rapid, Novo-Nordisk, Crawley) are useful for fasting as they work immediately with the Seher and Iftar meals. This limits a postprandial rise in glucose and also reduces the risk of hypoglycaemia during the period of fasting because of the short duration of action. In an open-label, randomized, cross-over study of 64 patients with type 1 diabetes, insulin lispro was compared with regular human insulin when given together with isophane insulin, twice-daily before the morning and evening meals, for 2 weeks. Glycaemic control, measured by postprandial glycaemic excursions, improved and hypoglycaemia was significantly reduced with insulin lispro compared with regular insulin (Kadiri et al, 2001). For premix insulins, the morning dose should be taken at Iftar and half of the evening dose should be taken at Seher.

The newer analogue mixes may provide better overall glycaemic control for type 2 diabetes (Mattoo et al, 2003). An open-label, multicentre, randomized, cross-over study involving 151 patients compared insulin Lispro Mix25 and human insulin 30/70. The evening pre-meal fasting blood glucose values (7.1±2.2 mmol/litre *vs* 7.5±2.6 mmol/litre, P=0.034) and the 2-hour postprandial glucose excursion following Iftar (3.4±2.9 mmol/litre *vs* 4.0±3.2 mmol/litre, P=0.007) were both significantly lower in patients on insulin Lispro Mix25 compared to human insulin 30/70 (Mattoo et al, 2003).

Patient self-management

Patients should be encouraged to self-manage their disease during Ramadan and report problems to their doctor. Thus the patient should continue physical activity,

increase water intake and minimize eating sweet or fatty foods. They must learn the warning signs of hypoglycaemia and hyperglycaemia and test their blood glucose as necessary during the fast (the patient must be reassured that taking a blood sugar test does not break the fast).

Exercise

Regular mild-to-moderate exercise during Ramadan does not carry any risk for patients with type 2 diabetes. Therefore patients may exercise, particularly in the morning, but should not exercise excessively 1–2 hours before Iftar. If the patient feels unwell during or after exercise, blood sugar levels should be checked.

Emergencies

Emergencies that may arise during fasting are likely to be related to either hypoglycaemia or hyperglycaemia. A study from Turkey showed that the commonest reason for attendance of fasting diabetic patients at accident and emergency was hypertension and uncomplicated headaches although the number of admissions related to hyperglycaemia or hypoglycaemia did not increase (Topacoglu et al, 2005). If emergencies do arise, the fast should be terminated and normal emergency protocols followed as if the patient were not fasting.

Conclusions

Safe fasting and feasting is possible for the majority of patients with type 2 diabetes, if they follow medical advice and actively self-manage their diet, exercise and drug regimen. Once-daily drugs may be easier for the patient to manage and should be taken along with the main meal at the end of the fast. Where written dietary and treatment advice and information is available, it should be supplied in the patient's language. BJHM

Conflict of interest: none.

KEY POINTS

- Diabetes is four times more common in Asians than in Caucasians in the UK.
- Fasting and feasting are central to the practice of Islam and Hinduism.
- Many Asian diabetic patients will fast and feast and risk hyperglycaemia or hypoglycaemia.
- This article provides a practical approach to help diabetic patients to fast and feast safely.

Further information

In the UK, Servier Laboratories have produced an advice pack entitled 'Focus on Fasting and Feasting' which is targeted at the Asian community. The leaflets give advice about safely participating in feasting and fasting and a more general overview of living with type 2 diabetes and are available in English and the main Asian languages of Bengali, Gujarati, Hindi, Punjabi and Urdu. This can be downloaded from www.servier.co.uk or by calling the diabetes team at Servier Laboratories on 01753 666 233

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