A double-blind, randomized, multicenter study evaluating the effects of pioglitazone in fasting Muslim subjects during Ramadan

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AIM: Hypoglycemia in fasting subjects with diabetes during Ramadan is a problem that demands attention. We aimed to assess the efficacy and cost-effectiveness of pioglitazone on subjects fasting during the Ramadan period and to determine its role in improving the glycemic control and reducing hypoglycemic episodes when used as an adjunctive form of therapy for subjects with type 2 diabetes mellitus.

METHODOLOGY: This multicenter, double-blind randomized controlled trial included 86 fasting Muslim subjects with type 2 diabetes mellitus. The study was initiated 74 days prior to Ramadan to optimize glycemic control. The subjects were randomized to 30 mg of pioglitazone once daily and placebo in addition to the existing oral hypoglycemic agents (OHAs) and the doses of other OHAs were titrated according to their glycemic status at each visit. Primary outcomes included were glycemic control, as assessed by serum fructosamine, and number of hypoglycemic episodes per week during Ramadan. Secondary outcome evaluated the cost-effectiveness in using pioglitazone as an adjuvant form of therapy to conventional OHAs.

RESULTS: Pioglitazone was tolerated well by subjects in this study. Glycemic control was better during early Ramadan (Fructosamine: 320.80 versus 360.94 µM/l, *P*=0.02), mid-Ramadan (fructosamine: 315.92 versus 374.79 µM/l, *P*=0.003), and 2 weeks post-Ramadan, (which reflects the glycemic control in the last week of Ramadan) (320.45 versus 375.12 µM/l, *P*=0.01) in patients in the pioglitazone arm versus those on placebo. There was no significant difference in the number of hypoglycemic events between the two groups (*P*=0.21). The common adverse effects in the pioglitazone arm were a mean weight gain of 3.02 kg (*P*=0.001) and ankle edema in 16 subjects (*P*=0.0002). Direct cost per month per subject in the pioglitazone group was INR 780.62 (US $17.36) vs INR 1232.50 (US $27.41) in the placebo group (*P*=0.02).

CONCLUSION: Pioglitazone is safe and efficacious in lowering blood glucose in fasting subjects during Ramadan in combination with other OHAs. There is no reduction in the number of hypoglycemic events when compared with conventional therapy without pioglitazone. There is a significant cost benefit when pioglitazone is added to other OHAs in this study.

KEY WORDS: Hypoglycemia, muslims, pioglitazone, Ramadan.

Introduction

Ramadan is a holy month observed by Muslims all over the world, during which fasting is rigorously observed. During the 30 days of Ramadan, those who observe the fast consume food only after sunset and do not eat during the daylight hours. Major alterations in mortality rates occur in both sexes around the time of Ramadan.[1] This may be owing to variability in the management of disease

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conditions, diabetes mellitus being one such disorder.[2] Many authors have suggested that fasting is possible in type 2 diabetes during Ramadan, provided the subjects that are involved are not insulin-requiring.[3,4] However, glycemic control may be erratic in patients with diabetes mellitus during Ramadan, owing to the ingestion of excessive calories at night, which in some situations may even exceed the estimated appropriate calorie intake by a subject with diabetes.[5] Moreover, the ingestion of oral hypoglycemic agents (OHAs) can result in hypoglycemic symptoms during the day. This, in turn, leads to subjects reducing their OHA dose and suboptimal glycemic control. Alertness in normal subjects drops during the Ramadan season owing to a combination of alteration in sleep patterns and the change in eating habits associated with fasting during the day.[6] The net result is that daytime sleepiness is significantly increased.[7] Thus, there is added concern that even mild to moderate hypoglycemic symptoms may precipitate confusional states that could adversely affect the quality of life. Hypoglycemia is seen in nearly 7% of subjects on conventional oral hypoglycemic therapy (glibenclamide) during the month of Ramadan.[8]

It has been shown that the use of lispro insulin significantly reduces the chances of developing hypoglycemia and diabetic ketoacidosis in type 1 diabetes during the Ramadan season.[9,10] Type 2 diabetes mellitus is far more common than type 1 diabetes mellitus, and hence, maneuvers with OHAs to control hypoglycemia in these subjects are very important. Studies have suggested that the morning dose of OHAs be shifted to night and the night dose be shifted to before dawn during the month of fasting. This maneuver has been shown to result in reasonable glycemic control with no significant increase in hypoglycemic episodes during Ramadan in one British study.[10]

There is still much apprehension in utilizing the same dose of sulphonylureas during Ramadan for fear of precipitating more severe hypoglycemic attacks in older subjects. Another recommended strategy is to utilize OHAs that are less likely to result in hypoglycemic symptoms or those with a shorter duration of action. Repaglinide has been studied during Ramadan, and has been established to be a drug that does not cause significant amounts of hypoglycemic side effects. However, repaglinide was compared with glibenclamide, which by itself has a significantly higher chance of causing hypoglycemic episodes, and the trial was an open-labeled one.[8]

The thiazolidinedione derivatives do not directly produce hypoglycemia, though they enhance the hypoglycemic action of other OHAs.[11] When used in combination with metformin or meglitinide derivatives, hypoglycemia is less likely to occur in spite of good glycemic control. Compliance with thiazolidinediones is better because only single dose of medication is usually required.

We hypothesized that pioglitazone when utilized in Ramadan may improve glycemic control and reduce the incidence of hypoglycemia. We compared pioglitazone with placebo and conventional OHAs in Muslim subjects with diabetes who undertake fasting during Ramadan in a randomized, double-blind placebo-controlled trial. Our primary objective was to determine whether pioglitazone was better than placebo in terms of improving glycemic control and reducing hypoglycemic episodes during fasting. Moreover, pioglitazone is inexpensive in India when compared with Western countries. We also evaluated the cost effectiveness of using pioglitazone. Till date, there have been no randomized, double-blind controlled trial involving oral hypoglycemic agents in Ramadan.

Methodology

This study was a randomized, controlled, double-blind trial evaluating the safety and efficacy of pioglitazone in fasting Muslim subjects during Ramadan. Eligible participants were Muslim subjects with type 2 diabetes mellitus who were planning to fast during the entire period of Ramadan. Written informed consent was obtained from all subjects recruited in the trial. We excluded subjects with type 1 diabetes and secondary diabetes (pancreatic, corticosteroid usage, acromegaly, thyrotoxicosis, etc.), subjects with systemic diseases inclusive of cardiac disease (New York Heart Association classes III and IV), myocardial infarction in the past 6 months, cardiac arrhythmias, hepatic disease including jaundice or SGPT/SGOT > 120 IU/l or documented sonological liver disease, deranged renal functions with a serum creatinine of more than 1.3 mg%, gastrointestinal disorders, clinically significant autonomic neuropathy (excluding impotence), symptomatic postural hypotension, uncontrolled hypertension (systolic of more than 190 mmHg or diastolic of more than 110 mmHg), central nervous system disorders such as recent stroke of 6 months of duration, or dementia. Subjects with uncontrolled painful persistent peripheral neuropathy or recent mononeuritis, patients with severe

nonproliferative retinopathy, maculopathy, and proliferative retinopathy were excluded, as they potentially require insulin therapy. Other exclusion criteria were intolerance for oral hypoglycemic agents, subjects already on thiazolidinediones (rosiglitazone and pioglitazone), hypoglycemia unawareness, more than two alcoholic drinks a day, and poor glycemic control prior to recruitment (fasting of more than 200 mg / dl or postprandial of more than 350 mg / dl). Women who were menstruating were excluded from the study because religious tradition obliges them to abstain from fasting during the menstrual period.

After 4 weeks of screening phase, subjects fulfilling the inclusion and exclusion criteria were enrolled to take part in this study after obtaining an informed consent signed by them. This study was conducted from July to December 2004. The holy month of Ramadan was in November 2004 when subjects who participated took a 30-day fasting from sunrise to sunset. The initiation began 74 days prior to Ramadan in order to optimize blood sugars with the conventional OHAs. Patients were individually educated at their first visit and a planned diabetic diet sheet was given to them based on their body mass index. Patients were instructed on all aspects of diabetes with special emphasis on recognition of hypoglycemic symptoms. They were provided with diaries to record any event of hypoglycemia, timing, and course of the event.

Patients were followed up every 2 weeks during the entire study period with serial monitoring of serum fructosamine. The baseline characteristics of the patients randomized in the trial are shown in Table 1. OHA doses were adjusted to achieve optimal glycemic control based on serum fructosamine reference ranges, fasting, and postprandial blood glucose levels. A standard protocol for dose adjustment of other OHAs was followed. Patients were re-educated and dietary modification in diabetes was re-emphasized before and during Ramadan. In the event of a hypoglycemic event recorded by the patient, they were re-educated and dosages of OHAs were reduced appropriately.

The outcome measures were the number of hypoglycemic episodes per week during Ramadan and glycemic control, as assessed by serum fructosamine levels, from pre-Ramadan to the point of termination of the study. The direct cost of treatment was computed and compared between the two groups.

Patients on conventional oral hypoglycemic agents had their dosages adjusted to reach optimal glycemic control prior to randomization. Patients were randomized 1 week after the run-in period, to receive either pioglitazone or placebo. Allocation concealment was achieved by double-blind study medication provided prepackaged and randomization was stratified centrally by blocks of four treatments. Patients were instructed to commence therapy with a single 30-mg tablet (pioglitazone or matching placebo) taken at night (after dinner).

Table 1: Baseline characteristics of patients randomly allocated to pioglitazone and placebo

	Pioglitazone (n=43)	Placebo (n=44)	*P* value
Age (Years)	45 ± 9	45 ± 9	1.000
Duration of diabetes	8.0 ± 2	8.5 ± 2.2	0.316
Body weight (Kg)	66.99 ± 12	62.04 ± 8.4	0.371
Sex ratio (M:F)	26 / 17	8 / 36	0.131
BMI (Kg/m^2)	29.8 ± 5	29.4 ± 5.4	0.745
Serum fructosamine* (umol /L)	320.45 ± 83.16	330.64 ± 92.27	0.652
ALT# (U/L)	18 ± 4.2	20 ± 8.3	0.421
Fasting glucose* (mg/dl)	157.47 ± 53.04	162.77 ± 55.19	0.665
Post pandrial glucose* (mg/dl)	229.62 ± 73.45	247.03 ± 75.68	0.303
Drug therapy			
Monotherapy†	24	15	0.023
Sulphonylureas	11	6	
Metformin	9	7	
Metglinides	1	0	
Acarbose	3	2	
Combination therapy†	19	29	0.032
Sulphonylurea + Metformin	17	25	
Sulphonylurea + acarbose	2	3	
Metformin + acarbose	0	1	

Data are means±SD*, †Number of subjects, #Alanine transaminase

Glycemic control was assessed by serum fructosamine, which was measured centrally by Boehringer Mannheim automated analysis (BM / Hitachi System 912). The intra- and interassay coefficients of variation were 0.526% and 5.21%, respectively (n=10). Capillary glucose was measured using Accu-Check® active glucometer by reflectance photometry. The ranges defining glycemic control in relation to serum fructosamine were deduced based on controls performed against HbA_{1C}; 185-285 µM/l signifies good glycemic control, 286-485 µM/l signifies suboptimal glycemic control, and more than 486 µM/l signifies poor glycemic control.

Hypoglycemia was used as the primary outcome measure to determine the sample size because it was the primary outcome variable. The sample size was

calculated using the software package EPIINFO, version 5.1, with a confidence level (1-α) of 95%, a power of 80% (1-β), and an expected frequency of hypoglycemic attacks of 30% in those subjects not on pioglitazone *vs* 10% in those on pioglitazone, the calculated sample size being 35 in each arm. Thus, a total of approximately 70 subjects were expected to be included in the trial, considering the possibility of drop-outs from the study, the plan was to recruit 90 subjects (45 in each arm). Statistical analysis was performed using SPSS windows 7.5 program on an intention-to-treat basis. ANOVA was used to compare the changes in repeated fructosamine measurements in the two groups at different points of time. Chi square test was employed to test differences in proportions. End points were assessed from randomisation to the end of the study and *P* values <0.05 were considered statistically significant. Chi square tests were also employed to analyse the number of hypoglycemic events during the study.

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Results

Out of 109 subjects screened for the trial there were 14 screen failures [Figure 1] 95 patients entered the run-in period (67 days prior to Ramadan) where 8 subjects opted out of the study prior to randomisation, remainder 87 subjects being randomised to blinded therapy and placebo. At the end of the study, the total number of subjects in the placebo arm was 39 and in the study drug arm was 37 (n=76). One subject withdrew consent after 4 weeks post-randomisation, 3 subjects were off-drug during the study due to protocol deviation and study drug was stopped in 1 subject due to impending cardiac failure. Six patients were lost to follow up post randomisation and therefore did not complete the study. 76 patients completed study.

The mean fructosamine level was significantly lower in the group of subjects on pioglitazone during early, mid and late Ramadan. Though both the groups had achieved good glycemic control at baseline [Table 1], subjects in the pioglitazone group maintained good glycemic control throughout the study period as assessed by stable serial fructosamine values. But, glycemic control deteriorated in subjects on the placebo arm with serial fructosamine values showing a steady increase. Serial values were analysed by ANOVA. In the placebo arm serial fructosamine values showed a progressive increase (*P*=0.031) [Table 2, Figure 2]. No such difference was seen in the pioglitazone group. Comparison between the two

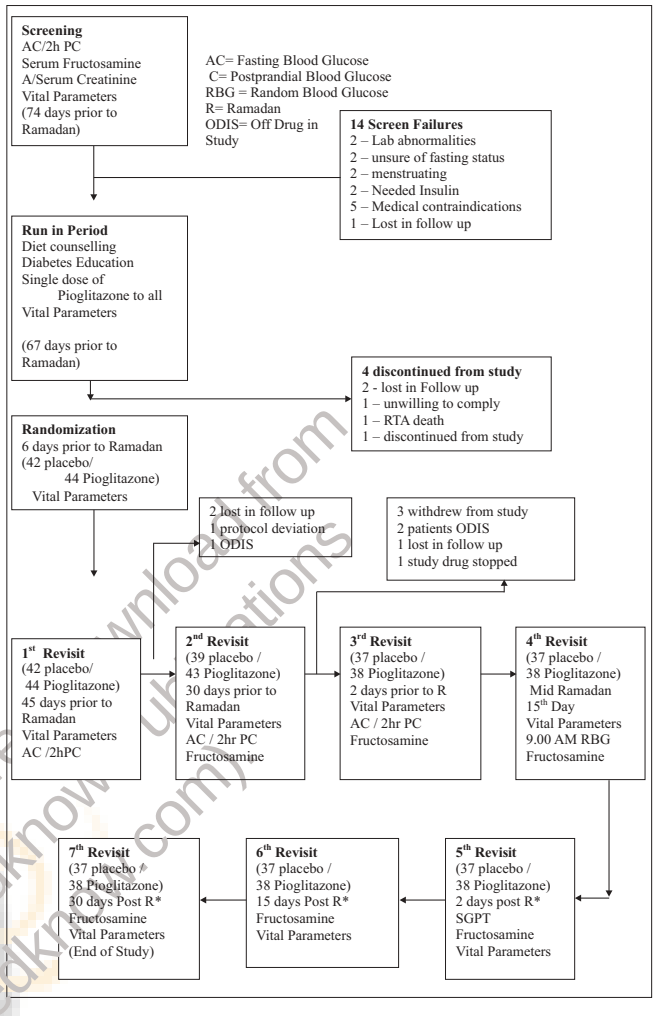


Figure 1: Flow chart of study

groups by ANOVA indicated significantly better overall glycemic control in the pioglitazone arm (*P*=0.027)

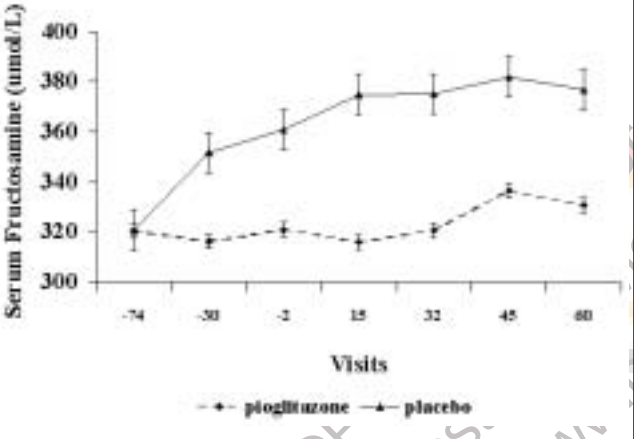
A hypoglycemic episode was defined as a sudden episode of hunger, diaphoresis, light-headedness, weakness, dysarthria, convulsion or coma that occurred more than one hour after the last meal or snack and was presumably precipitated by low blood glucose. The episode described above may necessitate food intake to terminate the event. The physician documented the hypoglycemic attacks at each visit by detailed questioning of the subject. In addition, the subjects were asked to maintain an account of each hypoglycemic attack in their diary.

It was observed that for the number of patients with hypoglycemia (chi-0.0 and *P*=1.0), there was no significant difference in the number of hypoglycemic events in both the study and the control group. The total number of hypoglycemic episodes was 39 in the

Table 2: Mean serum frutosamine (umol/l) levels in the two randomized groups (Pioglitazone and Placebo)

Visits since randomization	Pioglitazone mean ± S.D	Placebo mean ± S.D	*P* value
Baseline 74 days prior to Ramadan	320.45 ± 83.16	320.64 ± 92.27	0.60
30 days prior to Ramadan	316.07 ± 80.37	351.07 ± 103.04	0.09
2 days prior to Ramadan	320.80 ± 63.31	360.94 ± 93.34	0.02
Early Ramadan	315.92 ± 63.08	374.79 ± 101.70	0.003
Mid Ramadan	320.45 ± 62.39	375.12 ± 116.29	0.01
2 weeks post Ramadan	336.45 ± 76.20	381.94 ± 112.99	0.04
End of study	330.62 ± 54.98	376.80 ± 110.45	0.02

Serial values were analysed by ANOVA. In the placebo arm serial Fructosamine values showed a progressive increase (*P*=0.031). No such difference was seen in the pioglitazone group. Comparison between the two groups by ANOVA indicated significantly better overall glycemic control in the pioglitazone arm (*P*=0.027).



Error bars represent standard error of mean. X axis represents the study visits in relation to Ramadan and Y-axis represents serial measurements of Fructosamine (umol/L)

Figure 2: Serial measurements of mean serum fructosamine (umol/l) before and after Ramadan

pioglitazone group and 32 in the placebo group. This difference was not statistically significant (*P*=0.21). In certain patients who were on monotherapy alone, the number of hypoglycemic events necessitated withdrawal of conventional OHA and hence they were on study drug alone**.** However severe hypoglycemia (a symptomatic event requiring the assistance of another individual) was reported in 2 patients in the placebo group and none in the study group. Nocturnal hypoglycemia was not reported in both the groups.

Drug safety was assessed in all subjects who were randomized. Hepatic enzymes (SGPT) Alanine transaminases was performed at screening, 2 months post randomization and at the end of the study. There was no significant elevation to the levels that necessitated discontinuation of subjects from the trial. Overall adverse events not related to the study drug in the pioglitazone group were 35 and in the placebo group were 9. The majority of the adverse events were mild. Gastrointestinal disorders (diarrhoea in particular) occurred more frequently in the placebo arm (26.4% vs 14.0%) but these events were not statistically significant (*P*=0.190). There was no difference in the incidence of cardiovascular events.

Adverse events attributable to the study drug included weight gain and oedema. The mean incremental weight gain was 3.02 kgs (*P*=0.001) in the pioglitazone group, which increased from baseline value of 66.99 kgs to 70.01kgs, and this difference was statistically significant (*P*=0.001). However in the placebo group there was no significant change in weight (62.05 kgs at baseline to 61.59 kgs at study termination (*P*=0.37). A definite incremental weight gain was observed in the study group. A total of 16 patients who were on pioglitazone complained of the ankle oedema while two patients on the placebo had a similar complaint (*P*=0.0002)

Direct cost analysis was done based on the amount spent by each subject on both pioglitazone and conventional OHAs in the study group and standard treatment in the placebo group. The expenditure per month per subject in the pioglitazone group was INR 780.62 (US $ 17.36) versus INR 1232.50 (US $ 27.41) in the placebo group (*P*=0.02). The expenditure was 65% more in the placebo group when compared to the pioglitazone group. (1US $ = 44.95 INR)

Discussion

The control of type 2 diabetes mellitus remains a challenge in the fasting individual with diabetes mellitus. The use of oral hypoglycemic agents in Ramadan has evolved in a stepwise fashion. Glibenclamide was shown to be safe when the doses were switched between morning and evening during Ramadan. Subsequently repaglinide was shown to be effective and more recently, in an open labelled study, glimeperide seems to be well tolerated. A logical step was attempting to use a drug which itself is not responsible for hypoglycemia as a side effect. The oral hypoglycemic drug combinations, which included pioglitazone, clearly achieved better glycemic control than those without pioglitazone. A previous study[12] has

shown that there is a reduced propensity for hypoglycemia when the morning and evening doses of sulphonylurea are exchanged during Ramadan, thus this practice was instituted on the night before Ramadan in this study subjects who were on sulphonylureas. During Ramadan the incidence of hypoglycemic episodes was 3% in newly diagnosed patients and 3.7% in already treated patients.[15] Repaglinide can reduce the frequency of hypoglycemia during fasting in Ramadan.[19] In our study there was no significant difference in the number hypoglycemic events in both the pioglitazone and the control group. According to the previous literature, patients arbitrarily modify the times of the doses, the number of doses, the time span between doses, and even the total daily dosage of drugs during Ramadan, often without seeking medical advice.[16] Hence in our study, we aimed at maintaining the same dose of pioglitazone through out the study. The only change in terms of dosage was the complete withdrawal of the study drug in 3 patients who experienced repeated hypoglycemic episodes and were on study drug only. With the use of generic brands in India combinations containing pioglitazone were more cost effective in controlling diabetes, though this effect is not necessarily applicable only to the control of diabetes in Ramadan.

Though our study is limited because of the multiple outcome evaluations and a substantial proportion of patients who were unable to continue in the study, the possible effect of pioglitazone in glycemic control is clinically important. One of the practical problems in assessing glycemic control during a period like Ramadan is the relatively short duration of time where glycemic control requires assessment and strict control to achieve target levels. Glycosylated hemoglobin measurements are unsuitable for assessment of glycemic control over such short periods. Fructosamine assays are useful for assessing mean glycemic control over short-term periods, (2 weeks to one month).[13,14] The Ramadan fasting in patients with well-controlled and fairly–controlled type-2 diabetes mellitus could cause a reduction in serum fructosamine.[17] In view of shorter time period of study and glycemic assessment during 30 days we used serum fructosamine. Hypoglycemic events were not documented by plasma or blood glucose measurements and clinical symptoms were taken into consideration in view of the fact that the patients were educated to identify all symptoms of hypoglycemia. However, the extent of under reporting would be expected to be similar in the both the groups in a randomised, double blind controlled study.

In conclusion this is the first ever-randomized double blind controlled trial of oral hyperglycemic agent using pioglitazone in Ramadan. When pioglitazone is added to other OHAs during Ramadan, there is significant improvement in glycemic control without an increase in reported hypoglycemic events. In addition to improving the glycemic control, pioglitazone containing regimens are effective in terms of cost. The major drug related adverse events included significant weight gain and ankle oedema.

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References

1. Anson O, Anson J. Surviving the holidays: gender differences in mortality in the context of three Moslem holidays. Sex Roles 1997;37:381–99.
2. Uysal AR, Erdogan MF, Sahin G, Kamel N, Erdogan G. Clinical and metabolic effects of fasting in 41 type 2 diabetic patients during Ramadan. Diabetes Care 1998;21:2033–4.
3. Burden M. Culturally sensitive care: Managing diabetes during Ramadan. Br J Commun Nur 2001;6:581–5.
4. Pinar R. Management of people with diabetes during Ramadan. Br J Nur 2002;11:1300–3.
5. Mafauzy M, Mohammed WB, Anum MY, Zulkifli A, Ruhani AH. A study of the fasting diabetic patients during the month of Ramadan. Med J Malaysia 1990;45:14–7.
6. Roky R, Iraki L, HajKhlifa R, Lakhdar Ghazal N, Hakkou SF. Daytime alertness, mood, psychomotor performances, and oral temperature during Ramadan intermittent fasting. Ann Nutr Metab 2000;44:101–7.
7. Mafauzy M. Repaglinide versus glibenclamide treatment of Type 2 diabetes during Ramadan fasting. Diabetes Res Clin Pract 2002;58:45–53.
8. Akram J, De Verga V. Insulin lispro (Lys(B28), Pro(B29) in the treatment of diabetes during the fasting month of Ramadan. Ramadan Study Group. Diabet Med 1999;16:861–6.
9. Kadiri A, Al-Nakhi A, El-Ghazali S, Jabbar A, Al Arouj M, Akram J, *et al*. Treatment of type 1 diabetes with insulin lispro during Ramadan. Diabetes Metab 2001;27:482–6.
10. Pavo I, Jermendy G, Varkonyi TT, Kerenyi Z, Gyimesi A, Shoustov S, *et al*. Effect of pioglitazone compared with metformin on glycemic control and indicators of insulin sensitivity in recently diagnosed patients with type 2 diabetes. J Clin Endocrinol Metab 2003;88:1637-45.
11. Belkhadir J, el Ghomari H, Klocker N, Mikou A, Nasciri M,

Sabri M. Muslims with non-insulin dependent diabetes fasting during Ramadan: treatment with glibenclamide. BMJ 1993;307:292–5.
12. Hom FG, Ettinger B, Lin MJ. Comparison of serum fructosamine vs glycohemoglobin as measures of glycemic control in a large diabetic population. Acta Diabetol 1998;35:48–51.
13. Petitti DB, Contreras R, Dudl J. Randomized trial of fructosamine home monitoring in patients with diabetes. Eff Clin Pract 2001;4:18–23.
14. Dello RC, Gavrilyuk V, Weinberg G, Almeida A, Bolanos JP, Palmer J, *et al*. Peroxisome proliferator-activated receptor gamma thiazolidinedione agonists increase glucose metabolism in astrocytes. J Biol Chem 2003 21;278:5828–36.
15. Glimepiride in Ramadan (GLIRA) Study Group. The efficacy and safety of glimepiride in the management of type 2 diabetes in Muslim patients during Ramadan. Diabetes Care 2005;28:421–2.
16. Aadil N, Houti IE, Moussamih S. Drug intake during Ramadan. BMJ 2004;2:778–82.
17. Roky R, Houti I, Moussamih S, Qotbi S, Aadil N. Physiological and chronobiological changes during Ramadan intermittent fasting. Ann Nutr Metab 2004;48:296–303.
18. Gustaviani R, Soewondo P, Semiardji G, Sudoyo AW. The influence of calorie restriction during the Ramadan fast on serum fructosamine and the formation of beta hydroxybutirate in type 2 diabetes mellitus patients. Acta Med Indones 2004;36:136–41.
19. Sari R, Balci MK, Akbas SH, Avci B. The effects of diet, sulfonylurea, and Repaglinide therapy on clinical and metabolic parameters in type 2 diabetic patients during Ramadan. Endocr Res 2004;30:169–77.

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Announcement

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