The Efficacy and Safety of Glimepiride in the Management of Type 2 Diabetes in Muslim Patients During Ramadan

THE GLIMEPIRIDE IN RAMADAN (GLIRA) STUDY GROUP*

There is widespread agreement that the incidence of diabetes is reaching epidemic proportions. Many of the countries in which diabetes has become a major health problem have sizeable Muslim populations, where the daylight, month-long, annual fast of Ramadan poses a potential problem for good glycemic control (1–3). Although there are clear religious exemptions from fasting for patients with serious diseases, many Muslim diabetic patients choose to participate (4). There is little information on the safety and efficacy of antidiabetic drugs during Ramadan fasting.

Glimepiride is a once-daily oral antidiabetic drug indicated for type 2 diabetes when diet, physical activity, and weight reduction alone do not adequately control the disease (5–7) and is available in many countries with a sizeable Muslim population. This study was undertaken to assess the effect of the changes in nutritional habits (eating and drinking starting at sunset instead of breakfast) and drug administration schedule during Ramadan on the control of type 2 diabetes in subjects in whom the disease is otherwise well controlled by glimepiride.

RESEARCH DESIGN AND METHODS

— The study included Muslim subjects aged 35–65 years with type 2 diabetes who presented good metabolic control with glimepiride in monotherapy for at least 3 months before Ramadan and were willing to participate in daylight fasting throughout the month of Ramadan. Subjects were excluded if they had no authorization to fast according to the Ramadan consensus recommendations (8), known hypersensitivity to glimepiride, diabetic ketoacidosis, progressive fatal disease, type 1 diabetes, or type 2 diabetes treated with insulin. Women who were pregnant or breast-feeding were also excluded from the study.

This was an open-label, prospective, observational study carried out in 33 centers in six countries (Algeria, Egypt, Indonesia, Jordan, Lebanon, and Malaysia).

Each subject attended a baseline visit at inclusion (V0) and three follow-up visits: V1 just before, or no more than 5 days after, the start of Ramadan (6 November 2002), V2 at the end of Ramadan (5 December 2002), and V3 between 45 and 75 days after the end of Ramadan.

During the two maintenance periods, pre- and post-Ramadan, subjects took glimepiride as usually prescribed, once daily before the first main meal of the morning. During Ramadan, the time of administration was switched to before the first meal after sunset without changing the dose.

The primary objective of the study was to monitor HbA_{1c} and fasting blood glucose (FBG) levels at V0, V1, and V3. The number of hypoglycemic events, either symptomatic or based on self-monitoring of blood glucose (defined as <70 mg/dl), was recorded for each period of the study.

Glycemic control was compared between newly diagnosed subjects (diagnosed in the 6 months preceding inclusion) and subjects already being treated for type 2 diabetes.

The study was conducted according to the Declaration of Helsinki (Hong Kong Amendment), Good Clinical Practices, and pertinent national legal and regulatory requirements.

RESULTS

— A total of 100 newly diagnosed and 232 already-treated subjects were included in the study between June and October 2002. The demographic characteristics and diabetes history of this population at baseline are given in Table 1. Few diabetes-related complications were reported, all of which concerned patients in the group that was already treated.

HbA_{1c} values (% ± SD) measured at V0, V1, and V3 were 9.2 ± 1.7, 7.7 ± 1.2, and 7.1 ± 0.9, respectively, in the newly diagnosed subjects and 8.4 ± 1.8, 7.7 ± 1.5, and 7.3 ± 1.3, respectively, in the subjects who were already treated.

The mean FBG value at the baseline visit (9.5 ± 3.2 mmol/l) decreased to 7.0 ± 1.7 mmol/l by the end of the study. As found with HbA_{1c}, FBG values were higher for the newly diagnosed subjects (10.4 ± 2.8 mmol/l) than for the group that was already treated (9.1 ± 3.3 mmol/l) at baseline, but by the end of the study these values were very similar (6.9 ± 1.2 mmol/l in newly diagnosed and 7.1 ± 1.9 mmol/l in already treated).

Reported hypoglycemic events ranged from 25 (in 13 subjects) in pre-Ramadan to 15 (in 11 subjects) during Ramadan and 8 (in 8 subjects) in post-Ramadan periods. The majority of these subjects were from the group already treated.

CONCLUSIONS

— Our results show that the efficacy and safety of glimepiride in type 2 diabetic patients is not altered

Address correspondence and reprint requests to Thomas Rohban, MD, Medical Department, Aventis Intercontinental Near East, Bloc C 1st Floor Starco Building, Georges Picot Street, P.O. Box 110697, Beirut, Lebanon. E-mail: thomas.rohban@aventis.com.

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Abbreviations: FBG, fasting blood glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Baseline characteristics and diabetes history of the intent-to-treat population*

	Newly diagnosed	Already treated	All
n	100	232	332
Sex			
Female [*n* (%)]	41 (41.0)	109 (47.0)	150 (45.2)
Male [*n* (%)]	59 (59.0)	123 (53.0)	182 (54.8)
Age (years)			
n	98	231	329
Means ± SD	48.7 ± 7.7	53.8 ± 9.2	52.3 ± 9.1
Min–max	24.0–66.0	32.0–75.0	24.0–75.0
Weight (kg)			
n	100	231	331
Means ± SD	82.5 ± 13.3	74.8 ± 14.3	77.1 ± 14.4
Min–max	55.0–124	40.0–137.5	40.0–137.5
Height (cm)			
n	99	231	330
Means ± SD	168.7 ± 8.6	163.4 ± 9.0	165.0 ± 9.2
Min–max	150.0–192.0	139.0–188.0	139.0–192.0
BMI (kg/m²)			
n	99	231	330
Means ±	28.9 ± 4.1	27.9 ± 4.5	28.2 ± 4.4
Min–max	21.1–45.5	17.1–53.0	17.1–53.0
Time since first diagnosis (months)			
n	75	224	299
Median	3.3	37.3	21
Glimepiride daily dose (mg)			
n	100	232	332
Median	2	2	2

during the month-long daylight fast of Ramadan, when the time of administration of glimepiride is changed from the morning to the evening. During Ramadan the incidence of hypoglycemic episodes was 3% in newly diagnosed patients and 3.7% in already-treated patients. These figures were similar to the pre- and post-Ramadan periods. These results are consistent with those of other published studies (9,10).

It can be concluded that with careful dietary management and a change in the time of drug administration from morning to evening, Muslim type 2 diabetic patients taking glimepiride who are normally well controlled can fast during Ramadan if they wish to do so, with no deterioration of glycemic control.

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References

1. Shichiri M, Kishikawa H, Ohkubo Y, Wake N: Long-term results of the Kumamoto Study on optimal diabetes control in type 2 diabetic patients. *Diabetes Care* 23 (Suppl. 2):B21–B29, 2000
2. Skyler JS: Diabetic complications: the importance of glucose control. *Endocrinol Metab Clin* 25:243–254, 1996
3. Stratton IM, Adler AI, Neil AW, Matthews DR, Mansley SE, Cull, C A, Hadden D, Turner RC, Holman RR, UK Prospective Diabetes Study Group: Association of glycemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 321:405–412, 2000
4. Azizi F, Siahkolah B: Ramadan fasting and diabetes mellitus. *Int J Ramadan Fasting Res* 2:8–17, 1998
5. Langtry HD, Balfour JA: Glimepiride: a review of its use in the management of type 2 diabetes mellitus. *Drugs* 55:563–584, 1998
6. McCall AL: Clinical review of glimepiride. *Expert Opin Pharmacother* 2:699–713, 2001
7. Schade DS, Jovanovic L, Schneider J: A placebo-controlled randomized study of glimepiride in patients with type 2 diabetes mellitus for whom diet therapy is unsuccessful. *J Clin Pharmacol* 38:636–641, 1998
8. Diabetes and Ramadan Advisory Board: International medical recommendations for Muslim subjects with diabetes mellitus who fast during the month of Ramadan. *Clinical Diabetes (Middle East Edition)* 3:143–145, 2004
9. 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* 307:292–295, 1993
10. Mafauzy M: Repaglinide versus glibenclamide treatment of type 2 diabetes during Ramadan fasting. *Diabetes Res Clin Pract* 58:45–53, 2002

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