Long-Term Treatment in Diabetics with Acarbose, a Glucosidase Inhibitor: Efficacy, Tolerability and Effect on GI Hormones

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12 months therapy with acarbose in 143 type I and type II patients markedly improved the metabolic control, assessed by fasting and postprandial blood glucose determination. During 5 year acarbose treatment GIP levels were decreased and enteroglucagon levels were elevated. After withdrawal of the drug for one week GIP levels increased and enteroglucagon concentrations fell. Thus, GI-hormone changes were reversible after discontinuation of acarbose. Tolerability of acarbose was good and clinical chemistry and haematology parameters showed no changes after 1-5 years acarbose therapy. Approximately 60% of the patients had intestinal symptoms which subsided again for most patients after 1-4 weeks therapy with acarbose. Body weight remained unchanged. The glucosidase inhibitor acarbose is a new effective and safe therapeutic concept in the treatment of diabetes mellitus.

Acarbose, a glucosidase inhibitor, reduces and delays the postprandial rise in blood glucose by competitive inhibition of enzymes in the upper part of the small bowel. This results in improved metabolic control for both forms of diabetes mellitus. Excessive postprandial hyperglycaemic peaks are avoided and the daily blood glucose profile is evened out, glucose excretion in the urine is reduced and the mean blood glucose levels lowered. This is all reflected in a reduction in MAGE, M-values and HbA1-values as reported by different authors and confirmed also in a longterm study by Sachse and co-workers: They treated 24 sulphonylurea patients first with placebo and then 12 of them for 6 months with 300 mg acarbose daily and 12 with placebo, then all 24 with sulphonylurea only. They found significant differences in the above mentioned parameters.

We investigated 245 type I and type II diabetics in a multicentre study which was carried out by 16 practitioners. The patients received an adjusted variable
dose of 100–900 mg acarbose per day for a mean duration of 1 year; the drug was then withdrawn for 1–3 months. 36 patients were excluded from the study for organisational or other reasons not related to the substance itself; a total of 13 patients i.e. 5%, were withdrawn from the study because of intestinal symptoms which in all cases were probably related to acarbose therapy. Complete data, i.e. fasting and postprandial morning blood glucose measurements taken at regular intervals, were available for 143 patients. Compliance of these patients measured by acarbose activity in the faeces - was good. The mean results for all 143 patients are depicted in Fig. 1. Over the 12 month treatment period with individually adjusted acarbose dose there was a marked reduction of the blood glucose levels compared with pre-treatment levels and the levels of the subsequent run-out period. Biochemical and haematological parameters were assessed during and following acarbose treatment and remained unchanged.

In another study we treated 4 non-insulin-dependent diabetics with acarbose 600–900 mg per day for 7 years. During the first year of treatment the effects of the drug were evaluated in comparison to placebo period and for the past 5 years the patients have been receiving acarbose continuously. The patients were monitored at 4–6 weekly intervals with blood glucose levels determined 3–4 times per day and quantitative urinary glucose measurements performed. In addition, 23 clinical-chemistry and haematology parameters were assessed at 6 weekly intervals and no changes were observed during the 7 year treatment with acarbose. For the past year these patients have been treated by their general practitioners and are continuing to take acarbose regularly. The improvement in metabolic control is documented also by the HbA1 levels. The mean HbA1 level measured in June 1982 wws 8.5±1.7%.

![Fig. 1. Effect of acarbose on mean fasting and postprandial blood glucose values in 143 diabetic patients.](image-url)
Long-Term Treatment with Acarbose

Fig. 2. Mean plasma GIP and enteroglucagon levels in 4 non insulin dependent diabetics after a standardized meal (814 Kcal, 50% CH, 30% fat, 20% protein) after 5 years of acarbose treatment and withdrawal of the drug for one week.

In a different study January 1981 we examined the behaviour of gastrointestinal hormones in the same 4 patients. On the first day of the study the patients received a standard breakfast and 200 mg acarbose; the drug was then withdrawn for one week, at the end of which a standard breakfast was again given without acarbose. Blood samples were taken 15 min before and at the start of the meal and at 15,30 and 60 min intervals for 4 hr following the meal by using an indwelling venous cannula in the arm. Blood glucose and serum insulin levels were determined. Plasma levels of GIP, enteroglucagon and pancreatic glucagon, motilin, gastrin, VIP (vasoactive intestinal polypeptide), neurotensin, somatostatin and pancreatic polypeptide were measured by Dr. Bloom at the Hammersmith Hospital, London.

During acarbose treatment blood glucose, serum insulin and plasma GIP levels were markedly depressed. After withdrawal of the drug these values increased again. Plasma enteroglucagon showed an opposite pattern. It was increased during treatment and fell after the withdrawal of acarbose. These findings are in accordance with those of Jenkins, Fölsch, Radziuk and Taylor et al.\textsuperscript{9–13)}

GIP is known to be a stimulator of insulin secretion under hyperglycaemic conditions. The lowered GIP levels may possibly be involved in the decrease of the serum insulin concentration. Enteroglucagon, however, was increased during acarbose treatment. GIP is secreted in the upper small intestine whereas enteroglucagon is secreted in the ileum and colon. It therefore appears that the secretion of these peptides is related to the intestinal availability of unabsorbed carbohydrate. After withdrawal of the drug the changes of the GI-hormones were
Changes in other gastrointestinal hormones after 5 years acarbose therapy were slight and remained within the normal range.

References


