A study of the effects of acarbose on glucose metabolism in patients predisposed to developing diabetes: the Dutch acarbose intervention study in persons with impaired glucose tolerance (DAISI)
Nijpels, G.; Boorsma, W.; Dekker, J.M.; Kostense, P.J.; Bouter, L.M.; Heine, R.J.

published in
Diabetes/metabolism Research and Reviews
2008

DOI (link to publisher)
10.1002/dmrr.839

document version
Publisher's PDF, also known as Version of record

Link to publication in VU Research Portal

citation for published version (APA)

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:
vuresearchportal.ub@vu.nl

Download date: 12. May. 2022
A study of the effects of acarbose on glucose metabolism in patients predisposed to developing diabetes: the Dutch acarbose intervention study in persons with impaired glucose tolerance (DAISI)

G. Nijpels1,2*, W. Boorsma2, J. M. Dekker2, P. J. Kostense2,4, L. M. Bouter2, R. J. Heine2,3

1Department of General Practice, VU University Medical Centre, Amsterdam, Netherlands
2EMGO Institute, VU University Medical Centre, Amsterdam, Netherlands
3Department of Endocrinology, VU University Medical Centre, Amsterdam, Netherlands
4Department of Clinical Epidemiology and Biostatistics, VU University Medical Centre, Netherlands

*Correspondence to: Prof. G. Nijpels, Department of General Practice, VU University Medical Centre, Amsterdam, Netherlands Van der Boechorststraat 7, 1081 BT Amsterdam, Netherlands. E-mail: g.nijpels@vumc.nl

Abstract

Background We hypothesized that acarbose would delay conversion from impaired glucose tolerance (IGT) to type 2 diabetes by alleviating postprandial hyperglycaemia. Our study’s main objective was to investigate the effect of acarbose in IGT-persons on their 2-h plasma glucose level and beta-cell function.

Subjects and Methods The study included a random sample of 45–70-year-old residents of Hoorn, Netherlands, with mean fasting plasma glucose <7.8 mmol/L and mean 2-h plasma glucose of 8.6–11.1 mmol/L (measured by two successive oral glucose tolerance tests). After a qualification period, participants were randomized to acarbose treatment or placebo. Insulin secretion and insulin sensitivity were measured by hyperglycaemic clamp. After a 3-year treatment, analyses were performed of both the intention-to-treat and the per-protocol groups.

Results Of the 12 093 residents who received postal invitations, 118 participants were randomized. The mean difference of the post-load plasma glucose after 3 years, was −1.16 mmol/L (95% CI: −2.03; −0.17). The absolute risk reduction for diabetes was 6% (95% CI: −9; 21). No effect was seen on insulin secretion and insulin sensitivity.

Conclusions In patients with IGT, treatment with acarbose was associated with beneficial effects on 2-h plasma glucose levels but not with improvement of beta-cell function. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords impaired glucose tolerance; randomized control trial; acarbose; prevention type 2 diabetes; beta-cell function; insulin secretion

Introduction

Approximately 11% of all Caucasians aged 40 and older suffer from impaired glucose tolerance (IGT) [1–3]. The World Health Organization distinguishes this glucose intolerance category for its two-fold risk of cardiovascular disease [4–9]. Moreover, approximately a third of persons with IGT develop type 2 diabetes within 5–10 years [10–14]. The main pathophysiological abnormalities responsible for IGT include a
compromised beta-cell response to hyperglycaemia with a loss of the first-phase insulin secretion and reduced insulin sensitivity both in muscle and liver.

In a previous large multi-centre intervention trial in persons with IGT (STOP-NIDDM), acarbose, an alpha-glucosidase inhibitor, delayed conversion to type 2 diabetes [15–20]. However, those results have been disputed as questions arose about the study’s methods, analyses, and interpretations. Not only do the postprandial glucose levels decrease, but also the fasting glucose levels [20–22]. It was therefore questioned if acarbose also improved insulin secretion or insulin sensitivity.

Our single-centre trial, started before the STOP-NIDDM trial results were published, studied the effect of chronic lowering of postprandial glucose excursions on beta-cell function and insulin sensitivity. Our primary objectives were to investigate the effects of acarbose on the distribution of the 2-h plasma glucose level following an intake of 75 g of glucose, the incidence of conversion to type 2 diabetes, on insulin secretion induced by hyperglycaemia, and on insulin sensitivity.

Materials and methods

In a randomized, double-blind, placebo-controlled, parallel-group study, we compared acarbose with placebo in patients with IGT. The 3-year intervention was preceded by three pre-randomization study phases: an initial screening, a 6-week qualification period, and a wash-out period. The ethical committee of the VU University Medical Centre approved the protocol. All participants gave written informed consent.

We defined the primary outcome measure as the plasma glucose level 2 h after oral intake of 75-g glucose after 3 years of treatment [oral glucose tolerance test (OGTT)]. Assuming that the mean 2-h post-load glucose level in patients with IGT, when treated with placebo, increases 0.25 mmol/L in 3 years, that the mean level in patients treated with acarbose decreases 0.25 mmol/L in 3 years [21,22], and that the standard deviation of the levels is stable in both groups and remains equal to the standard deviation in the comparable subpopulation of the Hoorn Study survey (0.67 mmol/L) [3], we determined that we would need 47 participants in each treatment group to demonstrate the resulting 0.5-mmol/L difference as statistically significant with alpha (two-sided) = 0.05 and beta = 0.05. Thus, we needed complete data from 94 participants to provide sufficient statistical power.

Using the population register of the town of Hoorn in the Netherlands, we mailed invitations to take a blood glucose test to 12,093 randomly selected 45–74-year-old persons. Of those, 6651 (55%) visited the study centre. We immediately excluded anyone who had: diseases or conditions likely to prevent completion of the study, known uncorrected endocrine disorders, documented gastrointestinal diseases, cholesterol >10 mmol/L or triglycerides >10 mmol/L, treatment with lipid lowering medication (with the exception of statins), a myocardial infarction within the previous 6 months, impaired liver function (AST/ALT >50 units/L), or impaired kidney function (creatinine >150 mmol/L).

Of the remaining participants, the 3147 with fasting plasma glucose levels >5.5 mmol/L underwent an oral glucose tolerance test. That test identified 554 participants with 2-h plasma glucose levels >7.8 mmol/L; they returned 2 weeks later for a second test. In the end, 171 participants met the inclusion criteria: a mean fasting plasma glucose level <7.8 mmol/L, a mean 2-h plasma glucose level of 8.6–11.1 mmol/L, an HbA1c level ≤7.0% and aged 45–70 years. These 171 participants were selected for the qualification period. The mean 2-h plasma glucose level of 8.6–11.1 mmol/L as inclusion criterion was chosen because of the higher incidence of conversion of diabetes [14].

At the start of the study, the World Health Organization (WHO) definition of 1985 classified type 2 diabetes as a fasting plasma glucose value of ≥7.8 mmol/L and/or a 2-h plasma glucose value of ≥11.1 mmol/L [22] and IGT as a fasting plasma glucose value of <7.8 mmol/L and/or a 2-h plasma glucose value of ≥7.8 and <11.1. In 1999, during the study, the WHO lowered the fasting plasma glucose value criterion for type 2 diabetes to ≥7.0 and for IGT a fasting glucose value <7.0 (the 2-h plasma glucose value remained unchanged) [23].

As the qualification period began, participants started with one tablet of acarbose per day in week 1 and two tablets per day in week 2; they reached the maintenance dose of 50 mg three times each day in week 3 and continued that dose through week 6. We selected this dose because previous studies had demonstrated that it significantly lowered postprandial blood glucose with fewer side effects than a dose of 300 mg/day [20–22]. Participants were instructed to take their tablets with the first bite of a meal.

At the end of the qualification period, participants were considered eligible for the wash-out period and subsequent trial if they met the following criteria: having complied with the study procedures, having taken more than 80% of the prescribed medication during week 3–6 of the qualification period (as determined from returned tablet blisters), and having reported no adverse effects that could threaten future compliance. All eligible participants received placebo tablets for the 4-week wash-out period.

After the qualification and wash-out periods, study numbers were randomly assigned to the placebo or the acarbose group generated by a computer at Bayer’s biometric unit. The numbers were assigned in ascending order in the sequence of the subject’s entry into the intervention study. The identity of the treatment groups was concealed until the final statistical analysis.

The intervention period lasted 3 years and 1 month. After an initial 2 weeks of up-titration, participants received either the maintenance dose of three 50 mg
tablets of acarbose per day or placebo. Placebo tablets matched the acarbose tablets in size, shape, and colour. Counts of tablets remaining at the end of each 3-month treatment period were recorded in a drug inventory form as an indication of compliance.

Measurements

At the start of the intervention, we measured participants’ height, weight, and body mass index [23]. Fasting plasma glucose was measured every 3 months, and participants took an oral glucose tolerance test twice at intervals of 18 months. Tablets were not taken on the morning of these measurements.

Fasting and 2-h post-load plasma glucose levels were measured with a hexokinase method (Boehringer, Mannheim, Germany). Plasma-specific insulin (milliunits/L) was measured by an immuno-radiometric assay (Medgenix Diagnostics, Fleurus, Belgium), and intact proinsulin (milliunits/L) by an immuno-radiometric assay based on antibodies (Dako, Cambridgeshire, United Kingdom). Total cholesterol, HDL cholesterol, and triglycerides were measured by enzymatic methods (Roche, Mannheim, Germany).

At the start of the intervention, participants underwent a hyperglycaemic clamp after at least 12 h of fasting. Lying down, they were administered a priming infusion of saline (0.9%) and glucose (20%). Blood was sampled through a cannula inserted into a vein on the back of the hand of the other arm. The hand was placed in a thermostatically regulated box at 45°C to arterialize the venous blood. After infusion of a bolus of glucose (150 mg/kg), blood glucose was measured with a glucose analyser (Yellow Springs Instrument, Inc., Yellow Springs, OH, USA) at 2.5-min intervals. Blood glucose was maintained for 170 min at a hyperglycaemic level of 10 mmol/L. Insulin samples were taken at 2.5-min intervals during the first 10 min and at 5–10-min intervals for the remaining 160 min.

We estimated beta-cell function by assessing the first-phase insulin secretion in the first 10 min of the clamp, calculating (using the trapezoidal rule) the area under the curve of the glucose infusion rate during the last 20 min of the clamp. The M value divided by the average plasma insulin concentration (I) during the same interval – the M/I ratio – provides a measurement of tissue sensitivity to insulin (mg/kg/min per milliunits/L). Finally, as a measurement of beta-cell function adjusted for insulin sensitivity, we calculated the ratio between the first insulin secretion phase and the M/I.

Participation in the intervention was terminated for any of the following reasons: refusal to cooperate, emergence of inter-current illness, serious side effects, or unacceptably high glucose levels.

We took final data measurements at the end of the treatment period or when a participant converted to diabetes. For participants who withdrew early, we tried to determine the reason for termination and to carry out as many scheduled follow-up measurements as possible, giving highest priority to the primary efficacy measure. In cases of loss to follow-up, we tried to determine the reason for the loss and to obtain a final assessment of the primary measure of efficacy.

Statistical analysis

We performed analyses of both the intention-to-treat and the per-protocol populations. We removed participants from the per-protocol analysis if a treatment code was broken, laboratory results were unacceptable, or data essential to statistical analyses were missing.

Using t tests, we compared fasting plasma glucose, 2-h post-load plasma glucose, HbA1c, and lipid levels between the treatment groups. We performed primary efficacy analyses for both the intention-to-treat and per-protocol groups. In cases where a patient needed blood glucose lowering treatment, we used the 2-h post-load level measured prior to the start of the treatment. We compared the mean differences between both fasting and 2-h post-load levels at the start of the intervention and the last visit (t tests). We performed multiple regression analysis with the last fasting and 2-h post-load levels as the dependent variables, and the following independent variables: an indicator variable for the treatment contrast (0 = placebo; 1 = acarbose), the baseline fasting and 2-h post-load plasma glucose levels, age, and sex. The effects of acarbose treatment on levels of insulin secretion and insulin sensitivity as measured by the clamp were evaluated using linear regression analysis with acarbose as the indicator variable adjusted for the baseline value, age, and sex. Finally, we calculated the rate of conversion to diabetes with relative risk reduction, attributable risk, and absolute risk reduction.

Results

Of the 171 participants who entered the qualification phase, 53 were ineligible to continue; therefore, 118 participants were randomized. From these participants, 25 persons (21.2%) had a fasting glucose value >7.0 mmol/L, and had type 2 diabetes according to the WHO99 criterion. By the end of the intervention, 52 participants had dropped out for various reasons, leaving 66 participants with complete data sets for the per-protocol analysis (Figure 1).

Table 1 summarizes demographic data of the participants. The treatment groups showed no important differences, with the exception of a statistically significant difference in their levels of HbA1c [acarbose 5.9% (95%
Subjects enrolled
Post-load glucose >8.5 and <7.8 mmol/l
N = 171

Completers
N = 30

Drop-outs
N = 22
Primary reason:
Adverse event (N=8)
Consent withdrawn (N=1)
Death (N=3)
Lack of efficacy (N=6)
Lost to follow-up (N=1)
Non-compliance (N=3)

Postal invitation
N = 12,093

First screening
N = 6,651

OGTT (FPG> 5.5 mmol/l)
N = 6,651

Subjects randomized
N = 118

Placebo
N = 58

Drop-outs
N = 22
Primary reason:
Adverse event (N=22)
Consent withdrawn (N=2)
Death (N=1)
Lack of efficacy (N=2)
Non-compliance (N=3)

Completers
N = 36

Acarbose
N = 60

Completers
N = 30

Table 1. Demographic characteristics of study participants at screening

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo n = 58</th>
<th>Acarbose n = 60</th>
<th>Non-randomized n = 53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.5 ± 7.0</td>
<td>58.5 ± 7.9</td>
<td>56.7 ± 8</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>50.0</td>
<td>50.8</td>
<td>42.0</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.5 ± 3.8</td>
<td>28.4 ± 3.9</td>
<td>28.8 ± 4.1</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.89 ± 0.07</td>
<td>0.89 ± 0.09</td>
<td>0.89 ± 0.09</td>
</tr>
<tr>
<td>Fasting glucose (mmol/l)</td>
<td>6.5 ± 0.6</td>
<td>6.6 ± 0.5</td>
<td>6.5 ± 0.6</td>
</tr>
<tr>
<td>2-h post-load glucose (mmol/l)</td>
<td>9.5 ± 0.7</td>
<td>9.6 ± 0.7</td>
<td>9.7 ± 0.8</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.6 ± 0.6</td>
<td>5.9 ± 0.5</td>
<td>5.7 ± 1.1</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>23.3</td>
<td>24.6</td>
<td>44.0</td>
</tr>
</tbody>
</table>

All data (except sex and smoking status) given as arithmetic mean ± (standard deviation).

CI: 5.77; 6.03) versus placebo 5.6% (95% CI: 5.44; 5.76); p < 0.05).

Tables 2 and 3 summarize the course of plasma glucose, plasma insulin, and lipid levels by comparing mean values at baseline and end of treatment. The 2-h post-load plasma glucose showed a decrease in the acarbose group. Fasting total triglycerides increased in participants on placebo and decreased in participants on acarbose. Table 3 shows the results of the regression analyses. In the intention-to-treat analysis but not in the per-protocol analysis, acarbose showed a statistically significant effect on the 2-h post-load levels.

Table 3 also shows the results of the regression analysis of the clamp-derived variables of insulin secretion and insulin sensitivity at baseline and after 3 years. For this analysis, 52 participants (27 placebo, 25 acarbose) underwent a hyperglycaemic clamp twice. Five of these participants had converted to type 2 diabetes. No statistically significant effect of acarbose could be determined.

The rate of conversion to diabetes according to the former WHO criterion (WHO85) in the placebo group was 24.1% and in the acarbose group was 18.3%. The relative risk was 0.76 (95% CI: 0.38; 1.53), the attributable risk:
Table 2. Descriptive course of test results

<table>
<thead>
<tr>
<th></th>
<th>Placebo group</th>
<th>Acarbose group</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-h post-load plasma glucose (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean value</td>
<td>9.51 ± 0.66 (58)</td>
<td>9.58 ± 0.74 (60)</td>
</tr>
<tr>
<td>Last visit (per-protocol) Mean value</td>
<td>8.57 ± 2.31 (36)</td>
<td>8.13 ± 2.41 (30)</td>
</tr>
<tr>
<td>Mean difference acarbose vs placebo</td>
<td>−0.49 (95% CI: −0.56; 1.56)</td>
<td></td>
</tr>
<tr>
<td>Last visit (intention-to-treat) Mean value</td>
<td>9.28 ± 2.71 (58)</td>
<td>8.18 ± 2.33 (60)</td>
</tr>
<tr>
<td>Mean difference acarbose vs placebo</td>
<td>−1.16 (95% CI: −2.03; −0.17)</td>
<td></td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean value</td>
<td>6.50 ± 0.61 (58)</td>
<td>6.59 ± 0.56 (60)</td>
</tr>
<tr>
<td>Last visit (per-protocol) Mean value</td>
<td>6.38 ± 0.99 (36)</td>
<td>6.34 ± 0.77 (30)</td>
</tr>
<tr>
<td>Mean difference acarbose vs placebo</td>
<td>0.06 (95% CI: −0.46; 0.34)</td>
<td></td>
</tr>
<tr>
<td>Last visit (intention-to-treat) Mean value</td>
<td>6.58 ± 1.05 (58)</td>
<td>6.39 ± 0.77 (60)</td>
</tr>
<tr>
<td>Mean difference acarbose vs placebo</td>
<td>−0.16 (95% CI: −0.48; 0.15)</td>
<td></td>
</tr>
<tr>
<td>Fasting total triglycerides (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean value</td>
<td>2.09 ± 1.03 (53)</td>
<td>2.34 ± 1.58 (49)</td>
</tr>
<tr>
<td>Last visit (per-protocol) Mean value</td>
<td>2.25 ± 1.43 (36)</td>
<td>2.19 ± 1.38 (30)</td>
</tr>
<tr>
<td>Last visit (intention-to-treat) Mean value</td>
<td>2.45 ± 1.52 (53)</td>
<td>2.12 ± 1.22 (49)</td>
</tr>
<tr>
<td>Mean difference acarbose vs placebo</td>
<td>−0.57 (95% CI: −1.08; −0.06)</td>
<td></td>
</tr>
</tbody>
</table>

All data given as arithmetic mean ± standard deviation (n).

*p < 0.05.

Table 3. Linear regression analysis with acarbose as independent variable

<table>
<thead>
<tr>
<th>Dependent</th>
<th>Added variables</th>
<th>Beta (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-load plasma glucose (mmol/L)</td>
<td>Baseline post-load glucose, age, sex</td>
<td>−1.18 (−2.11; −0.24)</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/L)</td>
<td>Baseline fasting glucose, age, sex</td>
<td>−0.16 (−0.46; 0.15)</td>
</tr>
<tr>
<td>First insulin secretion phase</td>
<td>Baseline first insulin secretion, age, sex</td>
<td>−5.07 (−11.96; 1.81)</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>Baseline insulin sensitivity, age, sex</td>
<td>1.34 (−2.28; 4.96)</td>
</tr>
<tr>
<td>Disposition index</td>
<td>Baseline disposition index, age, sex</td>
<td>−7.28 (−80.56; 66.0)</td>
</tr>
</tbody>
</table>

aInsulin sensitivity, M/I value (M, amount of metabolized glucose/l, average plasma insulin concentration).

*b p < 0.05.

−0.14 (95% CI: −0.46; 0.21), and the absolute risk reduction 6% (95% CI: −9; 21).

The number of dropouts due to adverse events was much higher with acarbose than with placebo (36.7% versus 13.8%). Acarbose had a significantly higher rate of side effects, mostly affecting the gastrointestinal system: abdominal pain (13.1% versus 3.3%), diarrhea (19.7% versus 1.7%), and flatulence (44.3% versus 3.3%). None of the documented gastrointestinal adverse events was regarded as serious. One participant in the acarbose group died from colon carcinoma approximately 8 months after the last treatment, but the death was not considered related to this treatment.

Discussion

In this study, we evaluated the effects of a 3-year treatment with acarbose in patients with IGT. The results partially support our initial hypothesis. In both the per-protocol and intention-to-treat analyses, acarbose lowered the mean 2-h post-load plasma glucose; in the intention-to-treat analysis the difference between acarbose and placebo was statistically significant. We also observed a statistically significant and clinically relevant decrease in total triglycerides in the acarbose group. We found no differences with regard to fasting glucose, HbA1c, or conversion to diabetes nor did we observe any beneficial effects of acarbose treatment on insulin secretion or insulin sensitivity. The frequency and pattern of observed adverse events did not deviate from the already known safety profile of acarbose, which is associated with gastrointestinal complaints. These results support those of the STOP-NIDDM trial [18–20].

Despite screening a large population (12,093), we identified only 118 eligible participants for the trial, due to a high dropout rate. The main reason for this premature dropout was gastrointestinal side effects. This phenomenon limits the use of acarbose. Because of the rate of premature dropouts (higher than in other acarbose studies), we had data for only 66 participants for the per-protocol analysis. This did not meet the requirement of 47 participants in each treatment group necessary for sufficient statistical power. We believe that this lack of power is the main reason that our results were not statistically significant in this analysis. Another limitation of this study is that we could not calculate a power-analysis on insulin secretion or insulin sensitivity, because of a lack of information on a meaningful difference in both measures and unknown standard deviations of these measures in this population. However, if a decrease of HbA1c and 2-h post-load glucose values would be explained by insulin secretion or insulin sensitivity, a statistically significant change should have occurred. Finally, there was a small but significant HbA1c difference between the acarbose and control group at baseline, although there was no significant difference between the post-load glucose levels.

Several other studies have looked at preventing or delaying conversion of IGT to type 2 diabetes. All of these studies had to screen large populations to find sufficient numbers of eligible participants [15–20]. In addition to the difficulty of finding participants, it is also
very difficult to motivate patients with IGT to comply with treatment protocols, especially when they are not yet suffering hyperglycaemia-related complaints. These are but two limitations of this kind of prevention study.

The STOP-NIDDM and a Chinese multi-centre study are the other trials that analysed acarbose as a diabetes prevention treatment. In contrast with our study, the STOP-NIDDM trial showed a delay in the conversion to diabetes [18–20]. In that study, the maintenance dose of acarbose was twice the dose in our study; this factor, among others, may explain the inconsistent results. However, a systematic review of alpha-glucosidase inhibitors concluded that dosages higher than 150 mg/day had no better effect on glycaemic control [23]. Moreover, the STOP-NIDDM trial results have been questioned because the study used a modified intention-to-treat analysis and there was a considerable difference in participants who already had diabetes at baseline. The Chinese study found no effect of acarbose on the prevention of the development of type 2 diabetes [24].

No other study has presented data on the effects of acarbose on insulin sensitivity and insulin secretion with clamp-derived measures. We hypothesized that acarbose would have a positive effect on insulin secretion and thereby on beta-cell function by delaying the gastrointestinal absorption of glucose and ameliorating postprandial hyperglycaemia. However, we found no such effect. This is in concordance with an acarbose intervention study with patients with early diabetes [25].

In summary, our study showed that acarbose lowers 2-h post-load plasma glucose, but failed to show that it delays conversion to type 2 diabetes. We observed no effect of acarbose on insulin secretion or insulin sensitivity.

Acknowledgements

We thank all patients who participated in this trial and the investigators, study nurses, and coordinators whose work made the trial possible. The study was supported by Bayer Healthcare AG, Wuppertal, Germany.

Conflict of interest

The authors declare that they have no duality of interest.

References