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Acarbose reduces body weight irrespective of glycemic control in patients with diabetes: results of a worldwide, non-interventional, observational study data pool

Oliver Schnell [a,*], Jianping Weng [b,c], Wayne H.-H. Sheu [d], Hirotaka Watada [e], Sanjay Kalra [f], Sidartawan Soegondo [g], Noriyuki Yamamoto [h], Rahul Rathod [i], Cheryl Zhang [h], Wladyslaw Grzeszczak [j]

[a] Forschergruppe Diabetes e.V. at the Helmholtz Center Munich, Munich, Germany
[b] Guangdong Provincial Key Laboratory of Diabetology, Guangzhou
[c] Department of Endocrinology and Metabolic Disease, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China
[d] Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan
[e] Juntendo University Graduate School of Medicine, Tokyo, Japan
[f] Bharti Research Institute of Diabetes & Endocrinology, Karnal, India
[g] University of Indonesia, Jakarta, Indonesia
[h] Bayer HealthCare, Beijing, China
[i] Bayer HealthCare, Thane, India
[j] Silesian University of Medicine, Zabrze, Poland

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ABSTRACT

Objective: The objective of this study is to examine the effect of acarbose, an alpha-glucosidase inhibitor, on body weight in a real-life setting by pooling data from post-marketing surveillance.
Methods: Data from 10 studies were pooled (n = 67,682) and the effect of acarbose on body weight was analysed taking into account baseline body weight, glycemic parameters and other baseline characteristics.
Results: The mean relative reduction in body weight was 1.45 ± 3.24% at the 3-month visit (n = 43,510; mean baseline 73.4 kg) and 1.40 ± 3.28% at the last visit (n = 54,760; mean baseline 73.6 kg) (both $p < 0.0001$). These reductions were dependent on baseline body weight (overweight: −1.33 ± 2.98% [n = 13,498; mean baseline 71.6 kg]; obese: −1.98 ± 3.40% [n = 20,216; mean baseline 81.3 kg]). When analysed by baseline glycemic parameter quartiles, the reduction was independent of fasting plasma glucose (FPG), postprandial plasma glucose (PPG), glycated hemoglobin (HbA_{1c}) and postprandial glucose excursion (PPGE). A bivariate analysis of covariance identified female sex, South East Asian and East Asian ethnicity, younger age, higher body mass index, short duration of diabetes, and no previous treatment as factors likely to impact positively on body weight reduction with acarbose.
Conclusions: This post-hoc analysis showed that acarbose treatment reduces body weight independent of glycemic control status but dependent on baseline body weight.

Conflict of interest: *O Schnell*: *Author, Speaker*: Bayer HealthCare, Merck Sharp & Dohme, Lilly, Roche, Lifescan, Boehringer Ingelheim Pharmaceuticals, AstraZeneca, BerlinChemie. *J Weng*: *Advisor, Author, Consultant*: Bayer HealthCare. *WHH Sheu*: *Advisor, Speaker*: AstraZeneca, Bayer HealthCare, Boehringer Ingelheim Pharmaceuticals., Daiichi-Sankyo, Eli Lilly and Company, Merck Sharp & Dohme, Mitsubishi Tanabe Pharma Corporation, Novartis Pharmaceuticals, Novo Nordisk, Pfizer, Sanofi-Aventis, Takeda Pharmaceutical Company. *H Watada*: *Advisor, Author*: Astellas Pharma, Boehringer Ingelheim Pharmaceuticals, Daiichi-Sankyo, Mitsubishi Tanabe Pharmaceutical Corporation, Sanofi-Aventis; *Author, Research Support*: Astellas Pharma, AstraZeneca, Bayer HealthCare, Boehringer Ingelheim Pharmaceuticals, Daiichi-Sankyo, Dainippon Sumitomo Pharma Co, Eli Lilly and Company, Merck Sharp & Dohme, Novartis Pharmaceuticals Corporation, Novo Nordisk, Pfizer, Sanofi-Aventis, Sanwa Kagaku Kenkyusho, Shionogi, Takeda Pharmaceutical Company; *Author, Speaker*: Bayer HealthCare, Boehringer Ingelheim Pharmaceuticals, Daiichi-Sankyo, Eli Lilly and Company, Merck Sharp & Dohme, Novartis Pharmaceuticals Corporation, Novo Nordisk, Sanofi-Aventis, Takeda Pharmaceutical Company. *S Kalra*: *Advisor, Author, Consultant*: Bayer HealthCare, Novo Nordisk. *S Soegondo*: *Author, Speaker*: Bayer HealthCare. *N Yamamoto*: *Author, Employee*: Bayer HealthCare. *R Rahod*: *Author, Employee*: Bayer HealthCare. *C Zhang*: *Author, Employee*: Bayer HealthCare. *W Grzeszczak*: *Advisor, Author, Consultant*: Bayer HealthCare.

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* Corresponding author. Tel.: +49 89 38 38 07 00.
E-mail addresses: Oliver.Schnell@lrz.uni-muenchen.de (O. Schnell), wengjp@cma.org.cn (J. Weng), whhsheu@vghtc.gov.tw (W.H-H. Sheu), hwatada@juntendo.ac.jp (H. Watada), brideknl@gmail.com (S. Kalra), sidartawansoegondo@me.com (S. Soegondo), noriyuki.yamamoto@bayer.com (N. Yamamoto), rahul.rathod@bayerzyduspharma.com (R. Rathod), cheryl.zhang@bayer.com (C. Zhang), wgrzeszczak@sum.edu.pl (W. Grzeszczak).

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1. Introduction

Many international and national bodies such as the American Diabetes Association (ADA), the European Association for the Study of Diabetes (EASD), the International Diabetes Federation (IDF) and the United Kingdom's National Institute for Health and Clinical Excellence (NICE) recommend body weight reductions in patients with diabetes, as even a modest weight loss can meaningfully contribute to improved glucose control (International Diabetes Federation, 2012; Inzucchi, Bergenstal, Buse, et al., 2012; National Institute of Health and Clinical Excellence (NICE), 2010). These modest reductions have many other health benefits, including a lower risk of diabetes-associated mortality and reduced cardiovascular risk (Gray et al., 2012). Higher waist circumference has been linked to increased cardiovascular disease risk, and this is something that naturally reduces when excess body weight is lost (Balkau, Picard, Vol, Fezeu, & Eschwege, 2007). Lifestyle interventions such as limiting calorie intake or increasing physical activity are recommended first line for weight loss (National Institute for Health and Clinical Excellence (NICE), 2012, 2006), but these interventions are often met with limited success, especially over the longer term. It may also prove difficult to maintain target weight due to rebound effects (Nguyen et al., 2012; Pan & Landen, 2007; Wing et al., 2013), so pharmacological options may become necessary. In addition to negative health effects, being overweight or obese has a considerable financial burden, including higher indemnity claim and medical claim costs, as well as lost productivity (Ostbye, Dement, & Krause, 2007).

In diabetes management, clinicians aim to reduce the patient's body weight to within a healthy range, as well as to control the patient's blood glucose levels. Treatment algorithms for type 2 diabetes (T2DM) from the IDF and American Association of Clinical Endocrinologists (AACE) list several options for the medical treatment of diabetes, including alpha-glucosidase inhibitors (aGIs) (Garber et al., 2013; International Diabetes Federation, 2012). Previous studies have investigated the effect of diabetes treatments on patient body weight, including a Cochrane review published in 2005. While this identified no significant body weight effect for acarbose, one of the most commonly used aGIs, it had favorable effects on body mass index (BMI), which decreased by 0.17 kg/m^2 (95% confidence interval [CI]: 0.08 to 0.26) (Van de Laar et al., 2005a). A systematic review and mixed-treatment comparison by McIntosh et al. (2011) showed a beneficial tendency for aGIs to reduce body weight when prescribed in patients already taking metformin. This beneficial effect was also seen in another meta-analysis that showed a significant weight reduction by acarbose in patients who were taking metformin and sulfonylurea (Gross et al., 2011). Weight loss was not seen when other agents, such as sulfonylureas, meglitinides, thiazolidinediones, dipeptidyl-peptidase-4 (DPP-4) inhibitors, basal insulin, and biphasic insulin, were added to metformin (Gross et al., 2011; McIntosh et al., 2011). Other studies, including a 5-year observational trial in Germany (Mertes, 2001), have also confirmed the ability of acarbose to reduce body weight when given as monotherapy or combination therapy. In addition, Pan & Landen (2007) and Yang (2013) showed that acarbose provides comparable reductions in glycated hemoglobin (HbA_{1c}) to vildagliptin and metformin, respectively, but greater reductions in body weight compared with each active comparator (Pan & Landen, 2007; Yang, 2013).

The aim of this post-hoc analysis was to investigate whether acarbose is able to reduce body weight under real-life conditions. This analysis also attempted to identify the profile of patients who might benefit more from acarbose treatment in terms of greater body weight reduction.

2. Methods

2.1. Patients

Data from 10 post-marketing non-interventional studies were pooled in one database (Acarbose pooled Database Integrated Analysis for Non-Interventional Studies; AcarDIA-NIS). This database included patients who were prescribed acarbose as part of standard clinical practice from 21 countries, provinces, and country groups between launch and 2011. Several of these studies have previously been published (Chiasson et al., 2003; Li et al., 2014; Bayer HealthCare Ltd, 2015; Nakhaee & Sanjari, 2013; Pan & Landen, 2007). Some of these studies enrolled patients with impaired glucose tolerance (IGT) if this was an approved indication for acarbose in that country.

The safety population for these studies included 67,682 patients. The efficacy population comprised 62,905 patients from 21 countries, provinces and country groups—China (27.9%), Germany (18.7%), Pakistan (11.0%), Taiwan (11.0%), Poland (6.8%), Japan (4.4%), Korea (3.9%), India (3.2%), Indonesia (3.1%), the Philippines (2.7%), the Middle East (2.5%), Morocco (1.5%), Russia (0.9%), Malaysia (0.8%), Vietnam (0.5%), Bosnia and Herzegovina (0.4%), Cambodia (0.2%), Hong Kong (0.2%), Thailand (0.2%), Algeria (0.1%), and Singapore (0.1%). Data from some patients were excluded from the efficacy population for the following reasons: patient data did not include at least two measurements of fasting plasma glucose (FPG) or post-prandial plasma glucose (PPG) from baseline and at least one follow-up visit (n = 4310), patient data were not available from follow-up visits (n = 2237), the patient had not taken acarbose (n = 467), the patient data were retrospectively documented (n = 166), and/or the patient was aged <18 years (n = 29) (some patients were excluded for more than one reason). The efficacy population therefore comprised 62,905 patients, and of these, baseline and 3-month body weight data were available for 43,510 patients and baseline and any post-treatment (last) visit body weight data were available for 54,760 patients.

2.2. Statistical analyses

All statistical calculations were carried out using Statistical Analysis System (SAS) software, version 9.2 (SAS Institute Inc.). The primary analysis examined the body weight change at the 3-month (±4 weeks) follow-up visit. Sensitivity analyses were performed using the change in body weight to baseline at the last follow-up visit.

2.2.1. Descriptive summary of data

Patient demographics were summarized in a descriptive way, presenting absolute and relative frequencies for discrete demographic factors and summary statistics for continuous variables factors.

Body weight and three glycemic parameters—HbA_{1c}, FPG, and PPG—were used to assess the efficacy of acarbose. Due to the non-interventional nature of the studies, PPG could have been measured at any time point after a meal, so the value closest to 1 h was selected for each patient. Descriptive statistics were provided for various subgroups. The p-values and 95% confidence intervals for the absolute and relative changes from baseline were also provided. Body mass index (BMI) was categorized according to regional standards. For patients of non-Asian race, the western standard of <25 kg/m^2 for underweight/normal, 25 to <30 kg/m^2 for overweight, and ≥30 kg/m^2 for obese was used. For patients of Asian race, the Asia-Pacific standard of <23 kg/m^2 for underweight/normal, 23 to <25 kg/m^2 for overweight, and ≥25 kg/m^2 for obese was applied.

The relative reduction versus baseline for all parameters was preferred to the absolute reduction in order for the efficacy outcome measure to reflect the effect size irrespective of baseline value.

It was not possible to collect specific details of previous diabetes treatments beyond the broad categories of oral anti-diabetic drug and/or insulin due to differences in trade name and the languages used on the case report forms (CRFs).

2.2.2. Bivariate analysis of covariance (ANCOVA)

The following subgroups of interest were investigated: region and ethnicity, sex, age, BMI, smoking, initial dose of acarbose, baseline HbA_{1c}, baseline FPG, baseline post-prandial glucose excursion (PPGE, e.g. PPG minus FPG), duration of disease and pre-treatment status.

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