The Efficacy and Safety of Acarbose compared with Voglibose in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis

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Abstract

Background: Acarbose and voglibose are alpha-glucosidase inhibitors and they are an effective therapy in patients with diabetes mellitus. Our aim is to directly compare the efficacy and safety of acarbose and voglibose for the treatment of patients with type 2 diabetes.

Methods: We searched the international web databases (PubMed, EMBASE, Cochrane Library, Web of Science) with an English language restriction (up to August, 2016). In addition, we checked bibliographies of each included study and the latest reviews to identify additional studies. For each clinical outcome, dichotomous data were analyzed by using the risk ratio (RR) with the 95% confidence interval (CI). Continuous outcomes measured on the same scale and units were analyzed by using weighted mean differences (WMD) with the 95% confidence interval (CI); if continuous outcomes were measured on the different scale or units, it were analyzed by using standardised mean differences (SMD) with the 95% confidence interval (CI).

Results: There are no differences in glycemic control between acarbose and voglibose while adverse events in acarbose group were higher than voglibose group.

Conclusion: Our limited evidence finds that voglibose is more suitable for the treatment of type 2 diabetes compared with acarbose. Further well-designed and multicentric RCTs with larger sample are required to confirm these findings.

Keywords: Acarbose; Voglibose; Type 2 diabetes; Systematic review; Meta-analysis

Introduction

Type 2 diabetes, a gradual and complex disease with one characteristic of impaired insulin secretion, is difficult to treat available in a long time [1,2]. Type 2 diabetes has become a global health problem because of a sharp rise in incidence [3]. The study have estimated that by 2030, global adult (20 to 79 years) diabetes was estimated at 439 million and the prevalence was 7.7% [4]. The morbidity and mortality in type 2 diabetes will increase in the future, which causes serious burden for human beings.

Acarbose and voglibose are alpha-glucosidase inhibitors which restrain the increase in postprandial blood glucose levels through restraining as well as delaying digestion and absorption of carbohydrates; therefore they are an effective therapy in patients with diabetes mellitus [5-10]. Alpha-glucosidase inhibitors have been at the as first-line and second-line therapies in the treatment for patients with diabetes mellitus in Asian [11]. An increasing number of randomized controlled trials report the efficacy and safety of alpha-glucosidase inhibitors in patients with type 2 diabetes.

Although the previous systematic reviews [12-14] had assessed the efficacy and safety of alpha-glucosidase inhibitors for patients with type 2 diabetes, there are still no any systematic reviews or meta-analysis that only directly summarize comparison data between acarbose and voglibose regarding the efficacy and safety for the treatment of patients with type 2 diabetes. We did a systematic review in order to directly compare the efficacy and safety of acarbose and voglibose for the treatment of patients with type 2 diabetes.

Methods

We reported this systematic review in accordance with preferred reporting items for systematic reviews and meta-analyses (PRISMA) [15].

Data sources and searches

The international web databases (PubMed, EMBASE, Cochrane Library, Web of Science) were searched with an English language restriction (up to August, 2016). We searched studies about the efficacy and safety of acarbose compared with voglibose in patients with type 2 diabetes from the international web databases using the following search terms: "diabetes mellitus, type 2", “niddm”, “maturity-onset diabetes”, “diabetes mellitus, noninsulin-dependent”, “diabetes mellitus, adult-onset”, “adult-onset diabetes mellitus”, “diabetes mellitus, onset”, “diabetes mellitus, ketosis-resistant”, “diabetes mellitus, ketosis resistant”, “ketosis-resistant diabetes mellitus”, “diabetes mellitus, maturity-onset”, “diabetes mellitus, non-insulin dependent”, “diabetes mellitus, non-insulin-dependent”, “non-insulin-dependent diabetes mellitus”,

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“diabetes mellitus, noninsulin dependent”, “diabetes mellitus, slow-onset”, “diabetes mellitus, slow onset”, “slow-onset diabetes mellitus”, “diabetes mellitus, stable”, “stable diabetes mellitus”, “diabetes mellitus, type II”, “maturity-onset diabetes mellitus”, “maturity onset diabetes mellitus”, “mody”, “type 2 diabetes mellitus”, “acarbose”, “bay g 5421”, “glumida”, “lasa brand of acarbose”, “precose”, “glucor”, “bayer brand of acarbose”, “glucobay”, “prandase”, “voglibose”, “basen”, “random”, and “randomized controlled trial”. Furthermore, we performed a hand search, such as checking bibliographies of each included study and the latest reviews. All articles from the above search were transferred to Endnote X7 software so as to efficiently select qualified studies.

**Inclusion criteria and exclusion criteria**

We selected eligible studies according to the following criteria: (1) participants were patients with type 2 diabetes; (2) participants were randomly placed on voglibose (with or without other drugs) or acarbose (with or without other drugs); (4) publication language was English; (5) not less than one of outcomes (glycosylated hemoglobin (HbA1c), fasting blood glucose (FBG), postprandial blood glucose, triglycerides, total cholesterol, LDL (low-density lipoprotein), HDL (high-density lipoprotein) fasting insulin, postprandial serum insulin, fasting glucagon, postprandial serum glucagon, body weight, hypoglycemia, hyperglycemia, adverse event); (5) randomized controlled trials (RCTs) or randomised cross-over studies. Moreover, we also excluded the following studies: duplicate publication, studies without original data.

**Data extraction**

We made a spreadsheet using Microsoft Excel 2010 before extracting data. We extracted the following data from each included study: the first author; publication year; study design; sample size; characteristics of patient (age, sex); acarbose (dose, administration frequency, duration); voglibose(dose, administration frequency, duration); outcomes (glycosylated hemoglobin (HbA1c), fasting blood glucose (FBG), postprandial blood glucose, triglycerides, total cholesterol, LDL (low-density lipoprotein), HDL (high-density lipoprotein) fasting insulin, postprandial serum insulin, fasting glucagon, postprandial serum glucagon, body weight, hypoglycemia, hyperglycemia, adverse event). The above data was imported in the spreadsheet. The process of data extraction was independently performed by two authors. All inconsistent results in the process of data extraction were resolved by detailed discussion.

**Assessment of bias**

Two authors independently assessed the risk of bias for each eligible study using the Cochrane Collaboration’s tool [16]. This tool includes seven items: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting; other bias. Each item has three options: low risk of bias; unclear risk of bias; high risk of bias. Authors selected each option according to detail description of each eligible study. All inconsistent results in the process of data extraction were resolved by detailed discussion.

**Statistical analysis**

For each clinical outcome, dichotomous data were analyzed by using the risk ratio (RR) with the 95% confidence interval (CI); if continuous outcomes were measured on the same scale and units, it were analyzed by using weighted mean differences (WMD) with the 95% confidence interval (CI); if continuous outcomes were measured on the different scale or units, it were analyzed by using standardised mean differences (SMD) with the 95% confidence interval (CI). We selected a fixed or random model according to heterogeneity among all included studies. We evaluated heterogeneity among all included studies using I-square (I²) [17]. If severe heterogeneity (I²>50%) with an associated p-value<0.05) occurred, the fixed model was chosen; otherwise, the random model was selected [18,19]. We used Stata14.0 software performed these analyses. In addition, we used to funnel plots examd publication bias. We explored sources of heterogeneity using subgroup analysis, sensitivity analysis and meta-regression analysis.

**Results**

**Study selection and risk of bias summary**

We got a total of 104 articles from the international web databases and hand search. There were 70 articles after duplicates removed. We excluded 59 articles through reading titles and abstracts. Eleven articles were required to read full text. Finally, a total of 5 articles [11,20-23] were included in this systematic review. We summarized characteristics of each included study in Figure 1 and Table 1. Risk of bias summary was shown in Table 2.

![Figure 1: Flow diagram of study selection. RCTs: Randomized Controlled Trials.](image-url)
Outcomes

**HbA1c**: No significant difference was found on change of HbA1c between acarbose group and voglibose group (WMD 0.04; 95% CI -0.39 to 0.47) (Figure 2).

**FBG**: No significant difference was found on change of FBG between acarbose group and voglibose group (WMD -0.09; 95% CI -0.46 to 0.28) (Figure 3a).

**Postprandial blood glucose**: No significant difference was found on change of postprandial blood glucose between acarbose group and voglibose group (WMD -0.29; 95% CI -1.11 to 0.52) (Figure 3b).

**Triglycerides**: No significant difference was found on change of triglycerides between acarbose group and voglibose group (SWM -0.02; 95% CI -0.33 to 0.29) (Figure 4a).

**Total cholesterol**: No significant difference was found on change of total cholesterol between acarbose group and voglibose group (SWM 0.12; 95% CI -0.18 to 0.43) (Figure 4b).

**LDL**: No significant difference was found on change of LDL between acarbose group and voglibose group (SWM 0.15; 95% CI -0.15 to 0.46) (Figure 4c).

**HDL**: No significant difference was found on change of HDL between acarbose group and voglibose group (SWM 0.14; 95% CI -0.17 to 0.45) (Figure 4d).

**Fasting insulin**: There was just one study [22] reported change of fasting insulin. Thus, it was impossible to compare.

**Postprandial serum insulin**: No significant difference was found on change of postprandial serum insulin between acarbose group and voglibose group (SWM 0.27; 95% CI -0.12 to 0.66) (Figure 4e).

**Fasting glucagon**: No any included studies reported change of fasting glucagon. Thus, no relevant data were analysed.

**Postprandial serum glucagon**: No any included studies reported change of postprandial serum glucagon. Thus, no relevant data were analysed.

**Body weight**: No significant difference was found on change of body weight between acarbose group and voglibose group (SWM 0.20; 95% CI -0.85 to 0.45) (Figure 5).
Our systematic review had several limitations. We only included in English studies, and it was a limitation. There may be some unpublished studies which we cannot find, which caused a potential limitation. What is more, our included trials had methodological limitations. Three included trials [11,22-23] had unclear risk of bias in random sequence generation. All included trials [11,20-22] had unclear risk of bias in allocation concealment. One included trial [20] had high risk of bias in blinding of participants and personnel. Four included trials [11,21-23] had unclear risk of bias in blinding of outcome assessment. Four included trials [11,21-23] had unclear risk of bias in allocation concealment. One included trial [20] had high risk of bias in blinding of participants and personnel. One trial [20] had high risk of bias in blinding of outcome assessment. Four included trials [11,21-23] had unclear risk of bias in allocation concealment. Finally, a limitation was caused due to lack of gray literatures (presentations, unpublished data, government reports, and other traditional or nontraditional sources of evidence).

**Conclusion**

Our insufficient evidence finds that voglibose is more suitable for the treatment of type 2 diabetes compared with acarbose. Further well-designed and multicentric RCTs with a larger sample to evaluate the efficacy and safety of acarbose compared with voglibose in patients with type 2 diabetes are required. These trials will clearly address the efficacy and safety of acarbose compared with voglibose in patients with type 2 diabetes.
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Ethical Approval
This article does not contain any studies with human participants or animals performed by any of the authors.

References