

Acarbose Monotherapy and Type 2 Diabetes Prevention in Eastern and Western Prediabetes: An Ethnicity-Specific Meta-Analysis

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ABSTRACT

Purpose: Acarbose is effective in delaying or preventing the progression of prediabetes to type 2 diabetes mellitus (T2DM). The aim of this study was to assess differences in the preventive effects of acarbose in Eastern and Western populations with prediabetes.

Methods: We performed a systematic search of databases and reference lists of clinical trials conducted through August 2013. Randomized controlled trials of acarbose alone, with a minimum intervention duration of 3 years and which provided data on T2DM incidence, were included for analysis. Analyses were conducted by using Review Manager version 5.1 software.

Findings: Eight randomized controlled trials with 2628 participants were included. Acarbose decreased the occurrence of T2DM (number needed to treat [NNT], 6.7). Compared with the control (placebo and/or lifestyle intervention), the incidence of T2DM was significantly lower in the Eastern group (NNT, 5.9) than in the Western group (NNT, 11.1) ($P < 0.0001$, $I^2 = 94.7\%$). At the end of follow-up, reversal of prediabetes to normal glucose tolerance was more likely in the Eastern group (NNT, 4.3) than in the Western group (NNT, 25) ($P = 0.004$, $I^2 = 92\%$). Among those remaining prediabetic, there was no significant difference between the subtotal estimates for the subgroups ($P = 0.17$, $I^2 = 46.5\%$). There was no positive correlation between preventive effect and dose, and no difference in studies with varying follow-up durations within and across either ethnic group.

Implications: The preventive effect of acarbose on the development of diabetes seems superior in Eastern populations with prediabetes compared with Western

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Key words: acarbose, ethnicity, diabetes prevention, prediabetes.

INTRODUCTION

Diabetes is a severe and increasing worldwide health burden, with a continual rise in the prevalence of type 2 diabetes mellitus (T2DM) predicted over the next few decades, from the currently predicted 382 million to 592 million by 2035.¹ More than 60% of people with T2DM develop cardiovascular disease, which is a more severe and costly complication than the diabetes itself.² Prediabetes, which is an intermediate stage between normal glucose tolerance (NGT) and diabetes mellitus, includes states of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and IFG combined with IGT.³ A total of 5% to 10% of populations with prediabetes develop diabetes yearly, with ~70% ultimately progressing to diabetes.^{4,5} The Da Qing study found that the 20-year average cumulative incidence of diabetes was 93% without any intervention.⁶ Both IFG and IGT are related to a high risk of developing diabetes and the progression of associated complications such as cardiovascular disease, which occur more frequently with increasing glycemia even in the prediabetic state.⁷ Such estimates present

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disturbing implications for global human morbidity and mortality related to diabetes.

Several trials have found reductions in the incidence of diabetes in prediabetic populations with the use of lifestyle and drug-based interventions.^{8–11} The Da Qing study with a 23-year follow-up found that a 6-year lifestyle intervention program for subjects with IGT in China led to a reduced incidence of cardiovascular and all-cause mortality and diabetes.¹² The International Diabetes Federation recommends the use of pharmaceutical interventions as preventive therapy for diabetes if lifestyle interventions cannot achieve the expected weight loss and/or glucose tolerance targets set by the health care provider. Acarbose is a recommended agent for tolerant subjects.¹³ α -Glucosidase inhibitors (AGIs), mainly acarbose, are commonly used oral hypoglycemic drugs, especially in East Asia. The antihyperglycemic effect of AGIs results from a competitive, reversible inhibition of pancreatic α -amylase and membrane-bound intestinal α -glucoside hydrolase enzymes, which block starch and sucrose degradation and delay the absorption of fructose and glucose in the digestive tract. Consequently, insulin and blood glucose are reduced, especially postprandial glucose (PPG).¹⁴ In patients with IGT, acarbose can decrease insulin resistance,¹⁵ which is a significant factor in the development of diabetes; thus, acarbose is associated with preventing or delaying IGT progression to diabetes. It also magnifies incretin secretion and changes gut microbiota flora, which may partly explain its benefits.¹⁶

STOP-NIDDM (Study to Prevent Non-Insulin-Dependent Diabetes Mellitus)^{11,17,18} and a systematic review¹⁹ of AGIs in prediabetes showed that acarbose effectively reduces IGT progression to T2DM and prevents cardiovascular events. A 3-year study in China found that acarbose decreased the risk of T2DM by 87.8%²⁰; however, because of its mechanism of action and predominant effects on PPG, acarbose's hypoglycemic effects might depend on the dietary starch content. This finding is in accordance with the widespread prescription of acarbose in Eastern countries, which have a high prevalence of isolated PPG.²¹ Our previous meta-analyses showed that the hypoglycemic and weight loss effects of acarbose are greater in Eastern hyperglycemic populations than in their Western counterparts.^{21,22} Thus, we conducted the present ethnicity-specific meta-analysis of the preventive effects of acarbose in Eastern and Western prediabetic populations.

MATERIALS AND METHODS

Search Strategy

Detailed search strategies were designed to detect randomized controlled trials conducted to August 2013. The Cochrane Central Register of Controlled Trials (CENTRAL) (from 1960), MEDLINE (from 1966), and EMBASE (from 1974) databases were searched. Chinese-language studies dating from 1989 were retrieved from Wanfang, the China National Knowledge Infrastructure, and the Chinese Technical Periodicals databases. The following search terms were used individually and in combination: *acarbose, prediabetes, impaired glucose tolerance, IGT, impaired fasting glucose, IFG, and controlled trial.*

Classification of Ethnicity

Retrieved studies were divided into 2 ethnic groups: Eastern (Asia) or Western (Europe and North America) according to the region in which the studies were performed. The differences between these 2 groups were mostly characterized by the dietary content, especially the proportion of dietary energy derived from cereals (Eastern, 50%–60%; Western, 30%).²¹

Study Selection

Studies published or unpublished in English or Chinese and documents in other languages with English abstracts were investigated.

The following inclusion criteria were used: (1) randomized or quasi-randomized controlled trials; (2) inclusion of adults (aged >18 years) in a prediabetic state (IGT and/or IFG meeting the American Diabetes Association [ADA] or World Health Organization [WHO] diagnostic standards); (3) comparison of a trial group receiving any dose of acarbose monotherapy versus a control group receiving placebo, a nonpharmacologic intervention (diet and/or exercise therapy), or other oral hypoglycemic agent; (4) trials with a minimum duration of 3 years; and (5) determination of prognosis as the outcome indicator (studies included had to report or provide data to calculate T2DM incidence). The following studies were excluded: (1) crossover trials; (2) studies without available data for calculating the incidence of T2DM; and (3) articles in which the intervention was tested in patients with preexisting diabetes. All the records identified were managed by using EndNote reference management software version X5 (Thomson Reuters, Philadelphia, Pennsylvania).

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