ORIGINAL RESEARCH

The Effects of Acarbose on Non-Diabetic Overweight and Obese Patients: A Meta-Analysis

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ABSTRACT

Introduction: This systematic review aims to verify the efficacy of acarbose monotherapy in treating obese or overweight patients without diabetes.

Methods: In the study, we conducted a systematic search on Pub-Med, EMBASE, Cochrane, and Science Citation Index Expanded databases in search of clinical trials on acarbose treatment, overweight and obesity. The crucial inclusion criteria were as follows: (1) the included population has been diagnosed as overweight or obesity (BMI≥25kg/m^2); (2) randomized controlled trials (RCTs); (3) patients have undergone acarbose monotherapy or placebo control; (4) acarbose treatment lasts for at least three months. Exclusion criteria were as follows: (1) patients diagnosed as diabetes mellitus (DM); (2) patients recieved a weight loss medication or surgery 3 months prior; (3) papers not published in English; (4) repeated research results of the same experiment or repeated published documents.

Results: A total of 7 studies involving 132 in acarbose group and 137 in placebo group，269 subjects in total，were included in this meta-analysis. From the selected 7 papers, we extracted the following clinical parameters: systolic blood pressure (SBP), diastolic blood pressure (DBP), body weight (BW), body mass index (BMI), triglyceride (TG), total cholesterol (TC), low density lipoprotein (LDL), high density cholesterol (HDL), and fasting plasma glucose (FPG). An important finding of our research is that TG is

the only significantly reduced parameter in acarbose group. Weight mean difference (WMD) was -0.21 (95% CI -0.33, -0.09) mmol/L between acarbose (P =0.0006) and the placebo. Reduction of BMI was also greater for acarbose than placebo subjects, although the discrepancy was not statistically significant (P=0.56). Moreover, no hypoglycemia occurred in either acarbose group or placebo group. A few subjects experienced gastrointestinal reactions, but these were mild or improved over time. Acarbose has no obvious influence on other metabolic indexes. **Conclusion:** Acarbose monotherapy is beneficial to reduce TG levels in obese or overweight patients, and will not result in hypoglycemia during medication. The side effects of acarbose are slight.

Keywords: Acarbose; Meta-Analysis; Obesity; Overweight

KEY SUMMARY POINTS

Why carry out this study?

- Obesity increases the incidence of cardiovascular disease, diabetes, hyper-lipidemia and other diseases, and led an economic burden.
- So far, the effect of the bariatric medications is poor, and there is no evidence that weight loss medications have a beneficial effect on morbidity and mortality of cardiovascular disease.
- Clinical studies have shown that acarbose treatment can lose weight, lower lipid levels, but the conclusion was not unified.
- Our study aimed to analyze the studies according acarbose and provides new thinking and evidence for the treatment of obese patients.

What was learned from the study?

- Our study confirmed that acarbose can reduce triglyceride levels of obesity or overweight people.
- Although the weight did not draw a statistically significant decline, our sensitivity analysis suggested the result was not stable, it might be related to the dose of the drug and the insufficient treatment duration.
- Therefore, acarbose was expected to improve metabolic markers such as triglycerides levels and may be used in the treatment of obesity and overweight people.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.13341464.

INTRODUCTION

Obesity is a chronic metabolic disease which develops with the excessive accumulation of adipose tissue in the body. Currently, almost one third of the world's population is defined as overweight or obesity [8]. Reilly JJ et al[9] indicated that the global prevalence of obese people has doubled from 1980 to 2015 after executing a epidemiological survey on obesity involving 195 countries, and the amount of obese people is continuously increasing. It is known that obesity-related diseases often exert a potential or significant effect on an individual's quality of life and economic level [9]. More importanty, obesity will increase the incidence of cardiovascular disease (CVD), DM, hyperlipidemia and musculoskeletal diseases [10]. Therefore, treating and managing obesity is of great urgency. Until now, medication of obesity has often failed, and there is no evidence revealing that weight loss medication plays a beneficial role in the incidence and mortality of CVD [11]. Acarbose, a glucose oxidase inhibitor, is a unique anti-diabetic drug used for reducing postprandial blood glucose. It has conventionaly been prescribed as an anti-diabetic medication. By competitively binding to α-glucosidase, which acts on the absorption of carbohydrates in the small intestine [12], acarbose reduces postprandial blood sugar and insulin levels [13]. The main side effects of acarbose are abdominal symptoms such as bloating and diarrhea[12]. The existing studies [4-6] and the latest study[14]have confirmed the effectiveness and safety of

acarbose in lowering postprandial hyperglycaemia and improving cardiovascular outcomes in obese and prediabetes patient. Studies have shown that acarbose can improve the metabolic indexes of obese and overweight patients, but conclusions are inconsistant: A study conducted by Noushin Khalili[14] revealed that the administration of acarbose in patients with MetS including overweight and obese patients can decrease weight, and also increases HDL. Rachmani R[1] and Malaguarnera M[7] reported a significant reduction in TG levels, Penna I[5] and Nakhaee A[15]reported a reduction in BMI after acarbose treatment in overweight patients, while other articles show a statistically meaningless decline in BMI[2,3] and TG levels[2]. Chiasson JL[6] suggest that acarbose treatment can improve insulin resistance. Studies[4-6] have shown that acarbose can be used in people with impaired glucose tolerance (IGT), and can improve their metabolic status and delay the development of diabetes. Obesity and overweight patients coexist with IGT. However, previous studies[1-2] have shown that taking acarbose can cause gastrointestinal side effects such as bloating and diarrhea. Additionally, there exists no meta-analysis studying the effects of acarbose treatment for obese and overweight people. To evaluate the effects of acarbose on obesity and overweight, we conducting the meta-analysis to compare the effect of acarbose and placebo on metabolic markers in overweight and obese patients.

METHODS

Search Strategy

We searched published articles from Pubmed, EMBASE, Cochrane and the Science Citation Index Extension Database, and searched the references of all the articles as supplementary materials. The search timeline began from the date of establishment of each database to December 2019. The search keywords comprised of "acarbose" and "humans" and "randomized controlled trials".

Inclusion and Exclusion Criteria

Two researchers independently reviewed the published articles and evaluated its potential inclusion in this meta-analysis. If the two researchers disagreed on the article, a third researcher would be brought in to consult and resolve the disagreement. The crucial inclusion criteria were as follows: (1) the included population had been diagnosed as obesity or overweight(BMI≥25kg/m^2); (2) randomized, double-blind comparison studies; (3) patients had undergone acarbose monotherapy or placebo control; (4) the duration of therapy was at least 12-weeks long. Exclusion criteria were as follows: (1) patients diagnosed with DM; (2) patients with a history of a weight loss medication or surgery 3 months prior; (3) papers not published in English; (4) repeated research results of the same experiment or repeated published documents.

Data Extraction

The extracted data included the document title, year of publication, the nationality of the subjects, patients' age, gender, number of cases, medication type, dosage, FBG, SBP, DBP, TG, LDL, HDL, BMI and BW.

Quality Assessment

In the process, we used the seven points of the revised jadad scale （Table 1）[16-17] to estimate the quality of the study. The revised Jadad scale describes whether the research is random and how the random sequence is generated (0-2 points), how to randomize and hide (0-2 points), blind method (0-2 points), and the number and reason of withdrawals or dropouts (0-1 points). The full marks are 7 points, among which 1 - 3 was classified as low quality and 4 - 7 as high quality.

Statistical Analysis

In the current study, we utilized the Review Manager 5.3 to analyze our data. In the included literature, change in all clinical indicators were all extracted as mean ± standard deviation (SD). 7 studies were ultimately selected for this meta-analysis and their heterogeneity was estimated by I^2 statistic. If $I^2 \geq 50\%$, heterogeneity was considered significant; otherwise, heterogeneity was considered insignificant. Considering that the data of the meta-analysis originated from different included articles and its own heterogeneity is remarkable, we used the random effect model to conduct our meta-analysis. The WMD was utilized to describe outcomes with a 95% confidence interval (CI). In this meta-analysis, 0.05 was used as the test

standard. If P ＜0.05, the result was considered statistically significant.

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

RESULTS

Study Selection

In total, 306 studies were eligible for study inclusion after searching the above-mentioned databases, and 7 studies were ultimately enrolled in our meta-analysis. 243 articles were excluded after reviewing article titles and abstracts, 35 articles were excluded for not meeting the inclusion criteria, 9 studies were excluded as they were summary articles, 9 studies were excluded because they are meta-analysis articles and 3 study was excluded for presenting repeat results of the same experiment (Fig.1). The characteristics of included studies are summarized in Table 1.

Effect of Acarbose on HDL

Five studies [1,4-7] were selected for the analysis of the effect of acarbose on HDL. In the five studies, 70 subjects were in the acarbose treatment group and 74 subjects were in the placebo group, for a total of 144 subjects. Among the five studies, the treatment duration of acarbose in two studies was 6 months [1,5], and the treatment duration of acarbose in the other three

studies [4,6,7] was 3, 4 and 5 months respectively, and the dose of acarbose in the five studies exceeded 100mg per day. The decline in HDL was slight between acarbose group and placebo group (p = 0.79, Fig.2); weighted mean difference was -0.01 (95% CI -0.11, 0.08) higher with the acarbose group than the placebo group. Heterogeneity was considered significant (I^2 = 76%).

Effect of Acarbose on FPG

Three studies [2,3,6] were selected for the analysis of the effect of acarbose on FPG. In the three studies, 70 subjects were in the acarbose group and 73 subjects were in the placebo group, for a total of 143 subjects. In these three studies, the subjects were diagnosed as obese patients, and the duration of acarbose treatment was more than 3 months. The reduction of FPG was insignificant (p=0.9, Fig.3) and weighted mean difference was -0.02 (95% CI -0.29, 0.26) higher than the control group. Heterogeneity was considered significant (I^2 = 80%).

Effect of Acarbose on TG

Five studies [1,2,4,5,6] were selected for the analysis of the effect of acarbose on TG. In the five studies, 80 subjects were in the acarbose group and 84 subjects were in the placebo group, for a total of 164 subjects. Among these five studies, the treatment duration of acarbose in two studies [2,4] was 3 months, and the treatment dose of acarbose was 100mg per day [4] and 150mg per day for the first two weeks, 50mg per in the rest of 14 weeks [2].

The treatment duration of the other two studies [1,5]was 6 months, and the treatment duration of acarbose was 50mg three times a day, and the remaining one was 4 months[6].The group treated with acarbose had a sharp reduction in TG compared with the placebo group (WMD = -0.21, 95%CI: -0.33 ~ -0.09, P =0.0006 Fig.4). The random effects model was used to compared with the placebo group (Heterogeneity: I^2 = 53%).

Effect of Acarbose on BMI

Five studies [1,2,4,5,6] were selected for the analysis of the effect of acarbose on BMI. In the five studies, 80 subjects were in the acarbose group and 84 subjects were in the control group, for a total of 164 subjects. There was no significant discrepancy in BMI between the acarbose group and the placebo group (WMD = -0.62, 95%CI: -2.67 ~ 1.44, P=0.56 Fig.5) and heterogeneity was significant (P＜0.00001 Heterogeneity: I^2 = 91%).

Effect of Acarbose on LDL

Four studies [1,2,5,7] were selected for the analysis of the effect of the effect of acarbose on LDL. In the four studies, 81 subjects were in the acarbose group and 83 subjects were in the placebo group, for a total of 164 subjects. There was no obvious difference between the acarbose group and the control group (WMD 0.06, 95%CI -0.03 ~0.15, P = 0.2, Fig.6) with insignificant heterogeneity (Heterogeneity: I^2 = 23%).

Effect of Acarbose on SBP

Four studies [1,4,5,6] were selected for the analysis of the effect of acarbose

on SBP. 55 subjects were in the acarbose group and 59 subjects were in the placebo group, for a total of 114 subjects. There was no statistical difference between the acarbose group and the placebo group (WMD -7.87, 95%CI -15.53 ~ -0.15, P=0.05, Fig.7) with high heterogeneity (P＜0.0001, Heterogeneity: $I^2 = 88\%$).

Effect of Acarbose on DBP

Four studies [1,4,5,6] were selected for the analysis of the effect of acarbose on DBP. In the four studies, 55 subjects were in the acarbose group and 59 subjects were in the placebo group, for a total of 114 subjects. There was a slight reduction in DBP in the acarbose group compared to the control group (p=0.79, $I^2 = 83\%$, Fig.8); heterogeneity was considered obvious and compared with the placebo group, weighted mean difference was -0.59 (95% CI -4.84, 3.66) higher with the acarbose group.

Sensitivity Analysis

An explanation for high heterogeneity can be explored through an analysis of sensitivity. Firstly, the reason for the high heterogeneity is found by excluding a certain document or subgroup analysis. However, due to the small number of articles we have included, the characteristics of the study in each article differ from one another, limiting this step to be carried out. Secondly, this meta-analysis is repeated by changing the statistical model, with the expectation that consistent calculations show higher reliability. If the two methods did not result in a high degree of heterogeneity, we

conclude that the quality of the literature, publication bias, differences in measurement results and other reasons could be the sources of the high heterogeneity. After changing the effects model for this meta-analysis, we found that the results of other indicators are consistent except BMI and SBP. The decline of BMI was significant in the acarbose group (WMD -1.82,95%CI（-2.3，-1.34） P＜0.00001， Fig.9), and there was significant reduction of SBP between the acarbose group and the control group ((WMD -3.23,95%CI（-5.29，-1.16） P=0.002, Fig.10) This indicates that acarbose has consistent results in reducing triglyceride levels in obese patients without diabetes compared with the placebo group, and acarbose has inconsistent results in reducing BMI and SBP.

DISCUSSION

The available data [9] suggests that obesity has become a global concern. Obesity has become a global public health problem and that reduces the longevity and quality of life [18]. Existing weight loss methods include dietary intervention, behavior modification and pharmacotherapy [19], but these have not result in satisfactory therapeutic effects. Pharmacotherapy has been utilized to manage obesity for more than ten years with little success in improving metabolic profiles [20]. Furthermore, diet pills can be expensive and have negative side effects and rebound effects, specifically metabolic side effects such as hypertension and cardiovascular damage,

limiting its use in the long term [21].

Acarbose can be used for the mono-treatment of DM or in combination with other hypoglycemic drugs or insulin injections to regulate blood glucose. It is well known that obesity is closely related to diabetes, and obese populations have a higher risk of developing IGT and diabetes [22-23]. Acarbose has already established as an overweight drug [24]. Research has demonstrated that acarbose can improve blood lipid metabolic disorders and reduce the incidence of CVD in diabetic patients [12]. Evidence has shown that it can aid in weight reduction [24-25]and lipid level reduction for patients with type 2 diabetes [26]. Diabetes often accompanied with obesity. On the basis of the above mentioned, we hypotesized that acarbose could also be beneficial for obese patients without diabetes. Concerning the documented literature of acarbose on obesity, there has been contradicting conclusion. Evidence shows acarbose may be beneficial for obese patients, with changes including weight loss [5,6,15,23], fat reduction [1,2,5,7,27], CVD events reduction [12] and other effects. Other research shows there is no influence of acarbose on weight [1,2,3,4,28], lipid levels [3,4,6,15], etc. Therefore, this meta-analysis aimed to compare the effect of acarbose monotreatment with a control group on obese patients without DM.

Our systematic results reveal that acarbose lowered TG level, and is

consistent with four other articles [20,29.30.31] that showed acarbose could induce TG drop in IGT populations [20,30,31,]and obese people with familial hypertriglyceridemia [29]. Consistent data has demonstrated that acarbose led to TG reduction in animals and human experiments [32-34]. Acarbose therapy reduces TG concentration with the following mechanism: Firstly, it reduces the TG concentration through its effects on postprandial serum glucose [35] by reducing the absorption of glucose in the small intestine; this reduces the conversion of excess sugar to blood lipids, indirectly regulating lipid metabolism; Secondly, acarbose may have some direct effect on lipid absorption in the intestine. Thirdly, acarbose reduces the TG level by acting on insulin levels [35]. Obese patients often suffer from insulin resistance, and the concentration of insulin receptors per adipocyte is reduced in obese patients [36]. As the level of insulin in serum increases, this results in an increase in free fatty acid, a decrease in lipoprotein enzyme activity, and an increase in liver lipase activity, which eventually leads to lipid metabolic disorders [37]. Acarbose can combat insulin resistance [1], thereby correcting lipid metabolic disorders and reducing triglyceride levels. Lastly, acarbose may reduce the generation of chylomicron residues by impairing the synthesis of triglycerides in the small intestine, thus affecting serum triglyceride levels [38].

In these two articles [1-2], the number of adverse events caused by taking

acarbose was reported. One [1] reported that 7/28 subjects in the acarbose treatment group experienced mild abdominal symptoms such as abdominal distension, while 3/28 subjects in the control group have mild abdominal symptoms. Two patients in the acarbose group stopped taking drugs. Another study [2] reported that 12/25 patients in acarbose treatment group had abdominal distension while the dose of acarbose is more than that of the former. The other five articles [3-7] only reported that a few patients had mild abdominal symptoms, but they did not affect the continued use of drugs, and did not report the specific number. A few subjects experienced gastrointestinal reactions, but these were mild or improved over time.

In addition, our meta-analysis found no statistically significant reduction in BMI between the acarbose and control group. We believe the reasons for this are as follows: Firstly, we found that the dose of acarbose used in the two articles [5,6] which showed a significant BMI reduction was larger, almost 300mg per day, while the dose of other three articles [1,2,4] without significant BMI reduction result was smaller, almost 150mg per day. We suspect this difference in the change in BMI is related to the dose of acarbose. Secondly, we found the study duration of the former articles is longer than the latter. We believe the change in BMI is related to the acarbose use duration. One study [24] by Siraj ES et al supports our view, showing that acarbose can lead to weight loss especially when used for a

long period of time. Thirdly, the lack of data for changes in weight after drug treatment from one [5] of the former two articles and the small number of articles included in the meta-analysis make it difficult for us to carry out data analysis and subgroup analysis. It may come a significant reduction if the dose of acarbose tablets and treatment duration is enough.

Although the BMI discrepancy was not statistically significant, we found the reduction of BMI was also greater for acarbose than placebo subjects, which is consistent with much literature [6,12,15].The latest article indicate that acarbose treatment in patients with obesity and overweight can decrease weight and abdominal obesity as well as the reduction of inflammatory and cardiovascular markers, including flow mediated dilation(FMD), intima media thickness(IMT), epicardial fat thickness(EFT), and C-reactive protein (CRP)[39].The possible mechanism may be the follows: Firstly, acarbose can reduce the digestion and absorption of carbohydrates, thereby reducing calorie intake [23] and achieving the goal of weight loss [40]. Secondly, by inhibiting appetite and fat absorption, leading to fat or calorie malnutrition, weight loss is more obvious in long-term use [24]. Furthermore, our meta-analysis showed that systolic blood pressure and body mass index decreased, although the results were not statistically significant. Some research has proposed that acarbose therapy can reduce blood pressure, but others speculate that this

reduction in blood pressure can be attributed to weight loss [5]. We do not have the data from each experimental sample to study the correlation between the two decrements. After conducting sensitivity analysis and repeated the meta-analysis using fixed effect model, we found that BMI and SBP decreased significantly after acarbose treatment with statistical significance. Due to the above mentioned, we believe acarbose has the potential effect of reducing blood pressure and for weight loss.

Our included articles are RCTs, with good baseline similarity, and our meta-analysis produced promising results. However, there are still some limitations. Firstly, the present meta-analysis was not registered in PROSPERO website, which is an important bias and limitation. Secondly, the heterogeneity among the research results is large, and the quality of some studies is not high. Thirdly, the number of studies and study subjects in each study was small, and tests for publication bias could not be carried out. Fourthly, after conducting sensitivity analysis, it was revealed that several of our results were not stable. Lastly, almost all studies were of short duration. Despite our limitations, it was still shown that acarbose could produce TG reduction. To add, most of the articles we included in the double group included an element of lifestyle changes (diet and exercise), which suggests that acarbose combined with lifestyle changes may have greater benefits on metabolic indexes for obese people. In

addition, there are few experimental studies on acarbose for simple obesity, most of which are combined with some metabolic diseases. If we explore the effects of acarbose on simple obesity patients, it may help delay the subsequent complications and complications of obesity. More research with larger sample sizes and conducted over a longer time period are certainly needed to produce more results in the future.

CONCLUSION

Our meta-analysis shows acarbose can reduce triglycerides and did not lead to hypoglycemia in obese or overweight people. Acarbose has potential to be considered a new and alternative drug in the treatment of obesity.

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Authorship

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosures

The authors Ai-Qing Yu, Jiong Le, Wen-Tao Huang, Bin Li, Hui-Xin Liang, Qun Wang, Yu-Ting Liu, Charlotte-Aimee Young, Mei-Ying Zhang, Shu-Lan Qin declare that they have no competing interests.

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability

All data generated or analyzed during this study are included in this published article/as supplementary information files.

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Fig.1 Flow chart of study selection process

Fig. 2 a. Forest Plot showed the baseline of HDL before the treatment in the acarbose group and placebo group. The difference was insignificant between acarbose group and placebo group. **b.** Forest Plot showed the change of HDL after the treatment in the acarbose group and placebo group. The decline in HDL was no significant in acarbose group than placebo group.

Fig. 3 a. Forest Plot showed the baseline of FPG before the treatment in the acarbose group and placebo group. The difference was insignificant between acarbose group and placebo group. **b.**Forest Plot showed the change of FBG after the treatment in the acarbose group and placebo group. The decline in FBG was no significant in acarbose group than placebo group.

Fig. 4 a. Forest Plot showed the baseline of TG before the treatment in the acarbose group and placebo group. The difference was insignificant between acarbose group and placebo group. **b.**Forest Plot showed the change of TG after the treatment in the acarbose group and placebo group.The decline in TG was more highly significant in acarbose than control.

Fig. 5 a. Forest Plot showed the baseline of BMI before the treatment in the acarbose group and placebo group. The difference was insignificant between acarbose group and placebo group. **b.** Forest Plot showing the change of BMI after the treatment in the acarbose group and placebo group.there was no remarkable difference in BMI between the acarbose and placebo

Fig. 6 a. Forest Plot showed the baseline of LDL before the treatment in the acarbose group and placebo group. The difference was insignificant between acarbose group and placebo group. **b.** Forest Plot showed the change of LDL after the treatment in the acarbose group and placebo group. The decline in SBP was insignificant.

Fig. 7 a. Forest Plot showed the baseline of SBP before the treatment in the acarbose group and placebo group. The difference was insignificant between acarbose group and placebo group. **b.** Forest Plot showed the change of SBP after the treatment in the acarbose group and placebo group. The decline in SBP was insignificant.

Fig. 8 a. Forest Plot showed the baseline of DBP before the treatment in the acarbose group and placebo group. The difference was insignificant between acarbose group and placebo group. **b.** Forest Plot showed the change of DBP after the treatment in the acarbose group and placebo group. The decline in DBP was insignificant.

Fig. 9 BMI sensitivity analysis by changing the statistical model

Fig. 10 SBP sensitivity analysis by changing the statistical model

Table 1 Characteristics of included studies and Jadad score of included studies

Study (first author + year of publication)	Nation	Duration	Blinding	Randomistation	Diagnoses	Intervention for Acarbose/control	Mean daily acarbose dose	The Jadad score
Rachmani, R. 2004	Israel	24weeks	Yes	Yes	Obesity, hypertension	Acarbose/Placebo	50mg tid	three
Bayraktar, F. 1998	Turkey	12weeks	Yes	Yes	Obesity	Acarbose/Placebo	150mgqd 2weeks/300mgqd 10weeks	three
Hauner, H. 2001	Germany	14weeks	Yes	Yes	Obesity	Acarbose/Placebo	5mg	three
M. Malaguarnera, 1999	Italy	20weeks	Yes	Yes	Familial hypertriglyc	Acarbose/Placebo	50mg bid	four
Laube, H. 1998	Germany	12weeks	Yes	Yes	Overweight with IGT	Acarbose/Placebo	100mg qd	three
Penna, I. A 2007	Brazil	24weeks	Yes	Yes	Obese, PCOS and insulin resistance	Acarbose/Placebo	50mg tid	six
Chiasson, JL1996	Canada	16weeks	Yes	Yes	Obese subjects with IGT	Acarbose/Placebo	50mg tid 2w /100mg tid 14w	three

Table 2 Sensitivity analysis

indicators	statistical model	WMD,95%CI	P
TG	the fixed effects model	WMD -0.25,95%CI（-0.30，-0.19）	＜0.00001
BMI	the fixed effects model	WMD -1.82,95%CI（-2.3，-1.34）	＜0.00001
SBP	the fixed effects model	WMD -3.23,95%CI（-5.29，-1.16）	0.002
DBP	the fixed effects model	WMD 0.04,95%CI（-1.45，1.53）	0.96
FPG	the fixed effects model	WMD -0.07,95%CI（-0.13，-0.01）	0.03
LDL	the fixed effects model	WMD 0.05,95%CI（-0.01，0.12）	0.12
HDL	the fixed effects model	WMD -0.01,95%CI（-0.05，0.03）	0.76