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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 availably 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, but their results are inconsistent. Thus, there are some systematic reviews [12-14] which assessed 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, adult onset”, “diabetes mellitus, ketosis-resistant”, “diabetes mellitus, ketosis resistant”, “ketosis-resistant diabetes mellitus”, “diabetes mellitus, maturity-onset”, “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 events). 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 (I^2) [17]. If severe heterogeneity (I^2 >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 examed 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.

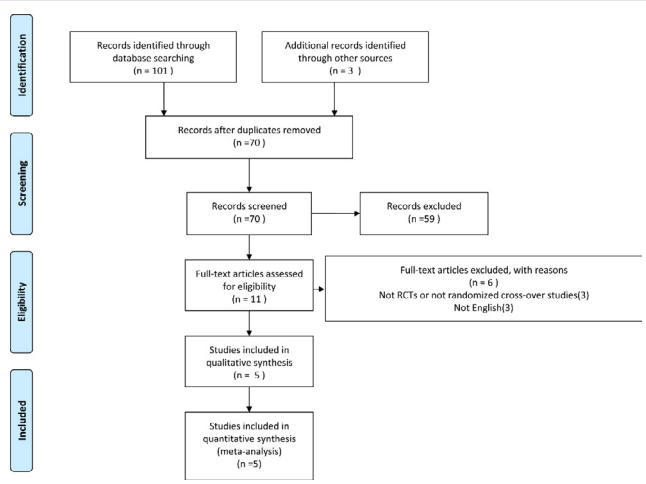

Figure 1: Flow diagram of study selection. RCTs: Randomized Controlled Trials.

Study (Year)	N (A/V)	Mean year	Sex (Male/ Female)	Intervention	Treatment duration
Ismail (2012)	90 (30/30)	NR	NR	A: 25 mg (1 month) T.D.S	4 months
				50 mg (3 months) T.D.S	
				V: 0.2 mg (1 month) T.D.S	
				0.3 mg (3 months) T.D.S	
Young Lee (2014)	102 (47/55)	A: 58.36 V: 58.73	A: 29/30 V: 33/22	A: Up to 100 mg T.D.S	24 weeks
				V: Up to 0.3 mg T.D.S	
Hitoshi (2014)	81 (22/19)	A: 61.8 V: 66.7	A: 13/9 V: 8/11	A: 300 mg/day	12 weeks
				V: 0.9 mg/day	
Apichati (2002)	30 (30/30)	NR	NR	A: 100 mg T.D.S	8 weeks
				V: 0.2 mg T.D.S	
Watanabe (2004)	20 (10/10)	A: 56.2 V: 54.2	A: 5/5 V: 4/6	A: 300 mg T.D.S	4 weeks
				V: 0.9 mg T.D.S	
Notes: A: Acarbose; V: Voglibose; NR: Not Report; T.D.S: Three Times One Day					

Table 1: Characteristics of each included study.

Study (year)	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Ismail (2012)	Low	Unclear	High	High	Low	Low	Unclear
Young Lee (2014)	Unclear	Unclear	Unclear	Unclear	High	Low	Low
Hitoshi (2014)	Low	Unclear	Unclear	Unclear	Unclear	Low	Low
Apichati (2002)	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Watanabe (2004)	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Notes: Low: Low risk of bias; High: High risk of bias; Unclear: Unclear risk of bias							

Table 2: Risk of bias summary.

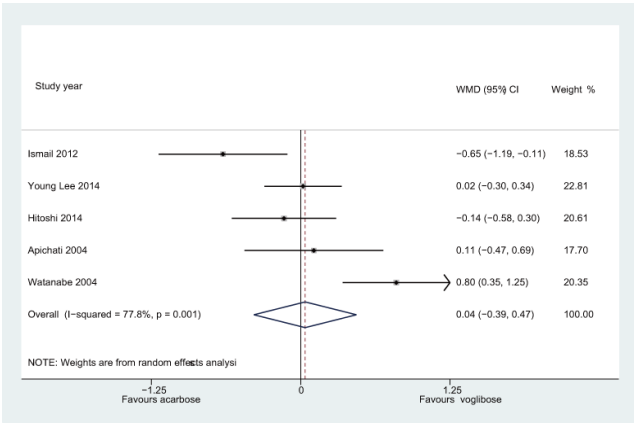

Figure 2: Weighted mean differences with 95% confidence interval in HbA1c between acarbose group and voglibose group.

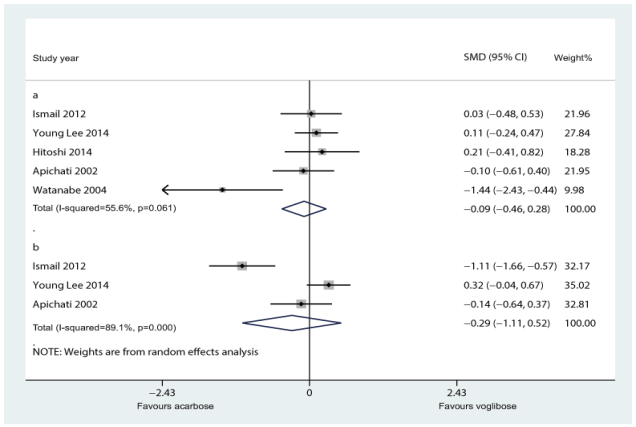

Figure 3: Standardised mean differences with 95% confidence interval in glycemic control parameters between acarbose group and voglibose group. **a:** FBG; **b:** Postprandial blood glucose.

Outcomes

HbA_{1c}: No significant difference was found on change of HbA_{1c} 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 (SWM -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 (SWM -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).

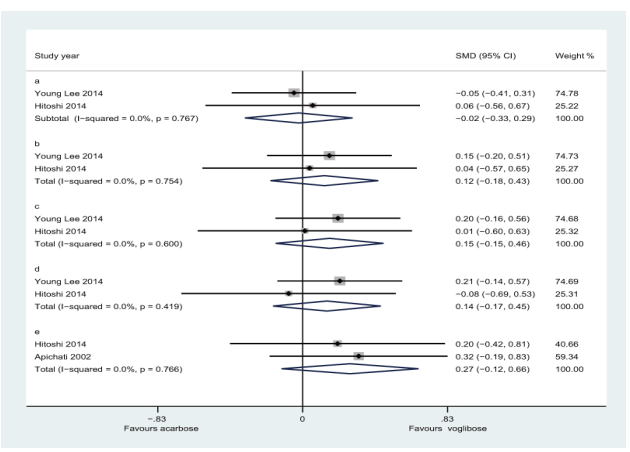

Figure 4: Standardised mean differences with 95% confidence confidence interval in glycemic control parameters between acarbose group and voglibose group. **a:** Triglycerides; **b:** Total cholesterol; **c:** LDL; **d:** HDL; **e:** Postprandial serum insulin.

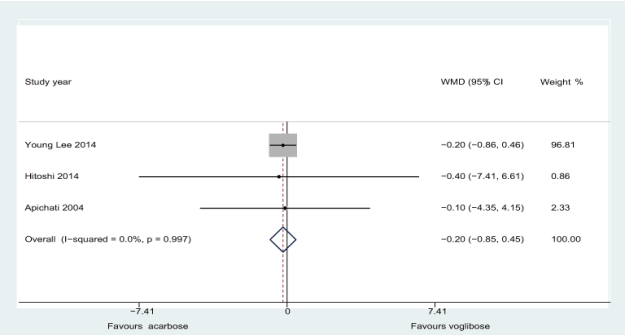

Figure 5: Weighted mean differences with 95% confidence interval in body weight between acarbose group and voglibose group.

Outcomes	Summery statistics	95% CI	I²
HbA_{1c}	WMD 0.04	-0.39 to 0.47	77.8%
FBG	SWM -0.09	-0.46 to 0.28	55.6%
Postprandial blood glucose	SWM -0.29	-1.11 to 0.52	89.1%
Triglycerides	SWM -0.02	-0.33 to 0.29	0.0%
Total cholesterol	SWM 0.12	-0.18 to 0.43	0.0%
LDL	SWM 0.15	-0.15 to 0.46	0.0%
HDL	SWM 0.14	-0.17 to 0.45	0.0%
Postprandial serum insulin	SWM 0.27	-0.12 to 0.66	0.0%
Body weight	SWM 0.20	-0.85 to 0.45	0.0%

Notes: HbA_{1c}: Glycosylated Hemoglobin; FBG: Fasting Blood Glucose; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; WMD: Weighted Mean Differences; SWM: Standardized Mean Differences; CI: Confidence Interval

Table 3: Results of meta-analysis summary.

Hypoglycemia: There was just one study [11] reported hypoglycemia event. Thus, it was impossible to compare.

Hyperglycemia: No any included studies reported hyperglycemia event. Thus, no relevant data were analysed.

Adverse events: Most included studies [11,20-22] reported adverse events. However, these adverse events were various and there were no appropriate data to perform meta-analysis. Dr. Teli Shaikh Emaran Shaikh Ismail et al. [20] reported the following adverse events in acarbose group: nausea (1 patient), flatulence (6 patients), diarrhea (2 patients), abdominal pain (1 patient); in voglibose group, adverse event was flatulence (2 patients). Mi Young Lee et al. [11] reported that "a total of 137 adverse events in 44/60 (73.3%) subjects in acarbose group and 143 adverse events in 42/62 (67.7%) subjects in voglibose group", including gastrointestinal disorders, general disorders, metabolic disorders, eye disorders, nervous system disorders, respiratory disorders, skin disorders. Hitoshi Sugihara et al. [21] showed that the incidences of persistent borborygmus, abdominal distension and flatulence in acarbose group were higher than voglibose group. Apichati Vichayanrat et al. [22] showed that incidences of adverse events in acarbose group were significantly higher than voglibose group ($P<0.05$). From the above, adverse events in acarbose group were higher than voglibose group.

All results of meta-analysis were presented in Table 3.

Sensitivity analysis: For all pooled results, our result of sensitivity analysis showed that there was not a single study may influence the whole results.

Subgroup analysis: Our systematic review only included 5 studies and a small number of studies were difficult to be divided into a subgroup by race or dose. Thus, we did not perform subgroup analysis.

Meta-regression analysis: We could not find the sources of heterogeneity by meta- regression analysis.

Publication bias: Funnel plot always was used to exam publication bias for large sample size and it is difficult to exam publication bias for small sample size. Our systematic review only included 5 studies, so we did not exam publication bias.

Discussion

The goal of this systematic review was to compare the efficacy and safety of acarbose and voglibose for the treatment of patients with type 2 diabetes. We included in a total of five randomised trials and drew a conclusion: acarbose could not gain a better efficacy in blood sugar control and body weight compared with voglibose; in contrast, voglibose is safer than acarbose.

In terms of efficacy, there are no differences between acarbose and voglibose; in terms of safety, voglibose is safer than acarbose. Thus, between the choice of acarbose and voglibose should be recommended for the treatment of patients with type 2 diabetes. This recommendation has some limitations. Firstly, some included trials reported the short-term efficacy and safety of acarbose and voglibose for the treatment of patients with type 2 diabetes. What is more, the patients with type 2 diabetes were different in age. Dosage of administration and administration route were also different. We did not perform subgroup analysis due to a small number of included trials. Significant heterogeneity was among the included trials, but we could not find it sources through sensitivity analysis and meta-regression. Instead, we selected random medol.

To our knowledge, a previous systematic review [14] had reported the effects of monotherapy with alpha-glucosidase inhibitors in patients with type 2 diabetes, but they only did a comparison of acarbose and miglitol versus placebo and sulfonylurea. The efficacy and safety of acarbose compared with voglibose in patients with type 2 diabetes have not been systematically summarized before. Our systematic review is the first one which systematically summarized the efficacy and safety of acarbose compared with voglibose in patients with type 2 diabetes.

Our systematic review had several limitations. We only included in five published studies, which was lack of credibility. In addition, 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 [11,20-23] 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 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 blinding of outcome assessment. 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

1. Krentz AJ, Bailey CJ (2005) Oral antidiabetic agents: Current role in type 2 diabetes mellitus. Drugs 65: 385-411.
2. Butler AE, Janson J, Bonner-Weir S, Ritzel R, Rizza RA, et al. (2003) β-cell deficit and increased β-cell apoptosis in humans with type 2 diabetes. Diabetes 52: 102-110.
3. Rydén L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, et al. (2009) Guidelines on diabetes, pre-diabetes, and cardiovascular diseases. Euro Heart J 9: C3-C74.
4. Shaw JE, Sicree RA, Zimmet PZ (2010) Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes res cln pract 87: 4-14.
5. Schmidt DD, Frommer W, Junge B, Muller L, Wingender W, et al. (1977) alpha-Glucosidase inhibitors. New complex oligosaccharides of microbial origin. Die Naturwissenschaften 64: 535-536.
6. Caspary WF, Graf S (1979) Inhibition of human intestinal alpha-glucosidehydrolases by a new complex oligosaccharide. Res Exp Med (Berl) 175: 1-6.
7. Puls W, Keup U, Krause HP, Thomas G, Hoffmeister F, et al. (1977) Glucosidase inhibition. A new approach to the treatment of diabetes, obesity, and hyperlipoproteinaemia. Die Naturwissenschaften 64(10): 536-537.
8. Coniff R, Krol A (1997) Acarbose: A review of US clinical experience. Clin Ther 19: 16-26.
9. Scheen AJ (1997) Drug treatment of non-insulin-dependent diabetes mellitus in the 1990s. Achievements and future developments. Drugs 54: 355-368.
10. Fujisawa T, Ikegami H, Inoue K, Kawabata Y, Ogihara T (2005) Effect of two alpha-glucosidase inhibitors, voglibose and acarbose, on postprandial hyperglycemia correlates with subjective abdominal symptoms. Metabolism 54:387-390.
11. Lee MY, Choi DS, Lee MK, Lee HW, Park TS, et al. (2014) Comparison of acarbose and voglibose in diabetes patients who are inadequately controlled with basal insulin treatment: Randomized, parallel, open-label, active-controlled study. J Korean Med Sci 29: 90-97.
12. Van De Laar FA, Lucassen PLBJ, Akkermans RP, Van De Lisdonk EH, De Grauw WJC (2006) Alpha-glucosidase inhibitors for people with impaired glucose tolerance or impaired fasting blood glucose. Cochrane Database Syst Rev 2006: CD005061.
13. Cai X, Yang W, Zhou L, Zhang S, Han X, et al. (2015) Comparisons of the efficacy of glucose control, lipid profile, and β-cell function between DPP-4 inhibitors and AGI treatment in type 2 diabetes patients: a meta-analysis. Endocrine 50: 590-597.
14. Van de Laar FA, Lucassen PL, Akkermans RP, Van de Lisdonk EH, Rutten GE, et al. (2005) Alpha-glucosidase inhibitors for patients with type 2 diabetes: results from a Cochrane systematic review and meta-analysis. Diabetes care 28: 154-163.
15. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 339: b2535.
16. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, et al. (2011) The cochrane collaboration's tool for assessing risk of bias in randomised trials. BMJ 343:d5928.
17. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21: 1539-1558.
18. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. Control Clin Trials 7: 177-188.
19. Mantel N, Haenszel W (1959) Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 22: 719-748.
20. Ismail TSES, Deshmukh SA (2012) Comparative study of effect of alpha glucosidase inhibitors-miglitol, acarbose and voglibose on postprandial hyperglycemia and glycosylated hemoglobin in type-2 diabetes mellitus. International Journal of Pharma and Bio Sciences 3: 337-343.
21. Sugihara H, Nagao M, Harada T, Nakajima Y, Tanimura-Inagaki K, et al. (2014) Comparison of three alpha-glucosidase inhibitors for glycemic control and bodyweight reduction in Japanese patients with obese type 2 diabetes. J Diabetes Investig 5: 206-212.
22. Vichayanrat A, Ploybutr S, Tunlakit M, Watanakejorn P (2002) Efficacy and safety of voglibose in comparison with acarbose in type 2 diabetic patients. Diabetes Res Clin Pract 55: 99-103.
23. Watanabe K, Uchino H, Ohmura C, Tanaka Y, Onuma T, et al. (2014) Different effects of two alpha-glucosidase inhibitors, acarbose and voglibose, on serum 1,5-anhydroglucitol (1,5AG) level. J Diabetes Complications 18: 183-186.