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Meta-analyses

Effect of niacin on lipids and glucose in patients with type 2 diabetes: A meta-analysis of randomized, controlled clinical trials

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SUMMARY

Background & aims: This study aims to conduct a meta-analysis to evaluate the effects of niacin on serum lipids and glucose in patients with type 2 diabetes mellitus (T2DM).

Methods: A comprehensive literature search in Medline, Scopus, AMED, Cochrane and Clinical trial registry databases was performed to identify randomized controlled trials investigating the effect of niacin on serum HDL cholesterol (HDL-c), LDL cholesterol (LDL-c), triglycerides (TG) and fasting plasma glucose (FPG). Pooled effects were measured by weighted mean difference (WMD) using fixed-effects or random-effects models. Quality assessment, and subgroup, meta-regression and sensitivity analyses were conducted using standard methods. Inter-study heterogeneity was assessed and quantified.

Results: The estimated pooled mean changes (95% confidence interval) with niacin were 0.27 (95% CI: 0.24 to 0.30; $P < 0.001$) mmol/L for HDL-c, −0.250 (95% CI: −0.47 to −0.03; $P < 0.05$) mmol/L for LDL-c and −0.39 (95% CI: −0.43 to −0.34; $P < 0.001$) mmol/L for TG compared with controls. There was a significant heterogeneity for the impact of niacin on LDL-c and FPG. Subgroup analyses revealed a significant increase in FPG 0.085 (95% CI: 0.029 to 0.141; $P < 0.05$) mmol/L compared with controls in patients with long term treatment. Our analysis also showed the absence of publication bias and any dose-response relations between niacin and effect size.

Conclusions: Analysis of the results showed that niacin alone or in combination significantly improved lipid abnormalities in patients with TDM, but requires monitoring of glucose in long term treatment.

1. Introduction

Diabetes mellitus is one of the most important public health burdens. Its prevalence has reached epidemic proportions worldwide [1]. It is well known that patients with type 2 diabetes mellitus (T2DM) are more prone to be dyslipidemic than the general population. Diabetic dyslipidemia plays a leading role in the progression of atherosclerosis. Lipid profile is a vital essential determinant of cardiovascular risk in type 2 diabetes. At present, HDL cholesterol (HDL-c) has been an important target for intervention efforts in the clinical management of dyslipidemia. Statin therapy is the cornerstone of treatment of dyslipidemia in diabetes mellitus. However, despite reaching the low-density lipoprotein (LDL) cholesterol target, only modest effects are exerted on triglyceride (TG) and HDL-c, and patients often have residual cardiovascular disease risk. This residual risk suggests that additional therapeutic interventions may be needed to reduce cardiovascular disease risk further [2].

Niacin, is an essential B-complex vitamin (vitamin B3). In pharmacological doses, it is a potent agent for raising HDL-c and lowering plasma TG with moderate effects on LDL cholesterol [3,4]. Niacin has been shown to regress coronary atherosclerosis [5] and reduce the rate of coronary mortal [6]. To address residual risk in the dyslipidemic diabetic population, clinical trials have demonstrated that the combination of statin–niacin may offer potent effects in lowering plasma TG and LDL-c and increasing HDL-c [7]. Niacin, however, has clinically insignificant negative impact on glycaemia: it can cause a modest, transient and reversible increase in fasting plasma glucose (FPG) [8]. There is a reluctance to use it among patients with T2DM.

To date, a substantial number of randomised control trials (RCTs) have reported that niacin affects lipid profiles and FPG in subjects with T2DM [9–15]. However, the sample sizes of these studies are relatively small and the conclusions are inconsistent. A meta-analysis of published clinical trials can offer a more accurate

Abbreviations: CI, confidence interval; FPG, fasting plasma glucose; HDL-c, HDL cholesterol; LDL-c, LDL cholesterol; RCT, randomised control trial; T2DM, type 2 diabetes mellitus; TG, triglycerides; WMD, weighted mean difference.

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and precise estimate of the overall effect of niacin on lipid levels and FPG. Therefore, we conducted a meta-analysis of all published randomized controlled trials that investigated the effects of niacin on blood lipids and FPG in TD2M.

2. Methods

2.1. Search strategy

A comprehensive and systematic literature search for articles was performed in the following data bases from inception through May 2014: PubMed, Web of Sciences, Embase and the Cochrane Library databases for intervention studies. Relevant studies were identified using the combination of the following search terms: (niacin or nicotinic acid or niaspan or vitamin B3) AND diabetes. To ensure a comprehensive identification of appropriate trials, we conducted a supplemental manual review of citations from all eligible studies and relevant systematic analyses [16–18]. The search was limited to clinical trials. Additionally, we evaluated the electronic databases Clinical Trials.gov and screened the references of the included studies for further relevant publications. The results of the systematic literature search are summarized in Fig. 1.

2.2. Study selection

Full articles were obtained if they met the following inclusion criteria: 1) published in English and on humans; 3) control groups included; 4) the research participants should be Type 2 diabetic patients. 4) weighted mean difference (WMD) and its 95% confidence interval (CI) could be calculated from the raw data extracted from the original literature. Outcome measures were: primary outcomes assessed were the changes from base-line in mean and HDL-c, LDL-c, TG and FPG levels.

2.3. Data extraction

The search, data extraction, and quality assessment were completed independently by 2 reviewers (YD and YWL) according to inclusion criteria. The following information was obtained from each trial: author identification, year of publication, study design, sample size, duration, niacin dose and statin utilized, and effect on lipid parameters (HDL-c, LDL-c, and TG) and FPG. Disagreements between the two reviewers regarding the eligibility of studies identified for inclusion were resolved by discussion.

2.4. Assessment of risk of bias

This data collection and assessment were performed independently by two investigators, wherein any disagreements were resolved by discussion. Risk of bias was assessed as described in the Cochrane handbook: by recording the method of random sequence generation, the method of allocation concealment, whether blinding was implemented, whether incomplete outcome data was reported, whether an intention-to-treat analysis was conducted, and whether there was evidence of selective reporting of outcomes.

2.5. Data synthesis and analysis

The main outcomes included in this meta-analysis were serum concentrations of HDL-c, LDL-c, TG and FPG in the studies included.

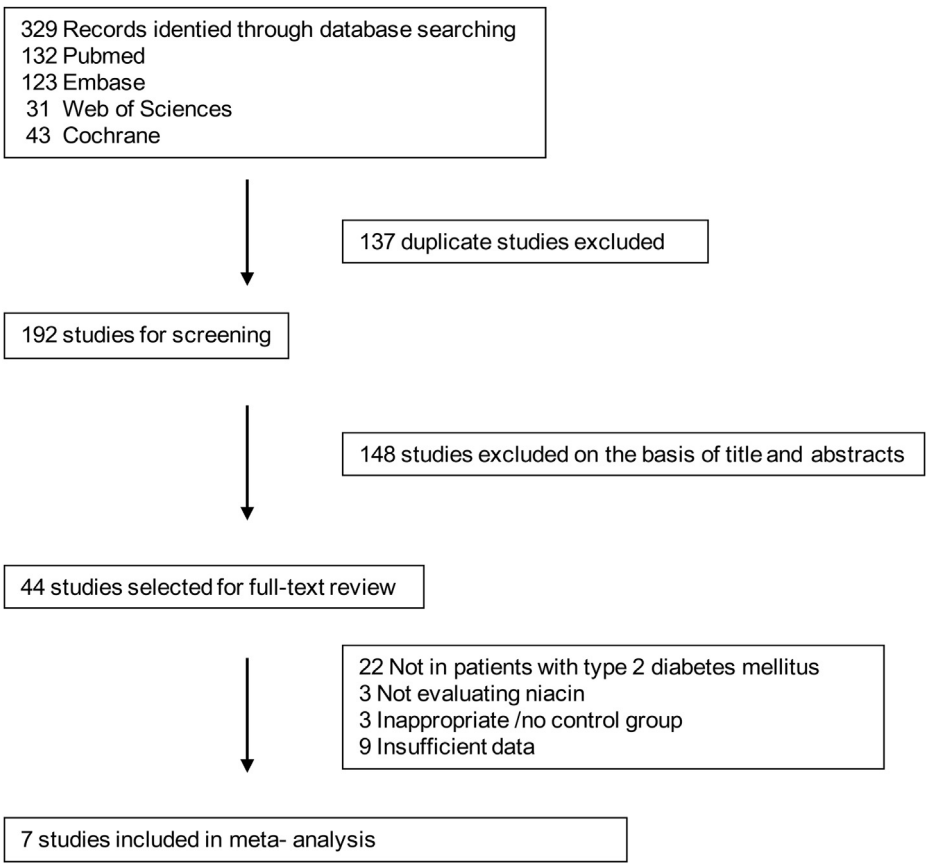

Fig. 1. Trial flow summary.

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