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EFFECT OF BLOOD 25-HYDROXY VITAMIN D [25(OH)] LEVELS ON PREDIABETES PATIENTS : A META-ANALYSIS OF RANDOMISED CONTROL TRIALS

Biochemistry

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ABSTRACT

Background: Emerging evidence suggests that vitamin D may play a role in the development of diabetes. This meta-analysis was done to evaluate effect of Vitamin D on blood glucose level among pre-diabetes patients.

Objective: To evaluate the effect of vitamin D on glycaemic control in Prediabetes in different RCT performed.

Methods: A literature search was conducted of MEDLINE, the Cochrane Library, (CINAHL), Scopus, Web of Science through the reference lists of relevant articles until end of November 2017. Studies were included if they were RCT of vitamin D or vitamin D analogues in pre-diabetes. Treatment effect was estimated according to mean difference in the changes 2-h oral glucose tolerance test plasma glucose, fasting plasma glucose and HbA1C between vitamin D and control groups.

Results: A total of 10 randomized controlled trials were included. Vitamin D did not significantly improve 2-h oral glucose tolerance test plasma glucose: the mean differences were - 0.06 (95% CI -0.36 to 0.24) and -0.23 mmol/l (95% CI -0.65 to 0.19), respectively.

Conclusions: Low beneficial effect of Vitamin D improving the blood glucose levels in prediabetes was identified.

KEYWORDS

25-hydroxy vitamin D, Prediabetes, Systematic review, Meta-analysis

Introduction

Prediabetes is defined as impaired fasting glucose (IFG) and/ or impaired glucose tolerance (IGT). People with prediabetes are at relatively high risk of developing diabetes [1,2]. The pathogenesis of prediabetes involves insulin resistance and defective beta cell function for secreting insulin [3]. Emerging evidence suggests that vitamin D may play a role in the development of diabetes. An indicator of vitamin D status, 25-hydroxyvitamin D [25(OH)D], has been reported to be inversely related to the risk of diabetes [4]. The progression to diabetes in subjects with low 25 (OH)D level was greater than in those who had a high 25 (OH)D level [4]. In addition, 25(OH)D level also had an inverse correlation with insulin resistance among individuals with prediabetes [4]. Low vitamin D levels have, therefore, been postulated to be associated with insulin resistance, resulting in diabetes. Several randomized controlled trials have been conducted to evaluate the effects of vitamin D supplementation in prediabetes, but the results are conflicting. A recent meta- analysis reported a negative effect of vitamin D on insulin resistance and glycaemic outcomes in prediabetes; however, that meta-analysis included a few randomized controlled trials with short duration [5]. The rationale behind conducting this study was to perform a systematic review and meta-analysis in an attempt to delineate the effect of vitamin D supplementation on glycaemic control in prediabetes.

Research Designs and Methodology

Literature search - Reports of randomized controlled trials of vitamin D or vitamin D analogues and glycaemic control in prediabetes were identified through a systematic literature search using the electronic databases MEDLINE, the Cochrane Library, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, Web of Science. The following Medical Subject Heading terms were used: vitamin D; glucose intolerance; prediabetic state; and hyperglycaemia. This was followed by search terms; [vitamin D or vitamin D2 or vitamin D3 or cholecalciferol or ergocalciferol or alfacalcidol or doxercalciferol or calcitriol or vitamin D analogues] AND [prediabetes or impaired glucose tolerance or impaired fasting glucose or impaired plasma glucose]. Databases were searched until the end of October 2017 and no language restriction was imposed.

Study Selection- Studies were included in this Meta-analysis if they were randomized controlled trials of vitamin D or vitamin D analogues in prediabetes (IFG and/or IGT, as defined by individual studies) and reported 2-h plasma glucose after an oral glucose tolerance test (OGTT). Studies reporting the effect of vitamin D in subjects with diabetes mellitus, metabolic syndrome, end-stage renal disease, or gestational diabetes were excluded. Citations retrieved as result of literature search (n=3447), articles excluded after review of title and abstract (n=3430). Reports identified for evaluation (n=17) in which non-RCT were (n=4), no control group (n=2), no pre-diabetes(n=1), so studies included for systematic review and meta-analysis are (n=10).

Data abstraction- Data abstracted from individual studies included year of publication, number of patients, dose of vitamin D, control group, BMI, outcome measures and baseline 25(OH)D level.

Data analysis - Our outcomes were categorized into primary and secondary outcomes. Our primary outcome was 2-h OGTT plasma glucose. Secondary outcomes included fasting plasma glucose (FPG) and HbA_{1c} levels. The inverse variance-weighted method was used for the pooling of mean difference and estimation of 95% CI [6]. Data were combined using the fixed-effects model if heterogeneity was non-significant. The random effects model was used if significant heterogeneity was detected at the level of 0.1. The degree of heterogeneity was quantified using the I^2 statistic [6], which is an estimate of percentage of total variation across studies. Publication bias was assessed for the primary outcome using a funnel plot. Review Manager Software (version 5.2.11) was used for analysing data in the form of forest plot only for primary outcome.

Results

Table 1: Characteristics of Included Studies

Study	Duration	N	Vit D group	Control	BMI	Baseline Vit D (nmol/l)
Pittas et al (2014)	3 years	92	45	47	28	76.31
Deboer et (2013)	7 years	384	189	195	25	NA
Jorde et (2013)	1 year	88	50	38	36	57.56
Mitri et (2012)	16 weeks	92	46	46	32	59.18
Harris et (2010)	12 weeks	100	49	51	32	61.12
Iraj etal(2009)	2 months	40	20	20	30	54.45
Davidson et (2009)	1 year	109	56	53	32.5	55.01
Dutta etal(2008)	2 years	125	68	57	26.6	43.34
Oosterweff et al (2007)	16 weeks	130	65	65	32.7	63.24
Solid et al(2007)	1 year	511	256	255	30	59.98

Table 1 shows characteristics of studies included in the present meta-analysis. Overall 10 RCT studies were included from the literature search along with total number of Vit D group and control group along with BMI and baseline Vit D values.

Figure 1: Forest plot for the included studies

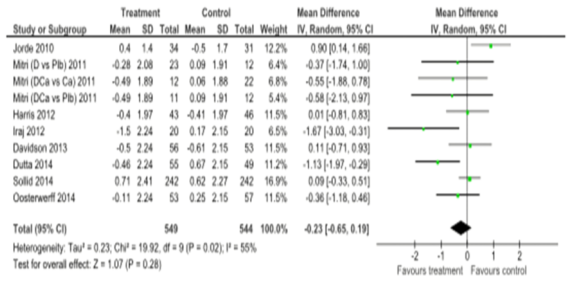

Figure 1 shows Vitamin D supplementation failed to show a significant effect on 2-h plasma glucose after OGTT. The pooled weighted mean difference was -0.23 mmol/l (95% CI - 0.65 to 0.19; Publication bias was not detected [Egger's bias -1.78 (95% CI -4.33 to 0.77); P = 0.15]. Meta-analysis of secondary outcomes -Fasting plasma glucose reduced significantly with vitamin D supplementation (mean difference -0.10 mmol/l (95% CI - 0.18 to -0.03); P = 0.006. People with prediabetes who received vitamin D supplementation had a lower HbA_{1c} level [mean difference -1 mmol/ mol(95% CI -2 to 0); P = 0.008] compared with control subjects.

Discussion

The results of the present meta-analysis failed to show a positive effect of vitamin D supplementation on 2-h plasma glucose after OGTT; it should be noted that the subjects included in the meta-analysis had a high BMI. Seven studies reported mean baseline BMI ≥ 30 kg/m^2 [9-12,15], while two studies reported BMI values of 25– 29.9 kg/m^2 [7,14]. The results of the meta-analysis are consistent with a previous meta-analysis [16]; however, that HbA_{1c} analysis included only three studies [10,11,13] with a small number of subjects and two studies had a short follow-up duration (only 3 and 4 months) [10,11]. The present analysis included an additional four, more recent, studies. Among these, three studies reported follow-up periods of 1 or 2.5 years [14,15,16]. A previous analysis suggested that a short duration of vitamin D treatment may be one of the factors explaining the lack of beneficial effect on glycaemic control [16]. The optimum vitamin D levels for diabetes prevention remain unknown. Lower baseline 25(OH)D concentration might be associated with improved 2-h OGTT plasma glucose in subjects with baseline 25(OH)D < 50 nmol/l. The effect of vitamin D supplementation based on baseline 25(OH)D was therefore inconclusive. The American Diabetes Association position statement of nutrition therapy recommendations for the management of adults with diabetes in 2013 did not recommend the routine use of vitamin D to improve glycaemic control in people with diabetes because of insufficient evidence, which has been proven to prevent the progression of prediabetes to diabetes by 58 and 31%, respectively [16].

Conclusion

The available evidence suggests there is low beneficial effect of vitamin D in improving 2-h OGTT plasma glucose level. The effects of lifestyle modification and metformin use were stronger than the effect produced by vitamin D intervention; therefore, the magnitude of the effect of vitamin D in itself may not be large enough to prevent diabetes.

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Conflict of interest: Nil

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