

# VU Research Portal

## The role of vitamin D in glycaemic control

Krul-Poel, Y.H.M.

2017

### **document version**

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

### **citation for published version (APA)**

Krul-Poel, Y. H. M. (2017). *The role of vitamin D in glycaemic control*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

### **General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

### **Take down policy**

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

### **E-mail address:**

[vuresearchportal.ub@vu.nl](mailto:vuresearchportal.ub@vu.nl)

## SUMMARY

This thesis highlights the role of vitamin D in glycaemic control in various populations. The aim of this thesis is to explore the role of vitamin D in patients with gestational diabetes mellitus (GDM), polycystic ovary syndrome (PCOS) and type 2 diabetes mellitus.

### Part I

Chapter 1 provides a systematic literature review and meta-analysis of the association between maternal vitamin D status and the onset of gestational diabetes mellitus (GDM). Seven observational studies were included, in which overall a significant inverse association was found between maternal vitamin D status and the incidence of GDM. Serum 25-hydroxyvitamin D (25(OH)D) was significantly lower in patients with GDM compared to normal glucose tolerance.

### Part II

The second part of this thesis focuses on the association between vitamin D status and metabolic disturbances in women with polycystic ovary syndrome (PCOS). This part is divided into two chapters. First, in Chapter 2 a summary of the literature is provided in a systematic literature review about the association between vitamin D and metabolic disturbances in women suffering from polycystic ovary syndrome (PCOS). Current evidence including 29 observational studies suggests an inverse association between vitamin D status and metabolic disturbances in PCOS. However, significance disappeared in PCOS women after correcting the results for BMI.

Second, in Chapter 3 the association between vitamin D and metabolic disturbances was explored in women with PCOS (Rotterdam PCOS cohort) compared to controls. A total of 639 PCOS women and 449 control women were included. The results demonstrated a significant lower serum 25(OH)D in PCOS versus control women (serum 25(OH)D 49.0 versus 64.5 nmol/l, respectively). As expected from the earlier systematic review a significant higher insulin resistance, measured using the homeostasis model assessment (HOMA-IR), was found in the lowest vitamin D group compared to PCOS women in the highest vitamin D group. Additionally, a significant adjusted association was seen between serum 25(OH)D and HDL-cholesterol and apolipoprotein A1 in PCOS women. Large randomised controlled trials are necessary to explore the causality of this linkage.

### Part III

This part of the thesis presents the data of our randomised placebo-controlled clinical trial in which 275 patients with type 2 diabetes without insulin treatment were randomised to either cholecalciferol 50,000 IU/month or placebo during six months. Chapter 4 presents the study protocol.

In Chapter 5 the primary outcome, the effect of vitamin D supplementation on glycaemic control after six months, is described. Mean baseline 25(OH)D was 59.1 versus 59.8 nmol/l in the vitamin D group versus the placebo group, respectively. Mean baseline HbA1c was 6.8% (51 mmol/mol) in both groups. After six months of vitamin D supplementation no improvement of HbA1c, and other indicators of glycaemic control, was found in the intervention group compared to placebo. Sub-group analysis revealed a significant decrease of HbA1c among 19 patients with a baseline serum 25(OH)D < 30 nmol/l.

The next two chapters describe the association between vitamin D status and health related qua-

lity of life in 241 patients with type 2 diabetes. In Chapter 6 cross-sectional analyses showed no association between vitamin D status and health related quality of life. In Chapter 7 longitudinal analyses were performed after six months of vitamin D supplementation versus placebo. Totally, 187 patients completed baseline and follow-up questionnaire (SF-36) after six months of intervention. No improvement of health related quality of life was seen after six months of vitamin D supplementation compared to placebo, despite an adequate rise in serum 25(OH)D from 58.5 to 106.0 nmol/l. In Chapter 8 the association between vitamin D status and advanced glycation endproducts (AGEs) is examined. AGEs were measured using skin autofluorescence. They are suggested to be one of the major agents in the pathogenesis and progression of diabetes related cardiovascular complications. 245 patients with type 2 diabetes were enrolled in this study. Vitamin D status was independently associated with skin autofluorescence. After six months of intervention no effect was seen on the amount of skin AGEs. Finally, Chapter 9 provides a systematic review and meta-analysis of all randomised clinical trials examining the effect of vitamin D supplementation on glycaemic control in patients with type 2 diabetes. Combining these studies no significant effect in change of HbA1c, fasting glucose or HO-MA-IR, was seen after vitamin D intervention compared to placebo. Subgroup analysis, including only studies with a mean baseline HbA1c  $\geq$  8.0% (64 mmol/mol), revealed a significant effect on fasting glucose. In conclusion, currently insufficient evidence exists to support vitamin D supplementation in patients with type 2 diabetes with the aim to improve glycaemic control.