

Vitamin D and diabetes

Improvement of glycemic control with vitamin D3 repletion

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Regular doses of vitamin D (VTD)—about 2000 IU/d—early in life have been shown to reduce the risk of developing type 1 diabetes (up to an 80% reduction projected over the next 30 years).¹ Vitamin D treatment has also improved glycemic control and insulin sensitivity in people with type 1 diabetes, people with type 2 diabetes, and normal individuals.²⁻⁴ Low VTD levels in elderly men have been associated with insulinemia and glucose intolerance.⁵ Low VTD levels in general have been associated with insulin resistance and obesity.⁶ Likewise, β -cell dysfunction and insulin resistance are also associated with low VTD levels.³ The following case reports demonstrate a substantial improvement in hemoglobin A_{1c} (HbA_{1c}) levels with the reversal of VTD deficiency. Changes in VTD levels and HbA_{1c} levels are summarized in **Table 1**.

Case 1

A 63-year-old woman of African descent had a 25-hydroxyvitamin D (25[OH]D) level of 25 nmol/L, which was determined by liquid chromatography mass spectrometry. She had been diagnosed with diabetes 5 years earlier. Her father had diabetes and had been taking insulin, and she had 2 older diabetic siblings who were both taking insulin as well. A younger sibling did not have diabetes.

Her care included regular exercise, a modified diet, and medication: 500 mg of metformin 3 times daily; 2 mg of repaglinide 3 times daily, which she had been using for the past 4 years; and 4 mg of rosiglitazone daily, which had been added in the past year. Her HbA_{1c} level was 8.4% after using rosiglitazone for several months. It was at that time she was found to be deficient in 25(OH)D, with a level of 25 nmol/L.

Repletion of her VTD levels began with 2000 IU of vitamin D3 daily, which was later increased to 3000 IU.

(This increase was made after reading that after a year of supplementation with 2000 IU of VTD, only 60% of African Americans return to normal 25[OH]D levels.) After using VTD for a little more than 6 months, a repeat HbA_{1c} test was done; HbA_{1c} levels had fallen to 7.4% and her VTD levels had risen to 140 nmol/L. A review of her diabetic testing showed improvement in her average pre- and post-meal sugar levels. The patient reported more hypoglycemic events during the 6 months she used VTD, and so she reduced her metformin dosage from 3 times daily to twice daily. She also admitted to not exercising as faithfully as before. Her weight, though, remained stable.

The patient had been previously warned that if there was no improvement in her diabetic status, we would need to consider insulin to manage her diabetes. She fully expected to hear this news when reviewing her diabetes with me and the primary care network diabetes nurse, and was pleasantly surprised that this was not the case. She has been encouraged to continue with the same medications, including VTD, and to return to her previous level of exercise.

Case 2

A 71-year-old white female patient was diagnosed with diabetes in 1988 and was prescribed medication. She lost 40 lbs within several months and was able to discontinue using the medication for several years. In 1996, she began taking 500 mg of metformin 4 times daily and 80 mg of gliclazide twice daily. Four-mg doses of rosiglitazone twice daily were added 3 years ago. She was on a diabetic diet and was strongly encouraged to exercise. She was found to have a 25(OH)D level of 34 nmol/L—by liquid chromatography mass spectrometry—which would be considered a severe insufficiency but not a deficiency by strictest criteria. Her HbA_{1c} level was 13.3% and she was told that she should be on insulin; however, she refused this intervention. Her VTD levels were

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Cet article a fait l'objet d'une revision par des pairs.

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Table 1. Changes in VTD levels and HbA_{1c} levels for Case 1 and Case 2 patients

PATIENT	STARTING VTD LEVEL (nmol/L)	STARTING HbA _{1c} LEVEL (%)	VTD REPLETION DOSE/D	FINAL VTD LEVEL (nmol/L)	FINAL HbA _{1c} LEVEL (%)	DROP IN HbA _{1c} LEVEL
Case 1	25	8.4	2000 IU for 2 mo; 3000 IU for 9 mo	140	7.4	1.0
Case 2	34	13.3	2000 IU for 9 mo	107	12.2	1.1

HbA_{1c}—hemoglobin A_{1c}, VTD—Vitamin D.

replenished with 2000 IU of vitamin D3 daily. Nine months later, her 25(OH)D level was 107 nmol/L. She did not change her medication, lifestyle, weight, or eating habits over the following 2 years. Her HbA_{1c} level on retesting was 12.2%. She was told that the best course of management for her diabetes would still be insulin, which she again refused.

Discussion

PubMed was searched for articles published in the past 26 years using the terms *diabetes*, *insulin resistance*, and *vitamin D deficiency*. There are many risk factors for VTD insufficiency or deficiency, including lack of sun exposure, inadequate dietary intake, darker skin colour, age, obesity, and use of various medications.

There is evidence that VTD is important in the prevention of islet cell death and might be useful to improve the survival of islet cell grafts.⁸ Vitamin D is required for and improves the production of insulin, and also improves insulin sensitivity.^{3,9} Studies have shown that insulin sensitivity is improved by as much as 60% when levels of VTD are increased from 25 to 75 nmol/L. This is better than troglitazone (54%) or metformin (13%).¹⁰ (These patients had been followed for less than a year and it is unknown if the drop in HbA_{1c} has been sustained or improved even further.) Recent studies suggested that supplementation with 500 mg of calcium and 700 IU of VTD prevented a rise in fasting glucose and slowed the progression of insulin resistance over a 3-year period, compared with the use of a placebo, in patients with impaired fasting glucose.¹¹

One study reported that glycemic control became worse in 3 Asian patients following VTD supplementation¹²; however, these patients received vitamin D2 and not vitamin D3. Vitamin D2 has several unknown metabolites with unknown effects. There is also evidence that there is increased 24-hydroxylase activity in Asian Indians, which inactivates the hormone 1,25-dihydroxyvitamin D.¹³ Certain VTD receptor genotypes are big determinants of insulin secretory capacity in various ethnic groups.^{14,15} It is apparent that not all patients will have the same improvement in glycemic control with VTD supplementation; much still needs to be learned.

The patients in this report were repleted with vitamin D3 into the normal range, a level usually found in people with adequate sun exposure. Toxicity has not been reported with levels lower than 220 nmol/L, and using up to 4000 IU of vitamin D3 to reverse states of deficiency is safe.¹⁶

Conclusion

These cases support information that is already known about VTD and its effect on the islet cell. As discussed above, this might be true only for vitamin D3 and not vitamin D2, although vitamin D2 has been shown to improve bone health. Vitamin D insufficiency

EDITOR'S KEY POINTS

- Vitamin D (VTD) deficiency has been shown to be associated with glucose intolerance, insulinemia, insulin resistance, and obesity in some groups. Studies have shown that insulin sensitivity improves with repletion of VTD stores.
- This case report describes 2 cases in which glycemic control improved with repletion of VTD stores using oral vitamin D3 in patients with VTD deficiency.
- Well-designed clinical trials are needed to further study the relationship between repletion of VTD stores and clinical outcomes in patients with diabetes.

POINTS DE REPÈRE DU RÉDACTEUR

- On a démontré qu'une carence en vitamine D (VTD) était associée à une intolérance au glucose, à l'insulinémie, à la résistance à l'insuline et à l'obésité dans certains groupes. Des études ont fait valoir que la sensibilité à l'insuline s'améliore avec le restockage des réserves de VTD.
- Ce rapport de cas décrit deux situations dans lesquelles le restockage des réserves de VTD a amélioré le contrôle glycémique au moyen d'un supplément de vitamine D3 par voie orale chez les patients ayant une carence en VTD.
- Il faut d'autres études cliniques bien conçues pour étudier plus en profondeur la relation entre le restockage des réserves de VTD et les résultats cliniques chez les patients atteints de diabète.

or deficiency is common, and repletion might improve glycemic control early in type 2 diabetes. Diabetes is one of the fastest growing chronic diseases worldwide. Vitamin D3 is inexpensive and readily available. Well-designed clinical studies are required to ascertain if improving 25(OH)D levels from an insufficiency or deficiency to sufficiency improves glycemic control in diabetes. These studies need to be properly designed: a randomized controlled trial with VTD deficiency or insufficiency identified in diabetic patients of various ethnic groups; VTD receptor genotyping; and VTD versus placebo repletion, with no other changes in diabetic management. 

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Competing interests

None declared

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