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Effects of vitamin D on insulin resistance in nursing home residents: an interventional study

Wpływ witaminy D na insulinooporność u pensjonariuszy domu opieki: kliniczne badanie eksperymentalne

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Abstract

Introduction: Insulin resistance is defined as reduction of insulin-stimulated glucose uptake in skeletal muscles and inadequate suppression of the production of endogenous glucose. The aim of this study was to assess the effect of vitamin D intake on insulin resistance in aged patients.
Materials and methods: This interventional study was carried out on residents of Sadeghieh Nursing Home in Iran. The participants were healthy adults aged ≥ 65. For eight weeks, the participants took pills containing 50,000 IU vitamin D_3 per week. Insulin resistance was defined as homeostasis model assessment of insulin resistance (HOMA-IR) > 2.5. We used McNemar's test, Wilcoxon test, chi-square, and Pearson correlation coefficient and SPSS software (v. 12) to analyse the collected data.
Results: The average age of the 76 participants was 78.7 ± 8 years and 52 of the participants were female. Before and after the study, 37 and four participants had vitamin D deficiency, respectively ($p < 0.001$). Impaired fasting plasma glucose (FPG) and insulin resistance was not more prevalent in the participants with vitamin D deficiency. In this study, vitamin D intake had no significant effect on FPG level ($p = 0.9$), but it increased the prevalence of insulin resistance significantly ($p < 0.001$).
Conclusions: In our study, before and after the intervention, vitamin D deficiency had no relationship with FPG level and insulin resistance. Vitamin D intake had no significant effect on FPG level, but it increased the prevalence of insulin resistance significantly. We believe that performing more studies, with a longer timespan and larger sample size, as double-blind clinical trials, is necessary. **(Pol J Endocrinol 2012; 63 (3): 191–195)**

Key words: *insulin resistance, diabetes mellitus type 2, vitamin D*

Streszczenie

Wstęp: Insulinooporność określa się jako zmniejszony insulinozależny wychwyt glukozy w mięśniach szkieletowych i niedostateczną supresję endogennej produkcji glukozy. Celem niniejszego badania była ocena wpływu stosowania witaminy D na insulinooporność u osób w podeszłym wieku.
Materiał i metody: To kliniczne badanie eksperymentalne przeprowadzono u osób przebywających w placówce opiekuńczo-leczniczej *Sadeghieh Nursing Home* w Iranie. Uczestnicy byli zdrowymi osobami dorosłymi w wieku ≥ 65 lat. Przez 8 tygodni podawano im witaminę D_3 w kapsułkach w dawce 50 000 jm./tydzień. Insulinooporność definiowano jako wskaźnik HOMA-IR > 2,5. W ramach analizy statystycznej danych przeprowadzono testy McNemara, Wilcoxona, χ^2 i określono współczynnik korelacji Pearsona, używając programu SPSS (wersja 12).
Wyniki: Średni wiek 76 uczestników badania (52 kobiety) wynosił 78,7 ± 8 lat. Niedobór witaminy D przed badaniem stwierdzono u 37 osób, a w trakcie badania — u 4 osób ($p < 0,001$). Nieprawidłowa glikemia na czczo (FPG, *fasting plasma glucose*) i insulinooporność nie występowały częściej u uczestników badania z niedoborem witaminy D. W niniejszym badaniu przyjmowanie witaminy D nie wpływało istotnie na FPG ($p = 0,9$), jednak powodowało istotne zwiększenie częstości insulinooporności ($p < 0,001$).
Wnioski: W niniejszym badaniu nie wykazano zależności między niedoborem witaminy D przed i w trakcie badania a FPG i insulinoopornością. Suplementacja witaminy D nie wpłynęła istotnie na wartości FPG, jednak spowodowała zwiększenie częstości insulinooporności. Zdaniem autorów konieczne jest przeprowadzenie kolejnych badań metodą podwójnie ślepej próby, o dłuższym okresie obserwacji i o większej liczebności próby. **(Endokrynol Pol 2012; 63 (3): 191–195)**

Słowa kluczowe: *insulinooporność, cukrzyca typu 2, witamina D*

Introduction

Insulin resistance is defined as reduction of insulin-stimulated glucose uptake in skeletal muscles and inadequate suppression of the production of endogenous glucose. These are critical for maintaining normal glucose homeostasis [1]. Genetic and environmental factors implicate insulin resistance aetiology [2]. Insulin resistance plays an important role in the development of type 2 diabetes (T2D) [3–7]. T2D has reached epidemic proportions: worldwide, more than 160 million individuals are diagnosed with this disease [8].

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Insulin secretion is influenced by vitamin D. Vitamin D increases the concentration of intracellular calcium via non-selective voltage-dependent calcium channels and thus influences the secretion of insulin by β-cell [9]. Many studies have suggested that vitamin D deficiency may be one of the factors participating in the development of insulin resistance. The relationship between vitamin D and insulin resistance has been reported in the early stages of chronic kidney disease [10], in a paediatric population at risk of diabetes [11], and in adults without physician-diagnosed diabetes in the United States [12]. But some studies have reported that there was no association between vitamin D and insulin resistance [13–15].

Also, the effect of vitamin D intake on insulin resistance is controversial. For example, vitamin D intake in T2D patients (as fortified yogurt) [16] and among participants with impaired fasting blood glucose (FBG) [17] improved insulin resistance. But vitamin D intake in T2D patients (as sub-therapeutic vitamin D treatment) [18], in Indian patients with moderately controlled T2D [19], and among participants with normal FBG [17], did not improve insulin resistance.

In light of the controversy about the effect of vitamin D intake on insulin resistance, we decided to determine whether vitamin D treatment improves insulin resistance in aged nursing home residents.

Materials and methods

This interventional prospective study was done on residents of Sadeghieh Nursing Home in Isfahan province in Iran. This trial was conducted by Isfahan University of Medical Sciences. The participants were healthy adults aged ≥ 65 who agreed to participate in the study. Exclusion criteria were: diabetes mellitus, consumption of drugs that could change glucose, insulin or vitamin D level, consumption of vitamin D supplements in the two months prior to the study, and occurrence of a severe or acute disease during the study. The participants' diet was unchanged before and throughout the study. Demographic data was collected via a questionnaire. For eight weeks, the participants took pills containing 50,000 IU vitamin D_3 per week. Before and after vitamin D consumption, to evaluate Fasting Plasma Glucose (FPG), insulin, 25-hydroxy vitamin D (25(OH)D), calcium (Ca), phosphorus (P), parathyroid hormone (PT H) and albumin, 10 cc blood samples were gathered from each participant. The samples were collected in the morning in a fasting state. All the samples were gathered by an expert and evaluated in the endocrinology research centre laboratory of Isfahan University of Medical Sciences. Insulin resistance was measured by homeostasis model assessment of insulin resistance (HOMA-IR). HOMA-IR is one of the indices of insulin resistance [2, 7, 20], and one study has reported that HOMA-IR is the best predictor of insulin resistance [20]. HOMA score is calculated using the formula: fasting glucose (mg/dL) ×fasting insulin (μU/mL)/405. Insulin resistance was defined as HOMA-IR > 2.5. Vitamin D deficiency was defined as < 8 ng/mL. 25(OH)D, PTH, and insulin were measured with enzyme-linked immunosorbent assay (ELISA, IDS-iSYS 25-hydroxy vitamin D, Immunodiagnostic Systems, Boldon, UK), immunoradiometric assay (IRMA, Immunotech, Prague, Czech Republic), and enzyme-linked immunosorbent assay (ELISA, Monobind, Lake Forest, CA, USA), respectively. FPG, Ca, P, and albumin were measured with enzymatic methods (Pars azmoon, Iran).

We used McNemar's test, Wilcoxon test, chi-square, and Pearson correlation coefficient to analyse the collected data. p values < 0.05 (two-sided) were regarded as statistically significant. The statistical analyses were done using SPSS software, v. 12.

Results

The average age of the 76 participants was 78.7 ± 8 years (mean ± SD) and 52 participants (68.4%) were female. The participants' ages were between 65 and 100 years. The participants were divided into subgroups according to age: 65–75 (Group A), 75–85 (Group B) and > 85 (Group C). There were 25 participants in Group A of whom 14 (56%) were female. In Group B, there were 28 participants of whom 19 (67%) were female. There were 23 participants in Group C of whom 19 (82%) were female.

Before the study, 37 participants (48.7%) had vitamin D deficiency. After the intervention, the mean 25(OH) D level significantly decreased ($p < 0.001$); it was seen in four participants (5.3%) (Table I). Before and after the intervention, there were no significant differences in vitamin D deficiency between the age groups or between female and male participants.

Before the study, 54 participants (71.1%) had normal FPG (FPG < 100 mM). After the intervention, 55 participants (72.4%) had normal FPG. Before and after the intervention, the mean FPG level was 97.4 ± 35 and 97.9 ± 37.5 mM, respectively, and there was no significant difference between them ($p = 0.9$) (Table II). Before and after the intervention, there were no significant differences in FPG levels between the age groups or between female and male participants.

Before the study, ten participants (13.2%) had insulin resistance. After the intervention, 28 participants (36.8%) had insulin resistance. Before and after the intervention, the mean HOMA-IR level was 1.34 ± 1.39 and 3.72 ± 5.27, respectively, and there was a significant difference between them ($p < 0.001$) (Table III). Before and after the intervention, there was no significant difference between HOMA-IR levels in the age groups.

Table I. *The prevalence of vitamin D deficiency, before and after the intervention, in the age groups*
Tabela I. *Częstość niedoborów witaminy D przed i po terapii w poszczególnych grupach wiekowych*

Age group	25(OH)D level before the intervention [ng/mL]		25(OH)D level after the intervention [ng/mL]	
	Normal	Deficient	Normal	Deficient
65–75 years	11 (44%)	14 (56%)	24 (96%)	1 (4%)
75–85 years	16 (57.1%)	12 (42.9%)	27 (96.4%)	1 (3.6%)
> 85 years	12 (52.2%)	11 (47.8%)	21 (91.3%)	2 (8.7%)
Total	39 (51.3%)	37 (48.7%)	72 (94.7%)	4 (5.3%)

Vitamin D deficiency was defined as < 8 ng/mL

Table II. *The FPG level, before and after the intervention, in the age groups*
Tabela II. *Wartości FPG przed i po terapii w poszczególnych grupach wiekowych*

Age group	FPG level before the intervention [mM]		FPG level after the intervention [mM]	
	Normal FPG	Impaired FPG	Normal FPG	Impaired FPG
65–75 years	18 (72%)	7 (28%)	18 (72%)	7 (28%)
75–85 years	20 (71.4%)	8 (28.6%)	21 (75%)	7 (25%)
> 85 years	16 (69.6%)	7 (30.4%)	16 (69.6%)	7 (30.4%)
Total	54 (71.1%)	22 (28.9%)	55 (72.4%)	21 (27.6%)

Impaired FPG was defined as FPG > 100 mM

Table III. *Insulin resistance, before and after the intervention, in the age groups*
Tabela III. *Insulinooporność przed i po terapii w poszczególnych grupach wiekowych*

Age group	Insulin resistance before the intervention		Insulin resistance after the intervention	
	Normal insulin status [IU/mL]	Insulin resistance [IU/mL]	Normal insulin status [IU/mL]	Insulin resistance [IU/mL]
65–75 years	19 (76%)	6 (24%)	16 (64%)	9 (36%)
75–85 years	25 (89.3%)	3 (10.7%)	17 (60.7%)	11 (39.3%)
> 85 years	22 (95.7%)	1 (4.3%)	15 (65.2%)	8 (34.8%)
Total	66 (86.8%)	10 (13.25)	48 (63.2%)	28 (36.8%)

Insulin resistance was defined as HOMA-IR > 2.5

Table IV. *Effect of vitamin D supplementation on changes of study parameters*
Tabela IV. *Wpływ suplementacji witaminy na zmiany badanych parametrów*

	Before the intervention	After the intervention	p value
Number	76	76	–
Insulin [IU/mL]	5.2 ± 4.3	13.1 ± 15	< 0.001
Ca [mmol/L]	7.6 ± 0.9	8.4 ± 0.6	< 0.001
P [mmol/L]	3.6 ± 0.3	4.1 ± 0.4	< 0.001
PTH [pg/mL]	81 ± 98.1	41.1 ± 62.5	< 0.001
Albumin [g/L]	3.7 ± 0.4	4.3 ± 0.5	< 0.001

Ca — calcium; P — phosphorus; PTH — parathyroid hormone

Before the intervention, insulin resistance in the male participants was significantly more than in the females ($p = 0.005$): seven male participants (29.2%) versus three female participants (5.8%). But after the intervention, there was no significant difference between HOMA-IR levels in the male and female participants.

The amount of insulin, Ca, P, PTH and albumin, before and after the intervention, is shown in Table IV.

After the intervention, insulin, albumin, Ca and P serum levels increased significantly. But serum level of PTH after the intervention decreased significantly.

Before the intervention, there was no relationship between vitamin D deficiency with FPG level and insulin resistance. Also, after the intervention, there was no relationship between vitamin D deficiency with FPG level and insulin resistance.

Discussion

Type 2 diabetes is a worldwide disease and insulin resistance plays an important role in its development [3–7]. The relationship between insulin resistance and vitamin D deficiency is controversial. Also, in different studies, insulin intake has been found to have different effects on insulin resistance.

In this study, the prevalence of vitamin D deficiency in aged persons was 48.7%, and this is in accord with similar studies done on aged persons [22–24]. According to previous studies, the prevalence of hypovitaminosis D is between 30% and 90% in developing countries, and old age has been reported as a risk factor for hypovitaminosis D [22]. In our study, insulin resistance before the intervention in the male participants was significantly more than in the females. This is in accord with Gayoso-Diz et al.'s study, which reported that HOMA-IR levels in men were higher than in women [25].

Our study showed that impaired FPG and insulin resistance were not more prevalent in the participants with vitamin D deficiency. Our results are consistent with Vilarrasa et al.'s study findings, which reported no associations between 25(OH)D and plasma glucose and insulin resistance in patients with morbid obesity [13]. Also, our results are in accord with Muscogiuri et al.'s findings in obese individuals [14] and Gulseth et al.'s findings in European subjects with metabolic syndrome [15].

In the present study, we found that consumption of 50,000 IU vitamin D_3 per week supplements has no significant effect on FPG, but it can increase insulin resistance significantly. These findings are consistent with Pittas et al.'s study results. Pittas reported that in Caucasian adults with impaired fasting glucose, daily consumption of 700 IU vitamin D and Ca for three years might attenuate increases in insulin resistance [17]. Our findings are not in accord with Nikooyeh et al.'s study, which reported that daily intake of a vitamin D-fortified yogurt drink (containing 500 IU vitamin D_3) twice a day for 12 weeks improved glycaemic status and insulin resistance in type 2 diabetes patients [16]. Furthermore, the results of our study and Von Hurst et al.'s study are not similar. Von Hurst reported that daily intake of 4,000 IU vitamin D_3 for six months improved insulin resistance in insulin resistant South Asian women [25].

The findings of Patel et al.'s study are different from our results. That study was done on type 2 diabetes patients and showed that four-month consumption of 1,200 IU daily of vitamin D (a subtherapeutic dose) had no significant effect on insulin resistance [18]. This difference may be due to the difference between doses of vitamin D in the studies. Also, Parekh et al, found that four-week consumption of vitamin D in 28 Indian patients with moderately controlled type 2 diabetes mellitus was not associated with improvement in insulin secretion or insulin sensitivity [19]. The difference between this study and our study results could be due to the timespan of this study.

Conclusion

In our study, before and after the intervention, vitamin D deficiency had no relationship with FPG level and insulin resistance. We found that vitamin D intake had no significant effect on FPG level, but it increased the prevalence of insulin resistance significantly. We believe that performing more studies, with a longer timespan and larger sample size, as double blind clinical trials, is necessary.

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