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Alexandria University
High Institute of Public Health
Department of Nutrition

EVALUATION OF IMMUNOMODULATORY ROLE OF VITAMIN D AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS HAVING INFECTION

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by

Doha Magdy Mohamed Naheed Abo Zahra

M.B.B.Ch. Faculty of Medicine, Alexandria University, 2007
M.Sc. (Internal Medicine) Faculty of Medicine, Alexandria University, 2013
Diploma in Public Health (Nutrition) HIPH, Alexandria University, 2014

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SUMMARY

Renewed interest in vitamin D, the so-called "sunshine vitamin," has occurred recently because it has been linked to everything from cancer and heart disease to diabetes. Research studies continue to pour into the literature stating that vitamin D is a superstar when it comes to health. However, most of the research is based on observational, epidemiological studies, which are important for generating hypotheses but do not prove causality. DM is also major health care challenge around the world.

Serum 25(OH) vitamin D is considered the most accurate marker for vitamin D status. The optimal 25(OH) vitamin D serum level regarding other aspects of human health is still under debate. For immune-mediated diseases, experts suggest that even higher serum 25(OH) vitamin D levels may be needed to lead to positive effects. Currently, no international consensus is available on the optimal level for vitamin D supplementation, in particular on the safe upper level. While the tolerable upper daily limit given by the Endocrine Society is 10,000 IU, the more conservative Institute of Medicine (USA) considers a supplementation of up to 4000 IU/day to be safe.

Vitamin D may have a suppressive effect on inflammation. Interestingly, vitamin D has also been shown to have a stimulatory effect on monocytes *in vitro*, suggesting a complex role in immune hemostasis rather than a purely suppressive effect on the immune system. The extent of this physiologic balance has yet to be fully elucidated.

The general objective of this study was to evaluate the immunomodulator role of vitamin D in patients with type 2 diabetes mellitus and infection. The specific objectives of the study were to determine the effects of vitamin D supplementation on serum 25(OH) vit. D, the metabolic profile and inflammatory markers.

The study was conducted on 170 adult patients with type 2 DM and infection. They were randomly allocated in two groups; 85 patients in the control group who received appropriate antibiotic therapy alone and 85 patients in the intervention group who received vitamin D supplementation (10,000 IU daily) together with appropriate antibiotic therapy. The duration of the study was 3 months. They were subjected to full history taking (medical and dietary) using pre-designed questionnaire and laboratory investigations.

The results showed no significant differences between the two studied groups as regard the sociodemographic data, dietary sources of vitamin D and sun exposure pattern. As regard the duration of type 2 diabetes in the studied groups; in the control group the mean value of the duration of diabetes was 11.69 ± 2.37 years, while in the intervention group the mean value was 10.46 ± 3.69 years. There was statistically significant difference between both groups as the duration of diabetes among the intervention group was longer than the control group ($p=0.001^{*}$).

The results of our study showed that no statistically significant association between vitamin D level and dietary sources of vitamin D but there was statistically significant association between vitamin D and sun exposure in both groups.

In both groups there was statistically significance association between vitamin D and both education level and income but there was no statistically significant association between serum vitamin D and residency

In our study; among the control group patients about 76.5% were overweight and 23.5% were obese while in the intervention group; 11.8% had normal BMI, 69.4% were overweight and 30.6% were obese. The differences between two groups was no statistically significant (p=0.300).

The mean value of random blood glucose (RBG) in the control group on admission was 341.18 ± 44.24 and after 2 months the mean value was 308.47 ± 67.05 and this difference was statistically significant (p<0.001). In the intervention group the mean value on admission was 339.52 ± 36.13 and after 2 months the mean value was 131.66 ± 20.20 and this difference was statistically significant (p<0.001).

In this study there was no statistically significant correlation between vitamin D and HbA1C in the control group (p=0.851) but there was statistically significant correlation between vitamin D and HbA1C (p<0.001).

Our study showed that the mean value of ESR in the control group on admission was 90.25 ± 16.0 and after 2 months the mean value was 61.46 ± 20.34 and this difference was statistically significant (p<0.001). In the intervention group the mean value on admission was 90.87 ± 16.52 and after 2 months the mean value was 28.71 ± 11.22 and this difference was statistically significant (p<0.001). When comparing both groups; on admission there was no statistically significant difference between both groups (p=0.803) while after 2 months there was statistically significant difference (p<0.001) between both groups as the ESR markedly decreased in the intervention the control groupn comparison to the control group.

The mean value of CRP in the control group on admission was 35.22 ± 14.04 and after 2 months the mean value was 25.98 ± 8.49 and this difference was statistically significant (p<0.001). In the intervention group the mean value on admission was 37.24 ± 12.44 and after 2 months the mean value was 5.02 ± 2.28 and this difference was statistically significant (p<0.001). When comparing both groups; on admission there was no statistically significant difference between both groups (p=0.173) while after 2 months there was statistically significant difference (p<0.001) between both groups as the CRP markedly decreased in the intervention the control groupn comparison to the control group.

The mean value of TNF-α in the control group on admission was 9.08 ± 1.04 and after 2 months the mean value was 8.82 ± 0.37 and this difference no was statistically significant (p=0.045). In the intervention group the mean value on admission was 11.29 ± 1.39 and after 2 months the mean value was 8.02 ± 0.92 and this difference was statistically significant (p<0.001). When comparing both groups; on admission there was no statistically significant difference between both groups (p=0.144) while after 2 months there was statistically significant difference (p<0.001) between both groups as the TNF-α markedly decreased in the intervention the control groupn comparison to the control group.

There was no statistically significant correlation between serum 25(OH) vitamin D and TNF- α both the control group and II on both admission and after 3 months.

There was no statistically significant correlation between serum 25(OH) vitamin D and CRP in the control group ($p=0.796$) but there was statistically significant correlation in the intervention group ($p<0.005$).

There was statistically no significant correlation between serum 25(OH) vitamin D in the control group (0.335) but there was statistically significant correlation in the intervention group ($p<0.001$).

From this study we concluded that

1. Vitamin D level was higher at the end of the study in the intervention group than the control group.
2. Vitamin D supplementation has improved the metabolic profile (Blood pressure and HbA1C) of the intervention group patients.
3. Serum vitamin D level is negatively correlated with BMI.
4. The clinical outcome of the intervention group was better at the end of the study from the control group.
5. Adequate serum level of vitamin D is negatively correlated with inflammatory markers (ESR, CRP and TNF-alpha).
6. Adequate serum level of vitamin D is positively correlated with lymphocytic count and negatively correlated with total WBCs.
7. Vitamin D supplementation has important immunomodulator effects in sepsis.

The most important recommendations from this study:

1. A study on a larger group of patients should be conducted to provide more statistically significant data.
2. Screening for vitamin D status should be done routinely in all subjects with T2DM especially those with infection.
3. Vitamin D supplementation should be considered as an important line of treatment together with antibiotic therapy for patients with T2DM and infection.
4. The role of vitamin D as an immunomodulator should be emphasized in all patients with infection and sepsis not only those with type 2 DM.
5. Educational programs should be done about the sources of vitamin D and the adverse effects of its deficiency especially for those at high risk.