Human beings are members of a whole,
In creation of one essence and soul.
If one member is afflicted with pain,
Other members uneasy will remain.
If you've no sympathy for human pain,
The name of human you cannot retain!

Saadi Shirazi (Persian Poet)

Middle Eastern Women's Health Study-Phase II

The Effect of Monthly 50,000 IU or 100,000 IU Vitamin D Supplements on Vitamin D Status in Pre-menopausal Middle Eastern Women Living in Auckland

A research report presented in partial fulfilment of the requirements for the degree of Master of Sciences in Human Nutrition

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Abstract

Background: Middle Eastern women are at increased risk of vitamin D deficiency/insufficiency due to a number of specific lifestyle risk factors. Vitamin D supplements (50,000 IU/month) are prescribed by General Practitioners to correct vitamin D deficiency in this population in New Zealand. However, no research has investigated whether this dose of vitamin D supplement is useful for vitamin D deficiency treatment in Middle Eastern women or if larger doses are needed.

Objectives: The primary objective of this study was to conduct a double-blind, randomised, placebo-controlled trial with vitamin D supplementation for 6 months. We aimed to assess the adequacy of supplementation with monthly 50,000 IU and 100,000 IU in optimising serum 25(OH)D concentrations (≥ 50 nmol/L and ≥ 75 nmol/L) in a group of Middle Eastern premenopausal women living in Auckland. The secondary objective was to identify those factors affecting serum 25(OH)D response to the given doses of vitamin D supplements. Results from this study will help medical practitioners to provide the best options for treating vitamin D deficiency in Middle Eastern women living in New Zealand.

Method: Women of Middle Eastern origin, ≥ 20 years old and in premenopausal stage, having no major illness, living in Auckland (n=62) were recruited for the study in winter 2013. All were required to take study tablets (50,000, 100,000 IU or placebo/month) for 6 months and were required to visit the Human Nutrition Research Unit at Massey University on 3 occasions (baseline, 3-months, and 6-months). Blood samples were collected to measure serum 25(OH)D concentrations and calcium levels. Participants were required to complete questionnaires about their demographics, medical history, skin colour, lifestyle change and physical activity level. Height, weight, body fat percentage (BFP) and blood pressure were measured. Participants were also required to complete four day food dairies. The primary outcomes were the changes in serum 25(OH)D concentration and serum calcium level.

Results: Mean baseline serum 25(OH)D was 46.0±15.0 nmol/L. Supplementation with 50,000 IU/month and 100,000 IU raised the mean serum 25(OH)D concentrations from a baseline of 44.0±16.0 and 48.0±11.0 nmol/L to 70.0±15.0 and 82.0±17.0 nmol/L at 6 months, respectively (P<0.001 for both treatment groups). The mean serum 25(OH)D concentration of women assigned to placebo group increased from 45.0±18.0 nmol/L at baseline to 54.0±18.0 nmol/L at 6 months (P<0.01). The mean serum 25(OH)D concentrations reached a

plateau after 3 months of supplementation. Of 62 women, 59.7% had serum 25(OH)D concentrations <50 nmol/L and only 3.3% had serum 25(OH)D ≥ 75 nmol/L. At 6 months, the proportion of subjects achieving serum 25(OH)D concentration of 75 nmol/L or more was 31.6% and 66.7% in women receiving monthly 50,000 IU and 100,000 IU, respectively (P=0.002). There were no reports of hypervitaminosis D (serum 25(OH)D >225 nmol/L) or hypercalcemia (serum calcium ≥ 2.7 mmol/L). Response to vitamin D supplementation varied widely (increasing 1.0 to 80.0 nmol/L). In a regression analysis, dose (P<0.001), baseline serum 25(OH)D concentration (P<0.001) and baseline BFP (P=0.01) were the only variables to reach statistical significance as predictors of the change in serum 25(OH)D over 6 months.

Conclusion: The prevalence of vitamin D deficiency/insufficiency was high in this study population highlighting the significance of the situation. Monthly intake of 100,000 IU vitamin D for 6 months was more effective than 50,000 IU in achieving serum 25(OH)D concentrations of 75 nmol/L, though it did not ensure a serum 25(OH)D concentration of 75 nmol/L or more in all people. Factors affecting serum 25(OH)D response to supplementation should be taken into account when an optimal dose for individuals is determined. The unexpectedly large variance in serum 25(OH)D response to a fixed dose of vitamin D highlights the importance of follow up and measurements of serum 25(OH)D when supplementation is used in clinical practice.

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List of abbreviations

-2LL	-2-Log Likelihood
1,25(OH)$_2$D	1, 25-dihydroxyvitamin D
24,25(OH)$_2$D	24, 25-dihydroxyvitamin D
25(OH)D	25-hydroxyvitamin D
25(OH)D-26,23 lactone	25-hydroxyvitamin D-26,23 Lactone
AI	Adequate Intake
ANCOVA	Analysis of Covariance
AUC	Area Under the Curve
BFP	Body Fat Percentage
BIA	Bioelectrical Impedance Analyser
BMC	Bone Mineral Content
BMD	Bone Mineral Density
BMI	Body Mass Index
BP	Blood Pressure
Ca	Calcium
CHD	Coronary Heart Disease
CI	Confidence Interval
CV	Cardiovascular
CVD	Cardiovascular Disease
CYP2R1	Cytochrome P450, Family 2, Subfamily R, Polypeptide 1
CYP24A1	Cytochrome P450, Family 24, Subfamily A, Polypeptide 1
CYP27B1	Cytochrome P450, Family 27, Subfamily B, Polypeptide 1
d	Day
D_2	Ergocalciferol
D_3	Cholecalciferol
DCs	Dendritic Cells
DHBs	District Health Boards
DHCR7	7-dihydrocholesterol Reductase
FGF23	Fibroblast Growth Factor 23
FPB	Fasting Plasma Blood
GC	Group Specific Component gene
g	Gram

List of abbreviations

GP	General Practitioner
HOMA-IR	Homeostatic Model Assessment of Insulin Resistance
HOMA-ß	Homeostatic Model Assessment of Beta Cell Function
IGI	Insulinogenic Index
IL-6	Interleukin 6
IL-10	Interleukin 10
IM	Intramuscularly
IOM	Institute of Medicine
IPAQ	International Physical Activity Questionnaire
iPTH	Intact Parathyroid Hormone
IU	International Unit
kg	Kilogram
LASA study	Longitudinal Aging Study Amsterdam study
log	Logarithm
MED	Minimum Erythemal Dose
MELAA	Middle Eastern, Latin American, African
mg	Milligram
Mg/dl	Milligram per Decilitre
MI	Myocardial Infarction
ml	Millilitre
mmHg	Millimetre of Mercury
mo	Month
MS	Multiple Sclerosis
MUFA	Monounsaturated Fatty Acid
m^2	Metre Squared
n	Number
N	North
ng/ml	Nanograms per Millilitre
nmol/L	Nanomol per Litre
NZPAQ-SF	New Zealand Physical Activity Questionnaire-Short Form
NZ$	New Zealand Dollar
OFELY	Os des Femmes de Lyon
OPRA Trial	Osteoporotic Prospective Risk Assessment Trial

List of abbreviations

OR	Odds Ratio
oz	Ounce
PHARMAC	The Pharmaceutical Management Agency
Pmol/mg	Picomole per milligram
PTH	Parathyroid Hormone
PUFA	Polyunsaturated Fatty Acid
QUICKI	Quantitative Insulin Sensitivity Check Index
RCT	Randomised Controlled Trial
RDA	Recommended Daily Allowance
RR	Relative Risk
SD	Standard Deviation
SNP	Single Nucleotide Polymorphism
SPF	Sun Protection Factor
SZA	Solar Zenith Angle
TNF-α	Tumour Necrosis Factor alpha
T1DM	Type 1 Diabetes Mellitis
UAE	United Arab Emirates
UK	United Kingdom
US NHANES III	The United States National Health And Nutrition Examination Survey 3
UV	Ultraviolet
UVB	Ultraviolet Beta radiation
US$	United States dollar
VDBP	Vitamin D Binding Protein
VDR	Vitamin D Receptor
vs.	Versus
y	Year
µg	Microgram
µmol/L	Micromole per litre