Optimal Dose of Vitamin D Replacement in Middle Eastern and North African Population: a Systematic Review and Meta-analysis

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BACKGROUND

Hypovitaminosis D, defined as a 25-hydroxyvitamin D [25(OH)D] level <20 ng/ml, is highly prevalent worldwide, especially in the Middle East and North African (MENA) region (1,2). Relevant risk factors in adults, and similarly to other countries, include advancing age, female gender, multiparity, clothing style, season, socio-economic status and urban living (3). The latest Institute of Medicine (IOM) recommendations for vitamin D dosing targeted populations from North America, and may not necessarily apply to the MENA region (4).

OBJECTIVES

The main objective is to define the mean 25-hydroxyvitamin D [25(OH)D] level reached with low (400-2,000 IU/d), moderate (800-2,000 IU/d) or high (>2,000 IU/d) daily dose of vitamin D in subjects in the MENA countries, by age and reproductive status. We will also deduce the proportion of subjects who reach a mean 25(OH)D level ≥20 ng/ml in the three above treatment groups. Other outcomes investigated are fracture rates, mortality, adverse events, change in metabolic parameters, bone mineral density, and muscle strength.

METHODS

Eligibility criteria: We included randomized clinical trials comparing different doses of oral vitamin D supplements or placebo in MENA countries, of both genders and all age categories, including pregnant and lactating women.

Search method: A systematic search for English and Non-English articles was conducted using Medline, PubMed, the Cochrane Library, EMBASE, Popline, Global Health Library,eligibility criteria. WHO-Evidence-based criteria were preferred. Additional studies were identified on ClinicalTrial.gov and the WHO registry for clinical trials (ICTRP). Authors were contacted for unpublished data.

Selection and data abstraction process: References retrieved were reviewed in duplicate (2 reviewers). We independently screened, excluded duplications, assessed risk of bias using the Cochrane risk of bias tool, 2011 (5), in duplicate and independently. We used RevMan software (version 5.2) for data entry and analysis.

ANALYSIS

The primary analysis was done using a random-effects model. Assumingly normality of the distribution of the 25(OH)D levels, the mean 25(OH)D level reached and the proportion of individuals reaching 25(OH)D ≥ 20 ng/ml was calculated for each group and vitamin D dose category.

RESULTS

2542 articles were screened for title and abstract. 192 full texts were assessed for eligibility. We judged 23 studies as eligible: 3 in elderly (≥ 65 years), 11 in adults, 3 in children, 2 in neonates and infants, and 4 in pregnant women.

DISCUSSION

• Our results show that the IOM recommended vitamin D doses in the Middle East and North Africa region may not be sufficient to raise 25(OH)D level to target levels in MENA countries, across different age and reproductive status categories.

• The proportion of subjects who reached a 25(OH)D level ≥20 ng/ml was below 50% at low doses (<800 IU/d), 54-83% at intermediate doses (800-2000 IU/d), and 80-93% at high doses (>2000 IU/d).

• In adults (18-65 years), a dose as high as 10 times the recommended IOM dose, allowed 93% of the population to reach a 25(OH)D level ≥20 ng/ml.

• In pregnant women, a dose equivalent to 6 times the IOM recommended dose, started early in the second trimester were needed to allow to 90% of the population to reach a 25(OH)D level ≥20 ng/ml.

• In children, a dose of 1600-2000 IU daily allowed to 75% of the population to reach the desirable 25(OH)D level.

Strengths:

• First systematic review in MENA assessing the dose response of vitamin D.

• Eligibility criteria have been chosen to avoid bias and limitations of previously published systematic reviews.

• Extensive search, inclusive of databases relevant to the MENA region.

Limitations:

• The majority of the included trials have been conducted in one country, Iran.

• Only five studies have been conducted on healthy individuals, while others were in individuals with various conditions, including obesity, multiple sclerosis, diabetes, PCOS, but excluding metabolic bone diseases and other conditions that affect vitamin D metabolism.

CONCLUSION

The IOM Recommended Daily Allowance (RDA) doses for vitamin D at different age categories may not be applicable to the MENA countries, thus vitamin D replacement guidelines in this region may need to target higher doses to achieve desirable level.