Vitamin D threshold ≥40ng/mL prevents arthralgia in aromatase inhibitors users: B-ABLE cohort study

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Introduction

Aromatase inhibitors (AI) are the gold standard treatment for estrogen receptor-positive breast cancer. However, it has been associated with emergence of arthralgia, defined as joint pain, severely affecting the patient's quality of life and their treatment compliance. Vitamin D (VitD) levels ≥40ng/mL were previously found associated with lower arthralgia incidence in the B-ABLE cohort. We performed a new analysis to confirm these results in an extended sample size.

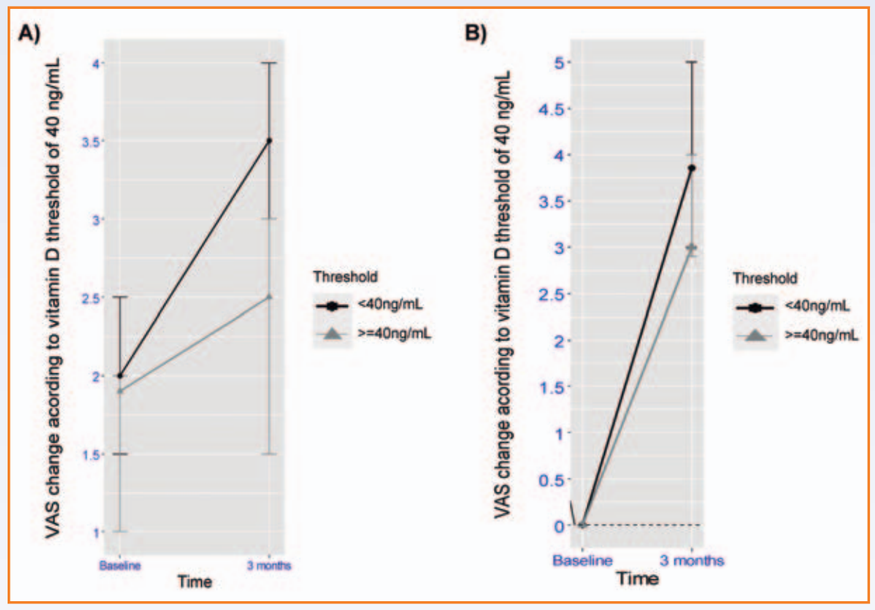

Fig 1. Median [95%CI] VAS change according VitD threshold 40ng/mL in **A)** all patients (n=741), and **B)** patients with incident pain (n=117)

Table 1. VAS and VitD levels at baseline and three months of AI treatment

Variables	Baseline	3 months
VAS median [Q1;Q3]	2.00 [0.00;4.00]	3.00 [0.00;5.00] *
VitD median [Q1;Q3] (ng/mL)	15.10 [10.8;21.00]	40.20 [30.90;52.50] *

*Abbreviations: Q, quartile; VAS, visual analogic scale; VitD, vitamin D. * P<0.001, compared with baseline.*

Methods

Data of 927 Caucasian postmenopausal women candidates for AI-treatment were collected in the B-ABLE cohort (Barcelona, Spain) from January 2006 to January 2019. Participants were supplemented with 25(OH)vitD3 tablets (800IU daily), and those with baseline VitD deficiency (<30ng/mL) received an additional dose of 16,000IU every 2 weeks. Visual analogic scale (VAS), used to score the intensity of self-reported joint pain, and serum levels of 25(OH)D were evaluated at baseline and 3 months of follow-up. Association between absolute VAS changes from baseline to 3 months and VitD threshold ≥40ng/mL was tested using a linear regression. Additionally, incident pain (patients with no initial joint pain but a VAS greater than 0 at 3 months) and VitD threshold ≥40ng/mL was evaluated by a logistic regression. All analyses were adjusted by age, body mass index, recent chemotherapy, previous tamoxifen use, and current antiresorptive treatment.

Results

A total of 741 participants had available data at 3 months and their baseline VitD levels were lower than 30ng/mL. VAS and VitD levels during follow up are described in Table 1. Lower VAS change from baseline to 3 months was significantly associated (p<0.05) with VitD threshold ≥40ng/mL at 3 months of follow-up (Fig. 1A; Table 2). Analyzing the subset of 301 patients with no baseline pain, 117 (38.87%) developed joint pain at 3 months with a VAS median [Q1;Q3] of 3.50 [2.20;5.00] (Fig. 1B). Occurrence of joint pain was lower in those patients that achieved levels of VitD ≥40 ng/mL (p<0.05; Table 3).

Table 2. Linear regression between VitD threshold ≥40ng/mL and absolute VAS changes from baseline to 3 months (All patients n=741)

Outcome	Unadjusted β coefficient [95%CI]	Adjusted β coefficient [95%CI]
Absolute VAS change	-0.39 [-0.74 to -0.03]	-0.39 [-0.75 to -0.04]

Abbreviations: CI, confidence interval; VitD, vitamin D. In 95%CI, values are compared with patients with VitD < 40ng/mL.

Table 3. Logistic regression among incident pain at 3 months of follow up and VitD threshold ≥40ng/mL. (Incident pain patients n=117)

Outcome	Unadjusted OR [95%CI]	Adjusted OR [95%CI]
Incident pain	0.53 [0.33 to 0.85]	0.55 [0.34 to 0.90]

Abbreviations: CI, confidence interval; OR, odds ratio; VitD, vitamin D. In 95%CI, values are compared with patients with VitD < 40ng/mL.

Conclusions

In summary, vitamin D levels ≥40ng/mL attenuate joint pain in AI-treated patients. Vitamin D supplementation is advisable to achieve this level.