The Effect of Vitamin D Replacement on Musculoskeletal Pain in Hypothyroid Patients with Vitamin D Deficiency

Azam Amini 1, Gholamreza Pourbehi 2, Fariba Karimi 3, Atefeh Amuzgar 1, Hamidreza Mosallaeepour 1, Katayoun Vahdat 2, Mohammadreza Kalantar Hormozi 1, Kamyar Asadipooya 4, Iraj Nabipour 1, Majid Assadi 5

1The Persian Gulf Biomedical Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran
2The Persian Gulf Tropical Medicine Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran
3Endocrinology and Metabolism Research Center, Shiraz University of Medical Sciences
4Department of Endocrinology and Metabolism, NYU Langone Medical Center, NYU school of medicine, New York, US
5The Persian Gulf Nuclear Medicine Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran

Abstract—Hashimoto’s thyroiditis [HT] is the most common chronic autoimmune thyroid disorder that can cause hypothyroidism. Environmental and genetic factors are playing role in its etiology. The role of vitamin D as an immune modulator has been emphasized in recent years. The goal of present study is to assess whether vitamin D supplements can reduce the musculoskeletal pain of HT patients who had vitamin D deficiency.

This is a single arm clinical trial that included 42 cases who have HT with musculoskeletal pain after becoming euthyroid. 25-hydroxy vitamin D was less than 32 nmol/L. We measured calcium, phosphorus, parathyroid hormone (PTH), thyroid stimulating hormone (TSH), 25-hydroxy vitamin D and severity of body pain at the beginning of the study and after 8 weeks of treatment with vitamin D (cholecalciferol 50,000 weekly). We used SPSS software version 16 to analyze data.

Vitamin D supplementation, after 8 weeks, improved musculoskeletal pain, and increased mean serum calcium, phosphorus, and 25-OH-Vitamin D levels significantly. There were no significant changes in mean TSH levels.

Vitamin D supplements can potentially helpful in reducing musculoskeletal pain of HT patients who also have vitamin D deficiency. High prevalent area of vitamin D deficiency should consider concomitant treatment of vitamin D deficiency in HT patient.

KEY WORDS: Hashimoto’s thyroiditis, vitamin D deficiency, musculoskeletal pain, Vitamin D replacement.

INTRODUCTION

Vitamin D deficiency is a public health challenges that outside of the bone system has possible relationship with cardiovascular disease, insulin resistance, infectious diseases, cancers, and autoimmune disorders such as rheumatoid arthritis and autoimmune thyroid disease (1-5). Vitamin D is a steroid hormone which plays an important role in regulating many genes. It also employs different effects on cellular proliferation, differentiation, apoptosis, angiogenesis, and inflammation (3-6). The role of calcitriol as a key hormone in the regulation of the musculoskeletal system is well described. However, after finding vitamin D receptor (VDR) in extra skeletal tissues, VDR was introduced as a transcriptional factor that carries various biological effects (7, 8), and contributes to orchestration of inflammatory processes in autoimmune diseases (9, 10). VDR probably has immunosuppressive, regulatory, and tolerogenic effects in autoimmune processes (11, 12).

Autoimmune thyroid disease (Hashimoto’s thyroiditis) and vitamin D insufficiency are linked together. TSH has negative correlation with serum vitamin D (13, 14). In addition, calcidiol (25-hydroxyvitamin D, 25VD) concentration has positive correlation with thyroid volume, and negative correlation with anti-TPO (thyroid peroxidase) and anti-TG (thyroglobulin) antibody levels (15, 16). Vitamin D supplementation may improve autoimmunity in patient with autoimmune thyroid disease (AITD) by reducing anti TPO-Ab levels (5).

Vitamin D deficiency and hypothyroidism are often associated with signs and symptoms of nociceptive pain and musculoskeletal discomfort (17, 18). Levothyroxine therapy can improve musculoskeletal symptoms of hypothyroidism (19). However, in accordance with vitamin D deficiency, musculoskeletal pain can potentially stay in euthyroid states, and may increase the risk of medication non-compliance. To
the best of our knowledge, in the setting of vitamin D deficiency and Hashimoto’s hypothyroidism, nobody tested effect of vitamin D supplementation on musculoskeletal pain of hypothyroid patients. We hypothesized that vitamin D supplementation in euthyroid patients with Hashimoto’s hypothyroidism (on levothyroxine with TSH < 4) can improve musculoskeletal symptoms and probably their compliance with medication.

MATERIALS AND METHODS:
This study is a single-arm clinical trial to investigate the effects of vitamin D supplementation on musculoskeletal pain in the patients with Hashimoto’s hypothyroidism (HT). Participants singed informed consent after having a broad explanation about the study course, interventions and benefit and side effects of prescribed medications (levothyroxine and cholecalciferol).

Our endocrinologist selected the enrollees between patients who came to Faculty Group Practice (FGP) clinic (Abolfazl clinic in Bushehr, Iran) from April to September 2010. All participants had Hashimoto’s hypothyroidism (TSH > 10 with positive anti-TPO antibody).

All patients with HT and musculoskeletal pain were treated with levothyroxine. Continued musculoskeletal pain after achieving normal TSH (TSH < 4) was considered for further investigation. HT with normal TSH (on levothyroxine), 25VD less than 32 ng/ml and continued musculoskeletal pain were criteria to be joined.

25-hydroxy Vitamin D, calcium, phosphorous serum level and body pain severity assessed before and after prescription of 8 weeks 50,000 IU in euthyroid HT patient with low vitamin D. Our data analyzed with SPSS software version 16 and paired t-test and Wilcoxon test used for descriptive statistics and Kolmogrov and Simonov test was done for evaluation of normality of data distribution. Cases had normal distribution and data analyzed using necessary tests.

Musculoskeletal pain scored per visual analogue scale (VAS) or 0-10 numeric pain rating scale. TSH, total T4, total T3 and anti-TPO-Ab were measured by using Monobite kit (ELISA method). Calbiotec PHASC (Pharm avaran e sabz co.) was used to check serum levels of 25VD (ELISA method).

Serum calcium and phosphorus were measured by using Pars azmoon kit (enzymatic method). Ethics committee of Bushehr University of Medical Sciences approved the study.

We excluded patients with history of concomitant autoimmune or rheumatologic disease (such as rheumatoid arthritis, systemic lupus erythematosus, and fibromyalgia syndrome), major systemic illness (included parathyroid disease, adrenal disease, diabetes mellitus, chronic renal failure, liver disease, or ischemic heart disease), hypertension or hyperlipidemia on medication, elevated liver enzymes (AST and ALT) and muscle enzyme (CK).

RESULTS
Out of 70 patients with Hashimoto’s thyroiditis and musculoskeletal pain, 63 patients who were complaining of musculoskeletal pain after receiving levothyroxine and having normal TSH (TSH 0.5 - 4) joined the study. During 3 months follow up, 21 patients had lost follow up assessment and 42 patients completed end of study questionnaire.

Our enrollee included 22 women (52.4%) and 20 man (47.6 %). Age distribution ranged between 15 and 70 with mean age of 40.88±15.77.

Vitamin D supplementation increased mean serum calcium (from baseline value 8.58 ± 0.23 to 9.04 ± 0.34), phosphorus (form starting value 2.3 ± 0.29 to 3.65 ± 0.55) and 25-OH-Vitamin D levels significantly. There were no significant changes in mean TSH levels during vitamin D supplementation (mean baseline values 3.46 ± 1.13, and end of study levels 3.3 ± 1.35) (Table 1).

Pain of 38 cases (90 %) improved significantly after vitamin D replacement (P-value < 0.0001).

DISCUSSION
In this single arm trial involving patients with history of Hashimoto’s thyroiditis, on levothyroxine, who had TSH < 4, 25-hydroxy vitamin D < 32, and musculoskeletal pain; vitamin D supplementation (cholecalciferol 50,000 weekly) improved musculoskeletal discomfort.

Hashimoto’s thyroiditis often causes musculoskeletal symptoms including joint pain, muscle weakness, cramps, and myalgias. On the other hand, vitamin D deficiency which is associated with autoimmune diseases such as HT, is a prevalent condition in different age groups from young children to middle-aged adults (2, 20).

Literature presents controversies around improvement of musculoskeletal pain after vitamin D supplementation in patients with low vitamin D (25-OD vitamin D < 20 ng/mL) with or without underlying diseases (21-23). However, vitamin D supplementation has some beneficial effects on musculoskeletal pain and fatigue, probably by increasing serum level of 25 OH vitamin D (24).

Higher prevalence of vitamin D deficiency in HT (25), may play a role in musculoskeletal pain, and thus medication noncompliance of these patients. Musculoskeletal pain of our patients (HT with vitamin D deficiency) improved after vitamin D supplementation. No change in TSH level, and increase in serum levels of calcium, phosphorus and 25 OH vitamin D after vitamin D supplementation may explain

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<td><strong>Patient’s data</strong></td>
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<tr>
<td>25(OH) vitamin D, nmol/L or ng /ml</td>
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<td>Calcium mg/dl</td>
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independent beneficial role of vitamin D supplementation in musculoskeletal pain of HT patients. Without measuring TPO and PTH after treatment, role of vitamin D supplementation as an immune modulator or regulator of calcium homeostasis in muscle is not completely explainable. Effects of Vitamin D on size, strength and function of muscle (6) may partially explain current improvement of musculoskeletal pain of HT. However, other possible mechanisms such as modulation of autoimmunity, increase efficacy of thyroid hormones, improvement of bone quality cannot be excluded.

CONCLUSION

Vitamin D deficiency should be considered as a possible cause of musculoskeletal pain in HT patients. Vitamin D supplementation may improve their musculoskeletal pain and possibly medication compliances.

REFERENCES