

# Successful Treatment of Isotretinoin Induced Musculoskeletal Pain by Vitamin B12 and Folic Acid

Amir Feily\*

*Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran*

## Abstract

**Citation:** Feily A. Successful Treatment of Isotretinoin Induced Musculoskeletal Pain by Vitamin B12 and Folic Acid. *Open Access Maced J Med Sci*. 2019 Nov 15; 7(21):3726-3727.  
<https://doi.org/10.3889/oamjms.2019.799>

**Keywords:** Isotretinoine; Vit B12; Folic acid

\***Correspondence:** Amir Feily, Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran. E-mail: [dr.feily@yahoo.com](mailto:dr.feily@yahoo.com)

**Received:** 10-Jun-2019; **Revised:** 11-Aug-2019;  
**Accepted:** 12-Aug-2019; **Online first:** 10-Oct-2019

**Copyright:** © 2019 Amir Feily. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

**Funding:** This research did not receive any financial support

**Competing Interests:** The authors have declared that no competing interests exist

**BACKGROUND:** Daily supplementation with vitamin B12 and folate, which are the cofactors of the enzymatic reactions involved in Hcy metabolism, can lower plasma levels of Hcy and prevent osteoporosis induced by retinoid

**CASE PRESENTATION:** We reported six patients with nodulocystic acne who reported musculoskeletal pain after taking isotretinoin which successfully treated with daily supplementation of folic acid and B12.

**CONCLUSION:** We suggest our colleagues consider these supplements when a patient suffers from musculoskeletal pain following starting isotretinoin and continue the treatment as well. In the end, the authors concluded that robust trials with more patients are needed to establish the efficacy of Vit B12 and folic acid in the treatment of isotretinoin induced musculoskeletal pain.

## Introduction

Acne vulgaris is a chronic inflammatory disease affecting the pilosebaceous unit in the skin. Isotretinoin is a vitamin A derivative is the most effective agent in the treatment of acne. A substantial amount of studies reports of adverse effects of isotretinoin on the skeletal system [1], [2], [3], [4], [5]. Namazi and Feily in 2010 suggested that retinoid-induced hyperhomocysteinemia may account for osteoclast overactivity, osteoporosis, and increased risk of bone fracture associated with retinoid use. As a hypothesis, they suggested Daily supplementation with vitamin B12 and folate, which are the cofactors of the enzymatic reactions involved in Hcy metabolism, can lower plasma levels of Hcy and prevent osteoporosis induced by retinoid [4], [5].

Accordingly, we reported six patients with nodulocystic acne who reported musculoskeletal pain after taking isotretinoin which successfully treated with daily supplementation of folic acid and B12.

Six patients (Table 1) had previously been treated with isotretinoin reported musculoskeletal pain after starting isotretinoin for their nodulocystic acne. Three of them around 20 days, one of them one month and the other two patients after 45 days of taking isotretinoin reported the musculoskeletal pain. Four of them reported back pain and two reported leg pain. Two of the patients had the history of taking isotretinoin and musculoskeletal pain which caused them to discontinue the treatment. There was not any other rheumatologic or other past history for all of them. Routine labdates were normal too.

**Table 1: Patients Treatment and Evolution**

Patient	Sex / Age (yrs)	Follow up	Area of musculoskeletal pain	Time of the pain after starting isotretinoin	History of pain after taking isotretinoin	Response to vitb12 and Folic acid
1	F/18	8 months	Back	Around 20 days after starting isotretinoin	Negative	Positive
2	F/21	6 months	Leg	Around 20 days after starting isotretinoin	Negative	Positive
3	F/24	8 months	Back	Around 45 days after starting isotretinoin	Positive	Positive
4	M/20	6 months	Back	Around 30 days after starting isotretinoin	Negative	Positive
5	F/29	8 months	Leg	Around 20 days after starting isotretinoin	Positive	Positive
6	F/22	6 months	Back	Around 20days after starting isotretinoin	Negative	Positive

In all patients, we started Folic Acid 1 mg daily and vitamin B12 injection every two weeks until more than 6 months follow up. After two weeks of treatment, the partial improvement was noted, and over the next week, further reduction in musculoskeletal pain was observed and After 6 weeks the symptoms completely disappeared, and all patients continued their treatment until 6 months.

It has been shown that the amino acid homocysteine level is elevated in patients on isotretinoin treatment for acne, which may be due to the inhibition of cystathionine-beta-synthase by the drug and/or the drug-induced liver dysfunction [4], [5], [6].

Higher levels of Hcy have been linked to higher fracture rate in the elderly and have been noted as a new risk factor for osteoporosis. Also, hyperhomocysteinemia has some adverse effects on the extracellular bone matrix by damaging collagen crosslinking [4], [5]. Accordingly, we think Daily supplementation with vitamin B12 and folate, maybe by affecting on enzymatic reactions involved in Hcy metabolism, could lower their plasma levels of Hcy

and musculoskeletal pain. We suggest our colleagues consider these supplements when a patient suffers from musculoskeletal pain following starting isotretinoin and continue the treatment as well. In the end, the authors concluded that robust trials with more patients are needed to establish the efficacy of Vit B12 and folic acid in the treatment of isotretinoin induced musculoskeletal pain.

## References

1. Rassai S, Rafeie E, Ramirez-Fort MK, Feily A. Adjuvant Narrow Band UVB Improves the Efficacy of Oral Azithromycin for the Treatment of Moderate to Severe Inflammatory Facial Acne Vulgaris. *J Cutan Aesthet Surg.* 2014; 7:151-154. <https://doi.org/10.4103/0974-2077.146664> PMID:25538435 PMCID:PMC4271294
2. Baykal Selçuk L, Aksu Arıca D, Baykal Şahin H, Yaylı S, Bahadır S. The prevalence of sacroiliitis in patients with acne vulgaris using isotretinoin. *Cutan Ocul Toxicol.* 2017; 36:176-179. <https://doi.org/10.1080/15569527.2016.1237521> PMID:27764978
3. Yaghoobi R, Feily A, Behrooz B, Yaghoobi E, Mokhtarzadeh S. Palpebral involvement as a presenting and sole manifestation of discoid lupus erythematosus. *Scientific World Journal.* 2010; 10:2130-1. <https://doi.org/10.1100/tsw.2010.209> PMID:21057726 PMCID:PMC5763936
4. Feily A, Namazi MR. Decrease of insulin growth factor-1 as a novel mechanism for anti-androgen effect of isotretinoin and its reported association with depression in some cases. *J Drugs Dermatol.* 2011; 10:793-4.
5. Namazi MR, Feily A. Hyperhomocysteinemia: can't it account for retinoid-induced fracture proneness? *Indian J Dermatol Venereol Leprol.* 2010; 76(2):186-7. <https://doi.org/10.4103/0378-6323.60557> PMID:20228554
6. Karlsson T, Vahlquist A, Kedishvili N, Törmä H. 13-cis-retinoic acid competitively inhibits 3 alpha-hydroxysteroid oxidation by retinol dehydrogenase RoDH-4: a mechanism for its anti-androgenic effects in sebaceous glands? *Biochem Biophys Res Commun.* 2003; 303:273-8. [https://doi.org/10.1016/S0006-291X\(03\)00332-2](https://doi.org/10.1016/S0006-291X(03)00332-2)