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Original Article

Incidence of low back pain and sacroiliitis in military families with acne vulgaris under isotretinoin therapy

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Abstract: Background: Acne vulgaris is a common complication that patients referred to dermatologist, also there are medications to manage of this such as isotretinoin, and incidence of low back pain in these patients is more than general population, so in this study we aimed to evaluate of Incidence of low back pain and sacroiliitis in military families with acne vulgaris under isotretinoin therapy. Methods: This cross-sectional study was performed on 113 acne vulgaris patients treated with isotretinoin (at least 3 months) referred to dermatology clinic of Imam Reza Hospital of Army Medical Sciences, Tehran, Iran during 2018 to 2019. All data of patients such as dosage and duration of medication, severity of acne, incidence of low back pain, sacroiliitis and inflammatory back pain and lab data were recorded. Results: 54% of patients had lethargy, 41.6% had myalgia and 46.9% had low back pain. Of the patients with low back pain, 54.7% had inflammatory low back pain and 45.3% had mechanical low back pain. 29 cases had inflammatory low back pain, 5 cases had sacroiliitis and one case had positive RF, the means of ESR, CRP and ANA were 19.01 ± 12.74 Mm/hr, 3.43 ± 1.27 Mg/litr and 1.31 ± 0.90, respectively. Conclusion: In patients with acne vulgaris under isotretinoin therapy much attention must be given regarding to sacroiliitis and rheumatoid diseases especially when symptoms such as low back pain are present.

Keywords: Acne vulgaris, isotretinoin, low back pain, sacroiliitis, rheumatoid diseases

Introduction

Acne vulgaris is chronic inflammatory disease of skin glans and is most common skin disease among Iranian soldiers that is not affected by gender, skin color, or race [1, 2]. Isotretinoin is a synthetic vitamin A product and is the most effective treatment for acne that has been used for nearly 4 decades. The limitations of using this medication are potential complication and need to laboratory tests during usage of drug but tremendous efficacy in treating acne lesions and improving the quality of life of patients are interesting therapeutic effect of this medication [3]. The use of isotretinoin in patients is associated with many complications, including musculoskeletal complications. The most common rheumatologic complications are musculoskeletal pain and arthralgia that has been seen in 20% of cases [4] and are mild complications that relief after discharging of drug [5]. Case reports of sacroiliitis in isotretinoin-treated patients are ambiguous because the exact pathogenesis of sacroiliitis in isotretinoin use is unclear [6]. However, it is thought that due to the detergent nature of isotretinoin, the lysosomal membrane of the joint may be affected and more susceptible to trauma [7]. The above theory is supported by reports of the occurrence of sacroiliitis in athletes treated with isotretinoin [7, 8]. Other proposed theories include the possible role of HLA-B27 that may predispose patients to this complication [9]. However, HLA-B27 has been negative in patients with sacroiliitis under isotretinoin therapy in many previous studies [9, 10]. Given the precise pathogenesis of sacroiliitis in the use of isotretinoin is still unclear and there is evidence from studies of the incidence of sacroiliitis in athletes under treatment with isotretinoin [7, 8]. It has not been investigated whether trauma or more physical activity can influence the incidence of sacroiliitis in patients treated with isotretinoin. According to more physical activity in the militaries than general papulation, high prevalence of skin disease such as acne vul-

garis in the Iranian soldiers [1] and also majority soldiers are under treatment with isotretinoin that may lead to complications such as sacroiliitis for conscripts and military personnel. Arthralgia and sacroiliitis can also impose costs on the country's military and medical system by increasing morbidity among soldiers. Previous studies on this complication have been the majority of case reports studies and only two studies have investigated the large sample size of this complication, which requires further studies with a larger sample size in this area. There are few studies on the prevalence of sacroiliitis in patients with acne vulgaris under treatment with isotretinoin and whether usage isotretinoin may be a prognostic factor for sacroiliitis. Therefore, we conducted the present study to evaluate the incidence of sacroiliitis in the military and their families with acne vulgaris under treatment with isotretinoin.

Materials and methods

This cross-sectional study was performed on 113 acne vulgaris patients treated with isotretinoin (at least 3 months) referred to dermatology clinic of Imam Reza Hospital of AJA University of Medical Sciences, Tehran, Iran during 2018 to 2019. It should be noted that the protocol of this study was approved by the Ethics Committee of the AJA University of Medical Sciences (IR.AJAUMS.REC.1398.103). Inclusion criteria were included patients with mod-to-severe acne vulgaris who had no other treatment modalities, patients with no previous history of low back pain, ankylosing spondylitis and spondyloarthropathy, and aged over than 18 years. Also, the patients with depression, psychiatric disorders, renal and liver failures, and not desired to continue cooperation in the study were excluded. Sampling in this study was convenience. Demographic data of patients were included age, gender, other clinical information such as dosage of isotretinoin and duration of drug use were recorded in a pre-prepared checklist. The severity of acne vulgaris was performed based on the recommended Tutakne and Chari ratings into four grades from 1 to 4 (mild to severe) [18]. Patients who were diagnosed with a new low back pain were examined further. ASAS criteria were used to differentiate of inflammatory and non-inflammatory low back pain. These criteria include: ages lower than 40 years at onset of pain, sudden onset of pain, improvement in pain with physical activity, no improvement in pain with physical activity, nocturnal pain (increased pain by lifting legs). Inflammatory low back pain was diagnosed in 4 items or more. Then patients with ASAS criteria for inflammatory low back pain were further evaluated by MRI imaging and laboratory tests including rheumatoid factor (RF), ANA, ESR and CRP.

After collecting the required data, all data were entered into SPSS software version 24. Data were shown based on means and standard division and also frequency or percentages. Statistical analysis was performed using chi-square test and nonparametric tests such as independent t test and one-way ANOVA. Logistic regression and Pearson correlation were also used significance level was less than 0.05.

Results

The study included 113 patients, 33 men and 80 women with mean aged of 22.32 ± 3.85 years. Acne severity was moderate in 22.1% and severe in 77.9%, respectively. The mean dose and duration of using isotretinoin were 0.55 ± 0.19 mg/kg and 7.11 ± 1.21 months, respectively. 54% of patients had lethargy, 41.6% had myalgia and 46.9% had low back pain. Of the patients with low back pain, 54.7% (29 cases) had inflammatory low back pain and 45.3% (24 cases) had mechanical low back pain (**Table 1**).

29 cases had inflammatory low back pain, 5 cases had sacroiliitis and one case had positive RF, the means of ESR, CRP and ANA were 19.01 ± 12.74 Mm/hr, 3.43 ± 1.27 Mg/litr and 1.31 ± 0.90, respectively (**Table 2**).

There was no significant correlation between dosage and duration of using isotretinoin with ESR, CRP and ANA (P>0.05), also there was no significant relationship between dosage and duration of using isotretinoin with sacroiliitis and positive RF (P>0.05). Also there was no significant relationship between severity of disease with ESR, CRP and ANA, sacroiliitis and positive RF (P>0.05). In addition, there was no significant relationship between age and gender with ESR, CRP and ANA, sacroiliitis and positive RF (P>0.05).

Discussion

Here in this study, we indicated that incidence of lethargy, myalgia, sacroiliitis, increased CRP and positive RF is more frequent among

Table 1. Variables of study

			Patients group (n=113)
Age, years, mean ± SD			22.32 ± 3.85
Gender	Male		33 (29.2%)
	Female		80 (70.8%)
Severity of acne	Moderate		25 (22.1%)
	Severe		88 (77.9%)
Dose, mg/kg/day, mean ± SD			0.55 ± 0.19
Duration of treatment, months, mean ± SD			7.11 ± 1.21
Symptoms	Lethargy		61 (54%)
	Myalgia		47 (41.6%)
	Low back pain		53 (46.9%)
		Mechanical	24 (45.3%)
		Inflammation	29 (54.7%)

Table 2. Para-clinical variables of patients

		Patients with inflammatory low back pain (n=29)
MRI finding	Sacroiliitis	5 (20.8%)
Lab data	ESR, Mm/hr, mean ± SD	19.01 ± 12.74
	CRP, Mg/litr, mean ± SD	3.43 ± 1.27
	ANA, mean ± SD	1.31 ± 0.90
	Positive RF	1 (4.2%)

patients who had been under treatments of isotretinoin for acne vulgaris. Recent studies have evaluated the effects and side effects of isotretinoin and reported that the use of isotretinoin might be associated with different complications. In a study by Baykal Selçuk and colleagues in 2016, they evaluated 73 patients who had received isotretinoin for treatments of acne vulgaris and indicated that the incidence of sacroiliitis is high among these patients and suggested that patients who receive isotretinoin must be questioned about any history of sacroiliitis or any sacroiliitis findings [11]. These findings are in line with our findings. We indicated that sacroiliitis is found in patients treated with isotretinoin. Furthermore, we showed that the frequency of sacroiliitis is more in those patients who already have low back pain. Different reports have also been published about the occurrence of sacroiliitis in patients treated with isotretinoin. Atabek, Dinçer, Pedraz, Kavadar and Levinson have reported some cases of sacroiliitis following isotretinoin usage [12-16]. All these data put emphasis on the possible relation of isotretinoin and sacroiliitis. We also indicated that sacroiliitis is more frequent among those patients with low back pain. Tasdelen and others have indicated that isotretinoin has some potentials to induce arthritis and mimic rheumatoid arthritis and axial spondyloarthritis [17]. They also suggested that rheumatoid laboratory data might be helpful for diagnosis of this complication. In this study we showed that positive RF and increased CRP levels are more frequent in patients with low back pain treated with isotretinoin. This issue might give us this clue that in those patients with physical symptoms, more attention must be given to laboratory data.

There have been also studies which evaluated other complications associated with isotretinoin treatments. In a study by Kaymak and colleagues in 2008, they evaluated 89 patients who were under treatments of isotretinoin for acne vulgaris. Finally they indicated that increased creatine phosphokinase (CPK) and myalgia is observed frequently among patients and this phenomenon is benign [18]. Here we also showed that myalgia is observed in 88.7% of patients who have low back pain and under treatments of isotretinoin. In another study by Qamar Masood and others, performed in 2010, they claimed that isotretinoin might induce reversible hypothyroidism and by this mechanism, lethargy could be observed in patients treated with isotretinoin [19]. An interesting issue of our study was that we showed that 100% of patients with low back pain had experienced lethargy. Unfortunately we cannot discuss this issue because we didn't evaluate thyroid hormone. Saklamaz and others have also showed that isotretinoin could increase CRP levels and this issue could be more significant when signs and symptoms be present [20]. These findings are also in line with our study. We showed that the amounts of CRP is higher in patients with low back pain. Taken together, based on the results of our study and former studies we conclude that much attention must be given to patients treated with isotretinoin regarding to sacroiliitis and rheumatoid diseases especially when symptoms such as low back pain are present.

Disclosure of conflict of interest

None.

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