Injection site reactions due to the use of biologics in patients with psoriasis: A retrospective study

To the Editor: Injection site reactions (ISRs) are localized reactions ranging from erythema, pruritus, and pain at the injection site.[1] However, real-world data on ISRs to various biologics are limited, and ISRs to those used to treat moderate to severe psoriasis can affect treatment compliance.

We identified 19 cases of ISRs in 18 out of 141 psoriasis cases treated with biologics at the CHA Bundang Medical Center from 2020 to 2021 (Table I). The highest prevalence of ISRs was to ixekizumab (55.0%) and guselkumab (14.3%). The demographics and clinical characteristics are shown in Table II.

Although the specific etiology is not identified, ISRs can be categorized as physical due to needle or injection techniques, irritant due to properties of injected solutions, and allergic due to immediate and delayed allergic reactions.[2] Although autoinjectors are known to reduce ISRs,[2] 2 patients (patients 3 and 8) developed ISRs after switching to autoinjectors, possibly because of injection techniques.

Moreover, female patients with a low body mass index (BMI) and comorbidities, such as fibromyalgia and depression, are more susceptible to ISRs.[3] In this study, 11 patients (61%) were women, and the mean BMI was 23.3 ± 5.3 kg/m^2, which was similar to the mean BMI of Korean patients with psoriasis.[4] Two patients (patients 3 and 4) had psychological factors and 1 patient (patient 11) had fibromyalgia.

The most common symptom was erythema (n = 14, 73.7%) and the most common location was the arm (n = 12, 63.2%). ISRs occurred after the first injection in 11 patients (57.9%) and appeared within 1 hour after the injection in 10 patients (52.6%). No patient underwent treatment for ISRs, and symptoms usually spontaneously resolved within several days. Patients were instructed the following to reduce ISRs: rotate injection sites, inject slowly, and warm biologics at room temperature before the injection. All but 1 patient showed recurrence of ISRs. None of them discontinued treatments.

In patient 11, ISRs occurred again even after shifting from ixekizumab to risankizumab, but symptoms were more tolerable and lasted for a shorter time. This was consistent with the result of our study that ixekizumab had a greater effect on ISRs than other biologics. Patient 11 could also be more susceptible to ISRs due to low BMI, fibromyalgia, and female sex.

Table I. Prevalence rates of injection site reactions

Biologics (N = 141)	Prevalence rate of ISRs, n (%)
Ixekizumab (n = 20)	11 (55.0)
Guselkumab (n = 42)	6 (14.3)
Adalimumab (n = 11)	1 (9.1)
Risankizumab (n = 14)	1 (7.1)
Ustekinumab (n = 22)	0
Secukinumab (n = 32)	0

ISRs, Injection site reactions.

Pain was more associated with ISRs to ixekizumab than to other biologics (7/11 [63.6%] vs 2/8 [25%]), albeit not significant (Fisher's exact test, P = .059). Unlike other biologics, ixekizumab contains citrate and sodium chloride, which contribute to injection site pain.[2] Chabra et al[5] compared patients treated with commercially available ixekizumab and citrate and sodium chloride–free ixekizumab, and they found that the latter was associated with reduced injection site pain and ISRs. Therefore, citrate and sodium chloride seem to contribute to the high prevalence of ISRs to ixekizumab.

This study was limited to a single center in Korea with a small sample size and dependent on the patients' self-report.

ISRs are tolerable and manageable and are not correlated with the efficacy of biologics.[1] However, ISRs can negatively affect treatment compliance of patients. Therefore, patients should be educated about ways to reduce ISRs.[2]

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Table II. Demographics and clinical characteristics of patients with injection site reactions

No.	Biologic	Sex	Age (y)	Location	Injection no. at onset of 1st ISR (inj)	Onset after inj	Duration	Symptom/s	Recurrence	BMI (kg/m$^{2)}$	Comorbidity
1	Ixekizumab	F	73	Thigh	1st	1 d	2-3 d	Erythema, pain, edema	Yes	—	
2	Ixekizumab	F	52	Arm	1st	Several hrs	1 d	Erythema, pain	Yes	22.7	Hyperlipidemia
3	Ixekizumab	F	54	Abdomen	14th	2-3 d	Continuous	Erythema, pain, eczema	Yes	38	Schizophrenia
4	Ixekizumab	F	60	Abdomen	1st	Immediately	1 h	Pain	Yes	—	Panic disorder
5	Ixekizumab	M	31	Arm	1st	1 h	2-3 d	Erythema, pruritus, edema	Yes	20.7	Hepatitis
6	Ixekizumab	F	55	Abdomen	1st	Immediately	3-4 d	Erythema, pruritus, pain, edema	Yes	26.1	Asthma
7	Ixekizumab	M	30	Arm	1st	1 h	1-2 d	Erythema, pain, edema	Yes	—	
8	Ixekizumab	F	40	Arm	25th	Several hrs	7 d	Erythema	No	16.6	Chronic kidney disease, urinary stone
9	Ixekizumab	M	31	Arm	1st	Immediately	2-3 d	Edema	Yes	—	
10	Ixekizumab	M	51	Arm	16th	Immediately	1 day	Pain, edema	Yes	23	
11	Ixekizumab	F	49	Abdomen	1st	Immediately	10 d	Erythema, pruritus, pain	Yes	18.5	Fibromyalgia
	Risankizumab			Arm	1st	1 d	2-3 d	Erythema, pruritus	Yes		
12	Guselkumab	M	49	Arm	5th	1 d	1-2 d	Erythema, pruritus	Yes	22.4	Diabetes mellitus
13	Guselkumab	F	54	Arm	5th	Several hrs	2-3 d	Erythema	Yes	24.1	Hypothyroidism
14	Guselkumab	M	40	Abdomen	7th	Several hrs	2-3 d	Erythema, pruritus, edema	Yes	22.5	
15	Guselkumab	F	28	Arm	3rd	1 h	3 h	Pruritus, wheal	Yes	23.1	Epilepsy
16	Guselkumab	F	64	Arm	1st	Several hrs	Continuous	Pain	Yes	—	
17	Guselkumab	F	32	Arm	4th	Immediately	1-3 d	Erythema, pain, edema	Yes	—	
18	Adalimumab	M	54	Abdomen	1st	1 h	1 d	Erythema, pruritus	Yes	21.4	

BMI, Body mass index; *ISR*, injection site reactions.

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Conflict of interest

None disclosed.

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