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. 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. Although autoinjectors are known to reduce ISRs, 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. In this study, 11 patients (61%) were women, and the mean BMI was 23.3 ± 5.3 kg/m², which was similar to the mean BMI of Korean patients with psoriasis. 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.

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. Chabra et al 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. However, ISRs can negatively affect treatment compliance of patients. Therefore, patients should be educated about ways to reduce ISRs.

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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.
| No. | Biologic   | Sex | Age (y) | Location | Injection no. at onset of 1st ISR (inj) | Onset after inj | Duration | Symptom/s                          | Recurrence | BMI (kg/m²) | 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                                    | Immediately    | 1 h      | 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                  |
| 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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