Which Areas Are Still Left in Biologics Responsive Korean Patients with Moderate to Severe Plaque Psoriasis

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Background: Psoriasis localized to certain body areas, such as the scalp, nails, palms, soles, intertriginous regions, and genital regions, is reportedly difficult to treat.
Objective: To investigate the biologics-resistant areas in South Korean patients with psoriasis treated with biologics.
Methods: The study included 50 patients with chronic moderate to severe plaque psoriasis from the Pusan National University Hospital and Chosun University Hospital between October 2019 and September 2020. The patients had at least one psoriatic lesion, were treated with biologics for more than six months, and exhibited a partial or good response (reaching a Psoriasis Area and Severity Index [PASI] score of 1~5 after biologics treatment).
Results: A total of 50 patients with psoriasis (32 male, mean±standard deviation 47.8±11 years), with a median PASI score of 1.8, were included. The most common biologics-resistant areas were the anterior lower leg (56.0%), followed by the knee (48.0%) and posterior lower leg (42.0%). The proportion of biologics-resistant areas were obtained for body regions traditionally considered as difficult-to-treat entities, including the fingernails (10.0%), toenails (14.0%), scalp (38.0%), palm (12.0%), sole (14.0%), and genital areas (10.0%).
Conclusion: This study determined the biologics-resistant areas in South Korean patients, successfully treated with biologics, in a real-world clinical setting.

Keywords: Biologics, Korea, Psoriasis, Quality of life

INTRODUCTION

Psoriasis is a common, chronic, inflammatory, multisystem disease of the skin and joints, which accounts for 2%~4% of the Western population and 0.5% of the South Korean population[1,2]. Psoriasis localized to certain areas of the body, such as the scalp, nails, palms, soles, intertriginous regions, and genital regions, is reportedly difficult to treat[3-5]. Several biologics have been widely used to treat patients with moderate to severe psoriasis[6]. Although many patients with moderate to severe psoriasis completely or partially responded to various biologics, biologics-resistant areas were observed in some patients[4]. Persistent lesions, even a small area, affect the quality of life of patients[7]. Therefore, it is necessary to identify the biologics-resistant body regions. However, only one Western study has been reported[8]. This study is aimed to investigate the biologics-resistant areas in Asian patients, especially South Koreans, who were reportedly less responsive to biologics than non-Asian patients[9,10].

MATERIALS AND METHODS

The study included 50 patients with moderate to severe plaque psoriasis from the Pusan National University Hospitals (Busan and Yangsan) and Chosun University Hospital between October 2019 and September 2020. The patients had at least one psoriatic lesion, were treated with biologics for more than six months, and exhibited a partial or complete response to biologics (reaching a Psoriasis Area and Severity Index [PASI]

score of 1~5 after biologics treatment). All 50 patients were treated with biologics on a regular basis as prescribed.

Body areas were divided into 24 regions, namely, the 1) body front side (13 regions), which included the scalp, face, neck, chest, abdomen, anterior upper arm, anterior forearm, palm, genital, anterior thigh, knee, anterior lower leg, and dorsum of the foot; 2) body backside (nine regions), which included the back, posterior upper arm, elbow, posterior forearm, dorsum of the hand, buttock, posterior thigh, posterior lower leg, and sole; and 3) nails (two regions), which included the fingernails and toenails.

All patients' medical records, PASI scores, and biologics-resistant areas were investigated. All analyses were performed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA). The Pearson's chi-squared test was performed to evaluate the difference in treatment-resistant areas, according to the types of biologics. In all analyses, values with a $p<0.05$ were considered statistically significant. The study was approved by the institutional review board of Pusan National University Hospital (IRB No. 2108-005-105). The patients in this manuscript have given written informed consent to publication of their case details.

RESULTS

A total of 50 patients with well-treated moderate to severe psoriasis were analyzed in this study (Table 1). The mean age was 47.8±11 years, and the male-to-female ratio was 1.78 (32:18). The mean duration of the disease was 17.5±7.5 years. The median PASI score upon initiating biologics treatment was 15, and the current median PASI score was 1.8. This indicated a PASI reduction of 87.9%. There were eight nail psoriasis and thirteen psoriatic arthritis cases. Approximately two-fifths (19/50, 38.0%) of patients had comorbidities, the most common of which was hypertension (n=10, 20.0%), followed by diabetes mellitus (n=5, 10.0%) and hypothyroidism (n=3, 6.0%). Twelve patients had a family history of psoriasis.

Various previous treatments were used before biologics (Table 2). All patients had been treated with narrow-band ultraviolet B. The most commonly used previous treatments included methotrexate (n=28, 56.0%), followed by cyclosporine (n=24, 48.0%) and acitretin (n=5, 10%). Eight patients were previously treated with biologics. Among the eight patients, four received one biologic agent, while the remaining patients received two biologic agents. The previously used biologics

Table 1. Patient demographics

Content	Variable
No. of patients	50
Male	32 (64.0)
Age (yr)	47.8±11
Body weight (kg)	69.3±8.3
BMI (kg/m^2)	23.7±2.2
Duration of disease (yr)	17.5±7.5
PASI at starting biologics	15 (12.2~18.1)
Current PASI	1.8 (1.4~2.8)
PASI reduction (%)	87.9 (81.3~92)
Nail psoriasis	8 (16.0)
Psoriatic arthritis	13 (26.0)
Comorbidities	
Hypertension	10 (20.0)
Diabetes mellitus	5 (10.0)
Hypothyroidism	3 (6.0)
Angina	1 (2.0)
Family history of psoriasis	12 (24.0)

Values are presented as number (%), mean±standard deviation, or median (interquartile range). PASI: Psoriasis Area and Severity Index, BMI: body mass index.

Table 2. Previous treatments and current biologics

Contents	Number (%)
Previous treatments	
NB-UVB	50 (100)
Methotrexate	28 (56.0)
Cyclosporine	24 (48.0)
Acitretin	5 (10.0)
Biologics	8 (16.0)
Number of biologics used	
One biologics	4 (8.0)
Two biologics	4 (8.0)
Type of biologics used	
Secukinumab	6 (12.0)
Ustekinumab	4 (8.0)
Adalimumab	2 (4.0)
Current biologics	
Ustekinumab	16 (32.0)
Secukinumab	14 (28.0)
Guselkumab	12 (24.0)
Ixekizumab	7 (14.0)
Adalimumab	1 (2.0)

NB-UVB: narrow-band ultraviolet B.

Table 3. Biologics-resistant areas

Content	Number (%)
Head and neck	
Scalp	19 (38.0)
Face	14 (28.0)
Neck	5 (10.0)
Trunk	
Chest	6 (12.0)
Abdomen	10 (20.0)
Back	17 (34.0)
Buttock	10 (20.0)
Genital	5 (10.0)
Nails	
Fingernails	5 (10.0)
Toenails	7 (14.0)
Upper limbs	
Anterior upper arm	8 (16.0)
Anterior forearm	10 (20.0)
Posterior upper arm	7 (14.0)
Elbow	11 (22.0)
Posterior forearm	9 (18.0)
Palm	6 (12.0)
Dorsum of hand	8 (16.0)
Lower limbs	
Anterior thigh	14 (28.0)
Knee	24 (48.0)
Anterior lower leg	28 (56.0)
Posterior thigh	13 (26.0)
Posterior lower leg	21 (42.0)
Dorsum of foot	8 (16.0)
Sole	7 (14.0)

Fig. 1. Distribution of the biologics-resistant areas among all included patients (n=50).

were secukinumab for six patients (12.0%), ustekinumab for four (8.0%), and adalimumab for two (4.0%).

In this study, the current biologics included ustekunumab (n=16, 32.0%), secukinumab (n=14, 28.0%), guselkumab (n=12, 24.0%), ixekizumab (n=7, 14.0%), and adalimumab (n=1, 2.0%).

The biologics-resistant areas are summarized in Table 3 and Fig. 1. The most common biologics-resistant areas were the anterior lower leg, followed by the knee, posterior lower leg, scalp, and back. Among the head and neck regions, the biologics-resistant areas were the scalp (n=19, 38.0%) and face (n=14, 28.0%). In our study, the category "neck" includes both the anterior and posterior necks. And the category "face" includes all areas of the face,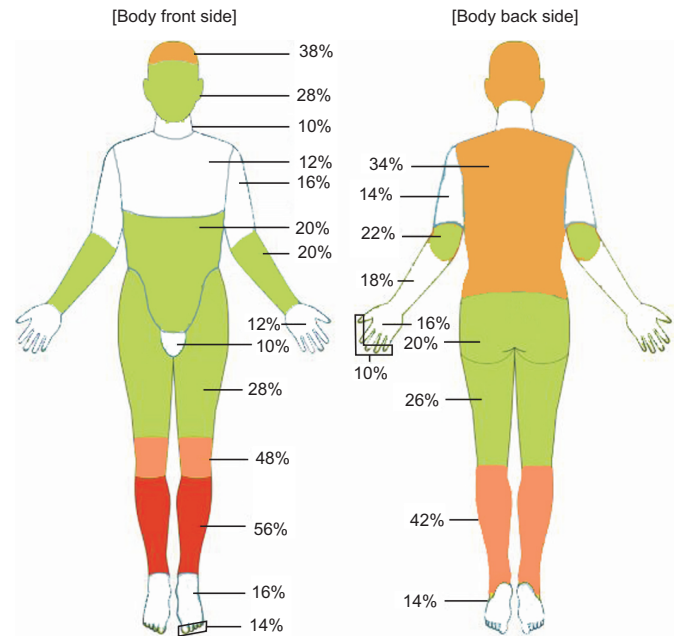 not just the area adjacent to the scalp. The thing is that the posterior neck adjacent to the scalp is more frequent than the anterior neck. And, the face adjacent to the scalp is more frequent than the rest area of the face. For the trunk region, the back (n=17, 34.0%), abdomen (n=10, 20.0%), and buttocks (n=10, 20.0%) were resistant to biologics. For the nails, the toenails (n=7, 14.0%) exhibited a poorer response than the fingernails (n=5, 10.0%). For the upper extremities, the elbow (n=11, 22.0%) and anterior forearm (n=10, 20.0%) were frequently resistant to biologics. Among the lower extremities, the anterior lower leg (n=28, 56.0%), knee (n=24, 48.0%), posterior lower leg (n=21, 42.0%), anterior thigh (n=14, 28.0%), and posterior thigh (n=13, 26.0%) were frequently resistant.

DISCUSSION

Psoriasis is a common, chronic, inflammatory, multisystem disease of the skin and joints, accounting for 2%~4% of the Western population and 0.5% of the South Korean population[1,2]. Several factors should be considered in psoriasis treatment. These include the site of the lesions, treatment history, cost, and comorbidities[4]. Psoriasis localized to certain areas of the body, such as the scalp, nails, palms, soles, intertriginous regions, and genital regions, requires special intervention[3-5,11]. In these areas, psoriatic lesions may be difficult to control due

to the unrealistic expectations of the patients, time-consuming applications, side effects, unsatisfactory cosmesis, restricted drug bioavailability, and treatment adherence[4]. Topical treatment is the first-line treatment for patients presenting with an isolated lesion involving these sites[12]. However, systemic therapy is warranted in severe cases, involving these sites, or cases, that were refractory to topical therapy[11,12].

Several biologics have been used in patients with moderate to severe psoriasis[6]. Although biologics are significantly more effective than conventional systemic therapy, some areas were resistant to biologics treatment[4]. These sites were classified as "biologics-resistant areas." Only one previous study has reported on biologics-resistant areas[8]. Hjuler et al.[8] described the biologics-resistant areas in 146 patients treated with biologics. Based on their results, the most common biologics-resistant areas were the anterior lower leg (n=72, 49.3%), followed by the posterior lower leg (n=36, 24.7%), elbow (n=52, 35.6%), scalp (n=28, 19.2%), knee (n=26, 17.8%), and back (n=26, 17.8%) (Table 4).

Compared with the study by Hjuler et al.[8], our study identified the regions which were more frequently resistant to biologics. These included the scalp, face, neck, back, anterior upper arm, anterior forearm, posterior upper arm, palm, anterior thigh, knee, posterior thigh, posterior lower leg, dorsum of the foot, and sole (Table 4).

The most common biologics-resistant areas in our study were the anterior lower leg (n=28, 56.0%), followed by the knee (n=24, 48.0%) and posterior lower leg (n=21, 42.0%). A possible cause for the predominance of the lower legs is the Koebner's phenomenon[13]. Physical trauma triggers psoriatic lesions at injured sites through proinflammatory cytokine secretion, autoantigen unmasking, or both[13].

Traditionally, there were the regions accepted as difficult-to-treat areas (scalp, nails, palms, soles, intertriginous or genital areas) in psoriasis[4]. Among them, except scalp responded well to biologics in our study.

According to Revicki et al.[7], the number of patients with "clear" skin, who had a Dermatology Life Quality Index (DLQI) of 0, was almost twice that of patients with "minimal" psoriasis. Achieving a DLQI of 0 is most significant when the PASI score is 100. Thus, achieving a PASI of 100 is important to improve the quality of life of patients. Therefore, it is crucial to treat biologics-resistant areas.

The Asian population was reportedly less likely to respond clearly to biologics, compared with the non-Asian population[9].

Table 4. Comparison with a previous report on biologics-resistant areas

Content	Hjuler et al.[8] (n=146)	Our study (n=50)	p-value
Head and neck			
Scalp	28 (19.2)	19 (38.0)	0.007
Face	0 (0)	14 (28.0)	<0.001
Neck	0 (0)	5 (10.0)	0.001
Trunk			
Chest	7 (4.8)	6 (12.0)	0.099
Abdomen	14 (9.6)	10 (20.0)	0.053
Back	26 (17.8)	17 (34.0)	0.017
Buttock	23 (15.8)	10 (20.0)	0.489
Genital	5 (3.4)	5 (10.0)	0.127
Nail			
Fingernails	19 (13.0)	5 (10.0)	0.575
Toenails	16 (11.0)	7 (14.0)	0.564
Upper limb			
Anterior upper arm	6 (4.1)	8 (16.0)	0.009
Anterior forearm	11 (7.5)	10 (20.0)	0.014
Posterior upper arm	6 (4.1)	7 (14.0)	0.023
Elbow	52 (35.6)	11 (22.0)	0.075
Posterior forearm	21 (14.4)	9 (18.0)	0.540
Palm	5 (3.4)	6 (12.0)	0.033
Dorsum of hand	18 (12.3)	8 (16.0)	0.509
Lower limb			
Anterior thigh	19 (13.0)	14 (28.0)	0.015
Knee	26 (17.8)	24 (48.0)	<0.001
Anterior lower leg	72 (49.3)	28 (56.0)	0.414
Posterior thigh	16 (11.0)	13 (26.0)	0.010
Posterior lower leg	36 (24.7)	21 (42.0)	0.020
Dorsum of foot	6 (4.1)	8 (16.0)	0.009
Sole	2 (1.4)	7 (14.0)	0.001

Values are presented as number (%).

Reich et al.[9] described that the proportion of patients, who achieved a PASI of 100, was greater in the non-Asian population than in the Asian population (South Korea and Taiwan) for both guselkumab and adalimumab. Based on these findings, biologics-resistant areas are more commonly detected among Asian populations than among non-Asian populations. Our study obtained meaningful results by comparing data, involving Asian populations, with that of the study by Hjuler et al.[8], which involved a non-Asian population.

Our study revealed no statistically significant difference

between the types of current biologics.

This study had some limitations. First, patients, who were unsuccessfully treated with biologics, were excluded. Second, the duration of biologics treatment varied between the patients. Third, relapsing and persistent lesions were not distinguished. Fourth, there was no information on the pretreatment body distribution of psoriasis. Lastly, there was no information on the effect of biologics-resistant areas on the quality of life of patients with psoriasis.

In conclusion, this study determined the biologics-resistant areas among patients with psoriasis, successfully treated with biologics, in a real-world clinical setting. The most common biologics-resistant areas were the anterior lower leg, followed by the knee and posterior lower leg. Since some body areas are more resistant to biologics than others, special attention is required to improve the patients' quality of life. The results of this study will aid dermatologists in understanding the biologics-resistant areas in South Korean patients with moderate to severe psoriasis.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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Research data are not shared.

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