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Algorithm for Selecting Ideal Biologic Treatment for Psoriasis

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Abstract

Biologics are the standard treatment for moderate-to-severe psoriasis due to their efficacy and safety. However, the selection of appropriate biologics is complicated by patient characteristics, treatment regimen, and cost. We constructed an algorithm to select biologics based on psoriasis type (psoriasis vulgaris or psoriasis arthritis), Psoriasis Area and Severity Index (PASI) score (≥ 20 or <20) and body mass index (≥ 25 or <25). To validate our algorithm, we retrospectively analyzed 134 patients treated with biologics. Based on the algorithm, patients were categorized into the following treatment groups: infliximab-appropriate (IFX-ap), n=33; adalimumab-appropriate (ADA-ap), n=44; and ustekinumab-appropriate (UST-ap), n=57. The relationship between each agent-appropriate group and the efficacy of each agent was analyzed. Among IFX-ap patients (n=33), the reduction in PASI with each treatment was as follows: inflximab (n=13), 93.2 ± 7.4%; adalimumab (n=10), 61.3 ± 29.2%; and ustekinumab (n=10), 87.4 ± 12.8%, with significant differences between infliximab and adalimumab. Among ADA-ap patients (n=44), the reduction in PASI with each treatment was as follows: infliximab (n=10), 83.3 ± 23.3%; adalimumab (n=12), 84.9 ± 23.6%; and ustekinumab (n=14), 73.0 ± 29.8%, with no significant differences between treatments. Among UST-ap patients, the reduction in PASI with each treatment was as follows: infliximab (n=15), 94.9 ± 6.0%; adalimumab (n=14), 73.0 ± 23.0%; and ustekinumab (n=28), 87.2 ± 18.0%, with a significant difference between treatment with adalimumab and ustekinumab. These results suggest that appropriate biologics selection results in increased efficacy of treatment.

Keywords: Psoriasis; Infliximab; Adalimumab; Ustekinumab; Algorithm

Introduction

Biologic agents have revolutionized the treatment of psoriasis by showing excellent efficacy without the severe adverse effects that can occur with conventional systemic therapies. These agents thereby provide relief to patients suffering from severe psoriasis who have failed or have contraindications for conventional systemic therapies. The biologics infliximab (IFX), adalimumab (ADA), and ustekinumab (UST) are currently available for use in psoriasis treatment in Japan. Clinical trials of these biologics in Japan have demonstrated their high efficacy and sufficient tolerability, which is consistent with previous international clinical trials [1-3]. However, despite the high efficacy of these biologics, 20% to 30% of patients remain insufficient responders or non-responders.

Improving the response rate of patients to treatment requires the appropriate selection of biologics. We therefore constructed an algorithm, based on current consensus and our own experience, to select biologics based on psoriasis type (psoriasis vulgaris [PsV] or psoriatic arthritis [PsA]), Psoriasis Area and Severity Index (PASI) (≥ 20 or <20), and body mass index (BMI) (≥ 25 or <25).

Here, we confirmed the efficacy and reliability of the constructed algorithm using the records of patients treated with biologics in our hospital. We then analyzed the relationship between the efficacies of IFX, ADA, and UST based on PASI improvement in treatment-appropriate groups based on the algorithm.

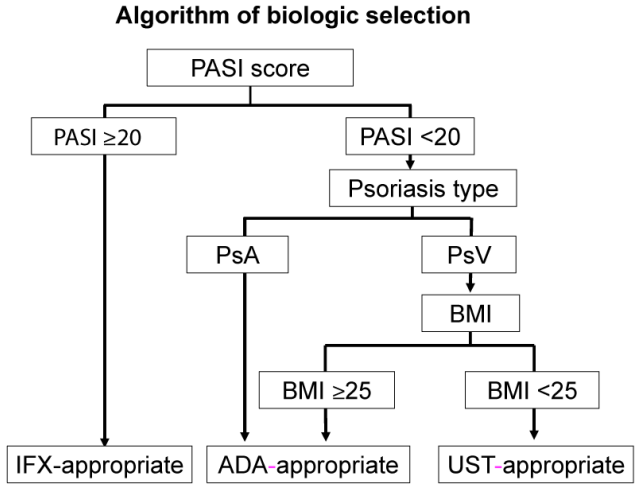

Figure 1: Algorithm of biologic selection. Patients were classified into IFX-, ADA-, or UST-appropriate groups based on PASI (≥ 20 or <20), psoriasis type (PsV or PsA), and BMI (≥ 25 or <25).

Material and Methods

Construction of algorithm

The algorithm was constructed according to the features of each biologic agent (Figure 1). For example, IFX has more potent efficacy

than ADA and UST, indicating its comparatively increased efficacy against severe cases with PASI 20 and over (PASI ≥ 20 [PsV and PsA]). Anti-TNF-α agents are more effective in treating arthritis than UST, indicating that these agents might be preferable over UST for the treatment of PsA [4-6]. In addition, as anti-TNF-α agents carry a reduced risk of cardiovascular events [7-9], they might be preferable for treating patients with high BMI. Given that UST shows higher efficacy in cases with lower BMI than 25 [10], this drug may be preferable for treating patients with PsV and BMI <25.

Patients

Patients previously treated with biologic agents between 2010 to 2013, aged ≥ 20 years, diagnosed with PsV or PsA, and with PASI ≥ 10 were retrospectively analyzed. Patients with previous exposure to biologics were excluded.

Efficacy assessments

Patients receiving each biologic treatment were assigned to the following agent-appropriate groups: infliximab-appropriate (IFX-ap), adalimumab-appropriate (ADA-ap), and ustekinumab-appropriate (UST-ap). Clinical efficacy was evaluated based on PASI score reduction after comparing PASI at baseline with that at Week 14 for IFX, Week 16 for ADA, and Week 16 for UST. Efficacies between IFX-ap, ADA-ap, and UST-ap groups for each treatment were assessed. In addition, the efficacies between treatment with IFX, ADA, and UST in each of the three groups were assessed.

Treatments

IFX was intravenously administered (5 mg/kg) at Weeks 0, 2, and 6 and every 8 weeks thereafter. ADA was administered via subcutaneous injection (80 mg/kg) at Week 0 and every 2 weeks (40 mg/kg) thereafter. UST was administered in patients via subcutaneous injection (45 mg/kg) at Weeks 0 and 4 and every 12 weeks thereafter. These patients did not receive other systemic medication during biologic treatment.

Statistical analysis

Statistical analysis was performed using the SPSS statistical package (SPSS Inc., Chicago, IL, USA). Data were analyzed using the Kruskal-Wallis test, and differences between groups were analyzed using the Mann-Whitney U test. All values were expressed as mean and standard deviation (S.D.). $P<0.05$ was considered statistically significant.

Results

Patients

A total of 134 patients who had been previously treated with IFX (n=46), ADA (n=36), or UST (n=52) to assess the validity of the algorithm were enrolled. Based on the algorithm, patients were assigned to one of three agent-appropriate groups (IFX-ap, ADA-ap, or UST-ap).

Table 1 shows baseline demographics and background characteristics by treatment. No significant differences were noted between patients treated with each biologic in terms of PASI at baseline, disease duration, body weight, or BMI. However, significant differences in terms of age and type of psoriasis were observed.

The number of IFX-treated patients assigned to each agent-appropriate group based on the algorithm was as follows: IFX-ap (n=13), ADA-ap (n=18), and UST-ap (n=15). The number of ADA-treated patients assigned to each agent-appropriate group based on the algorithm was as follows: IFX-ap (n=10), AD-ap (n=12), and UST-ap (n=14). The number of UST-treated patients assigned to each agent-appropriate group based on the algorithm was as follows: IFX-ap (n=10), ADA-ap (n=14), and UST-ap (n=28). The total number of patients assigned to each agent-appropriate group based on the algorithm was as follows: IFX-ap (n=33), ADA-ap (n=44), and UST-ap (n=57).

	Infliximab (IFX)	**Adalimumab (ADA)**	**Ustekinumab (UST)**
Number of patients	46	36	52
Age, years (mean ± SD)	22-74 (48.6 ± 12.1)	22-77 (51.2 ± 13.8)	24-88 (60.1 ± 16.7)*
Gender (Male:Female)	38:8	25:11	41:11
Psoriasis type (PsV:PsA)	38:8	26:10	49:2*
BMI (mean ± SD)	18.4-34.9 (24.6 ± 4.1)	18.4-34.9 (24.6 ± 4.1)	18.4-34.3(24.3 ± 3.6)
PASI score (base line)	10.2-65.0 (21.2 ± 12.7)	10.0-54.0(19.1 ± 9.7)	10.1-33.6 (16.3 ± 6.0)
PASI score (end point)	0.0-16.0 (2.0 ± 2.9)	0.0-31.2(8.5 ± 9.6)	0-20.0 (2.3 ± 3.3)
Improvement of PASI	90.2 ± 14.0%	77.3 ± 24.7%	85.7 ± 21.1
PASI-75	42/46 (91.3%)	25/35 (71.4%)	44/52 (84.6%)
IFX-appropriates (n)	13	10	10
ADA-appropriates (n)	18	12	14
UST-appropriates (n)	15	14	28
*Significant differences in terms of age and type of psoriasis were observed			

Table 1: Patient characteristics for each treatment group.

Treatment efficacy of each biologic agent

Figure 2 shows the PASI score reductions for each group and treatment. When evaluating outcomes by each agent-appropriate group, the reduction in PASI among IFX-ap patients in each treatment group was as follows: infliximab-treated (IFX-treat) (n=13), 93.2 ± 7.4%; adalimumab-treated (ADA-treat) (n=10), 61.3 ± 29.2%; and ustekinumab-treated (UST-treat) (n=10), 87.4 ± 12.8%. Significant differences were observed between IFX-treat and ADA-treat, and UST-treat and ADA-treat groups. The reduction in PASI among ADA-ap patients in each treatment group was as follows: IFX-treat (n=10), 83.3 ± 23.3%; ADA-treat (n=12), 84.9 ± 23.6%; and UST-treat (n=14), 73.0 ± 29.8%. No significant differences were observed between each treatment. The reduction in PASI among UST-ap patients in each treatment group was as follows: IFX-treat (n=15), 94.9 ± 6.0%; ADA-treat (n=14), 73.0 ± 23.0%; and UST-treat (n=28), 87.2 ± 18.0%, with a significant difference between treatment with ADA- and

UST-treat groups. These results suggest efficacy may increase when using appropriate biologics for treatment.

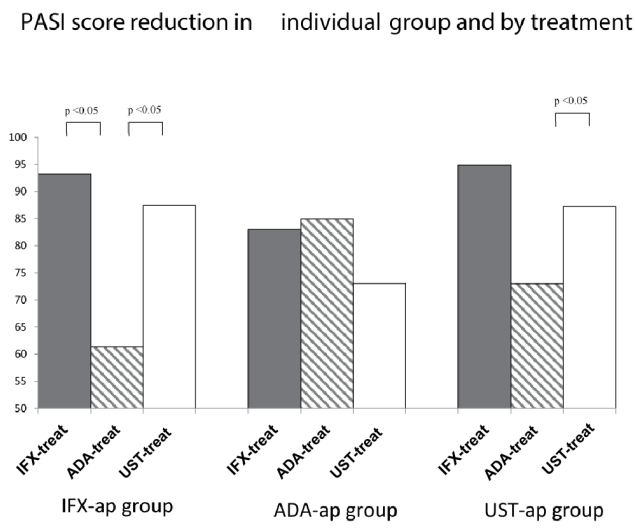

Figure 2: PASI score reduction in each group and by treatment. In cases classified as IFX-appropriate, a significant difference in score reduction was noted between patients treated with infliximab and those treated with adalimumab, and between patients treated with ustekinumab and those treated with adalimumab. In cases classified as ADA-appropriate, no significant differences were noted between any treatment groups. In cases classified as UST-appropriate, a significant difference in score reduction was noted between those treated with adalimumab and those treated with ustekinumab.

Discussion

In Japan, IFX and ADA were approved to treat psoriasis in 2010, with UST receiving approval in 2011. Biologics have greater efficacy and lower risk for organ toxicity than conventional treatments, such as cyclosporine, retinoids, and methotrexate. In clinical trials, rates of achieving 75% or greater improvement in PASI (PASI-75) in Weeks 10 to 16 for each biologic were as follows: IFX, 68.6% to 80.4% [1,11]; ADA, 62.8% to 71.0% [2,12]; and UST; 59.4% to 66.7% [3,13]. These results suggest that approximately 20% to 30% of patients did not achieve sufficient efficacy and were considered insufficient responders or non-responders. Identifying patient clinical factors associated with responses to biologic therapies in psoriasis patients will help in selecting an appropriate drug. Although factors such as smoking, severity of psoriasis, high body weight, BMI, and previous incidence of biologic treatments have been reported to be associated with clinical efficacy [14-18], how these factors affect treatment efficacy and the degree of those effects remain unclear. Here, we constructed an algorithm for the selection of biologics based on psoriasis severity, psoriasis type, and BMI.

Infliximab has shown superior treatment of psoriasis compared to ADA and UST [1-3,11-13], which might make IFX preferable to UST and ADA in cases with of more severe (PASI ≥ 20) psoriasis. Further, IFX and ADA exert potent efficacy on PsA [4-6], making these drugs preferable in patients with arthritis. In addition, anti-TNF-α agents have a decreased risk of cardiovascular events in patients with severe psoriasis [8,9,19]. Therefore, IFX and ADA might be preferable to UST in obese patients with moderate psoriasis. UST is more effective in treating PsV than PsA, and also is also more effective in patients with BMI<25 than in those with BMI ≥ 25 [4,20]. We considered these characteristics of biologic agents in creating an algorithm based on psoriasis type (PsV or PsA), severity of psoriasis (PASI ≥ 20 or <20), and BMI (BMI ≥ 25 or <25).

Given that IFX is extremely potent, patients respond well to this biologic, regardless of their characteristics. However, ADA and UST respond differently based on patient characteristics and should therefore be administered on a targeted basis. For example, patients with PASI ≥ 20 (IFX-ap) do not respond well to ADA, while those with BMI ≥ 25 and PASI<20 (ADA-ap) do not respond well to UST.

Although the current algorithm only accounts for psoriasis type, PASI score, and BMI, we were still able to appropriately assign treatment regimens based on patient characteristics. Biologic agents have demonstrated considerable efficacy and safety for the treatment of psoriasis; however, approximately 20% of patients still withdraw from treatment due to insufficient efficacy [21,22]. Therefore, appropriate agents should be selected for each patient when possible. A limitation of the present study is its retrospective design and small number of cases. To further validate the algorithm, this study should be evaluated using a prospective design with a larger number of patients.

Despite the retrospective nature of our study, our findings suggest that the efficacy of treatment might be improved by the selection of biologic agents deemed appropriate based on patient characteristics.

Conflicts of Interest

HN has received consultancy and speaker honoraria and grants from Tanabe Mitsubishi and AbbVie, and speaker honoraria from Janssen.

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