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Original Article

Comparison of two omalizumab dose-reduction strategies in patients with chronic spontaneous urticaria during the control phase: standard dose maintenance therapy versus extended interval dose reduction

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Abstract: Objective: To compare standard dose maintenance treatment (SDMT) and extended interval dose reduction treatment (EIDRT) in controlling patients with chronic spontaneous urticaria (CSU) during disease control phase, mainly focusing on time to treatment discontinuation, relapse rate, and pharmacoeconomic outcomes. Methods: This retrospective cohort study included 258 CSU patients treated with omalizumab (Xolair®) between May 2023 and April 2025. Patients were divided into SDMT (n=120) and EIDRT (n=138) groups according to their dose-reduction strategy received during disease control phase. Patients in the SDMT group continued to receive omalizumab at a dose of 300 mg every 4 weeks until complete disease control (Urticaria control test [UCT] score ≥ 16) was obtained, followed by treatment discontinuation. In the EIDRT group, the dosing interval was gradually extended to every 8 weeks during the control phase. Demographic characteristics, clinical data, Urticaria Activity Score over 7 days (UAS7), UCT, Chronic Urticaria Quality of Life Questionnaire (CU-QoL), Dermatology Life Quality Index (DLQI), relapse rate after discontinuation, and pharmacoeconomic indicators were collected and analyzed. Results: The EIDRT group demonstrated a significantly longer time to treatment discontinuation (10.27 ± 1.23 mo vs 9.82 ± 1.18 mo, P=0.003) and a lower relapse rate within 6 months after discontinuation (11.59% vs 23.33%, P=0.012), compared to the SDMT group. The EIDRT group required fewer omalizumab administrations (8.21 ± 0.76 vs 9.82 ± 1.25 doses, P < 0.001) and outpatient visits (9.08 ± 1.37 vs 11.35 ± 1.42 visits, P < 0.001) than the control group, with superior pharmacoeconomic outcomes. Multivariate logistic regression analysis identified EIDRT as an independent protective factor for relapse (OR=0.373, 95% CI: 0.189-0.739), whereas higher disease duration (OR=1.063, 95% CI: 1.014-1.115) and concomitant angioedema (OR=2.399, 95% CI: 1.330-4.329) were independently associated with an increased risk of relapse. Conclusion: Compared to SDMT, EIDRT was associated with a longer time to treatment discontinuation, a lower post-discontinuation relapse rate, and improved pharmacoeconomic outcomes in patients with CSU during the control phase.

Keywords: Chronic spontaneous urticaria, omalizumab, standard dose maintenance therapy, extended interval dose reduction therapy

Introduction

Chronic spontaneous urticaria (CSU) is characterized by recurrent wheals, angioedema, or both for over six weeks without an identifiable cause. Although common, CSU substantially impairs patients' quality of life and remains challenging to manage due to its heterogeneous pathophysiology and variable responses to treatment [1, 2]. Omalizumab is a humanized anti-IgE monoclonal antibody (mAb) and represents a major breakthrough in CSU therapy, demonstrating excellent clinical efficacy [3]. However, the optimal strategy for disease control, particularly during dose reduction, remains unclear [4, 5]. Current practice generally involves maintaining the effective dose until complete disease control is achieved, followed by

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discontinuation, which frequently results in relapse and is suboptimal for long-term disease management [6, 7].

The primary goals of CSU treatment are to achieve symptom control, minimize adverse effects, and optimize healthcare resource utilization. Under standard dose maintenance therapy (SDMT), patients continue taking the same dose of omalizumab once every 4 weeks following disease control. While widely adopted, this strategy may not be optimal, as it leads to unnecessary drug exposure and increased healthcare costs. Moreover, abrupt discontinuation after prolonged SDMT often results in rapid symptom recurrence, posing burden on both patient care and healthcare systems [8-10]. Therefore, alternative strategies aimed at reducing drug exposure while maintaining disease control are needed.

Extended interval dosing and reduction therapy (EIDRT) has emerged as an alternative to SDMT. By prolonging the dosing interval, EIDRT allows better adaptation of the immune system and potentially reduce relapse risk. Evidence from other chronic situations suggests that gradual tapering of biologic therapies can promote prolonged remission and improved patient well-being [11]. In CSU, this approach aligns with the 'stepwise' treatment concept, whereby therapy is adjusted according to disease activity and treatment response. EIDRT may help identify balance between efficacy and cost, while offering greater flexibility in managing mild disease fluctuations without compromising overall disease control [12, 13].

Despite its theoretical advantages, robust evidence comparing the efficacy and safety of EIDRT with SDMT in CSU remains limited. An in-depth understanding of the benefits and risks associated with each strategy is essential for developing individualized treatment plans that achieve durable disease control while minimizing economic burden. Therefore, this study aims to address these gaps to provide evidence to guide more rational and cost-effective management of CSU.

Materials and methods

Study design and patients

In this retrospective cohort study, a total of 258 patients with CSU who were treated with omalizumab at Shanghai First People's Hospital Jiuquan Hospital's and Xi'an Fifth Hospital between May 2023 and April 2025 were included. This study was approved by the Institutional Review Board (IRB) of Xi'an Fifth Hospital. Given the retrospective nature of study without additional patient intervention, the requirement for informed consent was waived.

Inclusion criteria: ① Meeting the diagnostic criteria for CSU [14]; ② Receipt of standard initial omalizumab therapy (Xolair®, imported formulation; 300 mg every four weeks for at least six consecutive months) with achievement of disease control (Urticaria Control Test [UCT] score ≥12) after treatment; ③ Age between 18 and 60 years; ④ Complete medical records and efficacy evaluation scales without any missing data.

Exclusion criteria: ① Coexisting chronic inducible urticaria; ② Use of immunosuppressants or other biologics other than omalizumab during the treatment period; ③ Presence of contraindications to omalizumab or experiencing severe adverse reactions necessitating treatment discontinuation; ④ Pregnancy or lactation; ⑤ Adjustment of concomitant medications or significant lifestyle changes during the treatment period that could affect disease control.

Grouping method and treatment plan

Depending on the treatment strategies applied after patients entered the CSU control phase, the 258 patients were assigned to either a SDMT group (n=120) or an EIDRT group (n= 138). Group allocation was based on treatment protocol changes and physician's empirical judgment. Specifically: SDMT was the standard protocol from May 2022 to June 2023, while EIDRT was implemented from July 2023 to April 2024 based on emerging real-world evidence and institutional guidelines. Patients were managed according to the protocol in effect at the time they achieved disease control.

Patients in the SDMT group continued with the standard omalizumab treatment dose and interval (300 mg every 4 weeks) until complete disease control was achieved (UCT score of 16), after which treatment was discontinued. In contrast, patients in the EIDRT group adopted a 'stepwise extended dosing interval' strategy. While maintaining a fixed dose of 300 mg per

administration, the dosing interval was progressively extended beyond the standard 4 weeks. Provided that disease control was maintained (UCT score ≥12), the dosing interval was extended by 1 week at each subsequent administration, up to a maximum interval of 8 weeks. If loss of disease control (defined as a UAS7 score >6 and/or a UCT score <12) occurred during the extension phase, the dosing interval was shortened to the most recent effective interval (e.g., from 7 weeks back to 6 weeks) for the next administration. Interval extension could be reattempted once disease control was re-established. According to international CSU diagnosis and treatment guideline [14], omalizumab treatment was discontinued after evaluation by the attending physician when complete disease control (UCT=16) was maintained for two consecutive follow-ups.

Medical records

Complete baseline demographic and clinical data prior to the adjustment of omalizumab treatment strategies were extracted from the electronic medical record system, including age, sex, body mass index (BMI), education level, smoking status, alcohol consumption, family history of urticaria, disease duration, comorbidities, serum total immunoglobulin E (IgE) level, and treatment for CSU prior to initiation of omalizumab therapy. Serum total IgE levels were measured using an automated chemiluminescence analyzer (MAGLUMI 2000, New Industries, China).

Efficacy indicators and follow-up

All patients were followed up in the outpatient clinic. Patients in the SDMT group were evaluated every 4 weeks, while the follow-up frequency in EIDRT group was adjusted according to the individualized dosing intervals (every 5-8 weeks). The mean duration of outpatient follow-up during treatment was 9.82 ± 1.18 months in the SDMT group and 10.27 ± 1.23 months in the EIDRT group, corresponding to the period until treatment discontinuation. After omalizumab discontinuation, all patients underwent a 6-month telephone follow-up to monitor recurrence. No patients were lost to follow-up, ensuring no missing data bias.

Urticaria Activity Score over 7 days (UAS7): UAS7 was used to assess disease activity at baseline (prior to treatment strategy adjustment and upon entry into the control phase), 3 months (the third month after strategy adjustment), and 6 months (the sixth month after strategy adjustment). The total score ranges from 0 to 42.

The score is calculated by summing the daily wheal count score (0: none; 1: 1-10 wheals; 2: 11-50 wheals; 3: >50 wheals) and daily pruritus severity score (0: none; 1: mild, no impact on daily life or sleep; 2: moderate, partial impact; 3: severe, marked impact), then multiplying by seven. Higher scores indicate greater urticaria activity, with a UAS score ≤6 indicating minimal disease activity, 7-15 indicating mild disease, 16-27 indicating moderate disease, and 28-42 indicating severe disease. The reported Cronbach's alpha coefficient for this scale ranges from 0.819 to 0.930 [15].

Urticaria Control Test (UCT): At baseline, 3 months, and 6 months, the UCT scale was used to assess overall disease control over the past 4 weeks. The total score ranges from 0 to 16 and consists of four items: frequency of itching/wheal episodes, impact on quality of life, difficulty controlling symptoms with treatment, and overall disease control.

Each item is rated on a 5-point scale. Higher scores indicate better disease control, categorized as complete control (16 points), good control (13-15 points), and poor control (<12 points). The intraclass correlation coefficient of the UCT is 0.93, indicating excellent reliability [16].

Chronic urticaria quality of life questionnaire (CU-QoL): At baseline, 3 months, and 6 months, the CU-QoL scale was used to assess disease-specific quality of life over the past 14 days. The questionnaire consists of 23 items on a 5-point scale (1: not at all bothered to 5: extremely bothered), yielding a total score range of 23-115. Higher scores indicate more severe impairment of quality of life. The Cronbach's alpha coefficient for this scale is 0.86 [17].

Dermatology life quality index (DLQI): At baseline, 3 months, and 6 months, the DLQI scale was used to assess the overall impact of CSU on patients' daily lives over the past week. The score comprises 10 items covering various aspects, including symptoms, sleep, emotional well-being, daily activities, social activi-

ties, work/study, leisure activities, personal relationships, treatment burden, and appearance. Each item is rated on a 4-point scale (0: not at all; 1: a little; 2: a lot; 3: very much), with a total score range of 0-30. Higher scores indicate more severe impacts on quality of life, with specific classifications as follows: 0-1 (no effect), 2-5 (small effect), 6-10 (moderate effect), and >10 (large effect). The Cronbach's alpha coefficient for this scale is 0.85 [18].

Relapse: In this study, relapse was defined as the recurrence of CSU symptoms after discontinuation of omalizumab, determined by a UCT score of <12 [19]. The time to discontinuation was calculated as the number of months from entry into the control phase (i.e., initiation of treatment strategy adjustment) to the final omalizumab administration.

All patients were followed up by telephone for 6 months after treatment discontinuation, with follow-ups conducted twice monthly during the first 3 months and once monthly for the subsequent 3 months. At each follow-up, patients were systematically questioned about typical CSU symptoms, and the UCT and a brief version of the UAS7 were completed through telephone interviews to determine disease recurrence.

Statistical analysis

Statistical analyses were conducted using SPSS software (version 29.0; Chicago, Illinois, USA). Continuous variables, after being tested for normal distribution using the Shapiro-Wilk test, were reported as mean ± standard deviation (SD) and compared between groups using independent samples t-tests. Categorical variables were expressed as count and proportions [n (%)] and compared using chi-square Tests. Multivariate logistic regression analysis was performed to identify independent risk factors for disease relapse during the control period, with "relapse within 6 months after omalizumab discontinuation" defined as the dependent variable. A *P* value <0.05 was considered significant.

Longitudinal changes in UAS7, UCT, CU-QoL, and DLQI scores at baseline, 3 months, and 6 months were analyzed using linear mixed-effects models (LMMs), including treatment group (SDMT/EIDRT), time (baseline, 3, 6 months), and group-by-time interaction as fixed effects and a random intercept for each patient. Additional models adjusted for age, sex, disease duration, and baseline total IgE level were evaluated; however, as these adjustments did not materially affect the primary estimates and resulted in less favorable AIC/BIC values, the unadjusted primary models were retained. When a significant group-by-time interaction was observed, post-hoc pairwise comparisons were performed with Bonferroni correction for multiple testing.

The sample sizes was determined by consecutively enrolling all eligible patients during the defined study period. A post-hoc power analysis for relapse rates (SDMT: 23.33%, EIDRT: 11.59%) demonstrated a statistical power exceeding 85%.

Results

General data

There were no significant differences in age (P=0.293), gender (P=0.474), BMI (P=0.236), level of education (P=0.584), smoking (P=0.610), drinking (P=0.472) or urticaria family history (P=0.604) between the two groups (**Table 1**).

Regarding clinical characteristics, no significant differences were observed between the two groups in disease duration (P=0.631), presence of concomitant angioedema (P=0.976), concomitant allergic disease (P=0.791), or baseline serum total IgE levels (P=0.505). In addition, prior use of H2 receptor antagonists (P=0.940), leukotriene receptor antagonists (LTRAs; P=0.804), and systemic corticosteroids (P=0.620) before initiation of omalizumab did not differ significantly between groups (**Table 2**). All patients in both groups had received H1 antihistamines.

UAS7

Comparison of UAS7 scores between the two groups at baseline, 3 months, and 6 months are presented in **Figure 1**. In the SDMT group, the UAS7 score decreased significantly from baseline (4.25 ± 1.32) to 3 months (2.15 ± 0.68; t=15.493, Bonferroni-corrected P<0.001) and 6 months (1.62 ± 0.47; t=20.561, Bonferroni-corrected P<0.001). Similarly, in the

Table 1. Comparison of demographic characteristics between the two groups

Data	SDMT group (n=120)	EIDRT group (n=138)	t/χ^2	P
Age (years)	38.25 ± 9.86	39.56 ± 10.12	1.053	0.293
Sex [n (%)]			0.513	0.474
Male	54 (45.00%)	56 (40.58%)		
Female	66 (55.00%)	82 (59.42%)		
BMI (kg/m^2)	22.15 ± 1.42	22.37 ± 1.56	1.188	0.236
Educational level [n (%)]			1.074	0.584
Junior high school or below	29 (24.17%)	30 (21.74%)		
Senior high school or secondary vocational school	24 (20.00%)	35 (25.36%)		
Junior college or above	67 (55.83%)	73 (52.90%)		
Smoking [n (%)]			0.260	0.610
Yes	23 (19.17%)	30 (21.74%)		
No	97 (80.83%)	108 (78.26%)		
Alcohol consumption [n (%)]			0.517	0.472
Yes	35 (29.17%)	46 (33.33%)		
No	85 (70.83%)	92 (66.67%)		
Family history of urticaria [n (%)]			0.269	0.604
Yes	18 (15.00%)	24 (17.39%)		
No	102 (85.00%)	114 (82.61%)		

Abbreviations: SDMT, standard dose maintenance therapy; EIDRT, extended interval dose reduction therapy; BMI, body mass index.

Table 2. Comparison of clinical features between the two groups

Data	SDMT group (n=120)	EIDRT group (n=138)	t/χ^2	P
Duration of disease (months)	20.13 ± 5.09	20.45 ± 5.31	0.481	0.631
Concomitant angioedema [n (%)]	45 (37.50%)	52 (37.68%)	0.001	0.976
Concomitant allergic disease [n (%)]	41 (34.17%)	45 (32.61%)	0.070	0.791
Total IgE level (IU/ml)	129.31 ± 42.83	132.89 ± 43.26	0.667	0.505
Treatments of CSU patients before the start of omalizumab				
H1 antihistamines [n (%)]	120 (100.00%)	138 (100.00%)	-	-
H2 receptor antagonists [n (%)]	36 (30.00%)	42 (30.43%)	0.006	0.940
LTRAs [n (%)]	40 (33.33%)	44 (31.88%)	0.061	0.804
Corticosteroids [n (%)]	21 (17.50%)	21 (15.22%)	0.245	0.620

Abbreviations: SDMT, standard dose maintenance therapy; EIDRT, extended interval dose reduction therapy; IgE, immunoglobulin E; CSU, chronic spontaneous urticaria; H1, histamine1; H2, histamine2; LTRAs, leukotriene receptor antagonists.

EIDRT group, the UAS7 score decreased significantly from baseline (4.31 ± 1.28) to 3 months (2.24 ± 0.72; t=16.558, Bonferroni-corrected P<0.001) and 6 months (1.73 ± 0.51; t=21.997, Bonferroni-corrected P<0.001). No significant inter-group differences at baseline (P=0.718) or at 3 months (P=0.339) were observed. At 6 months, lower UAS7 scores in the SDMT group were observed (P=0.058); however, the difference did not reach statistical significance.

UCT

UCT scores for both groups at baseline, 3 months, and 6 months are presented in **Table 3**. No significant inter-group differences were observed at baseline (P=0.444), 3 months (P=0.297), 6 months (P=0.114). Within-group comparisons showed significant improvements in disease control over time. In the SDMT g-oup, the UCT score increased significantly fr-om baseline (13.32 ± 0.66) to 3 months

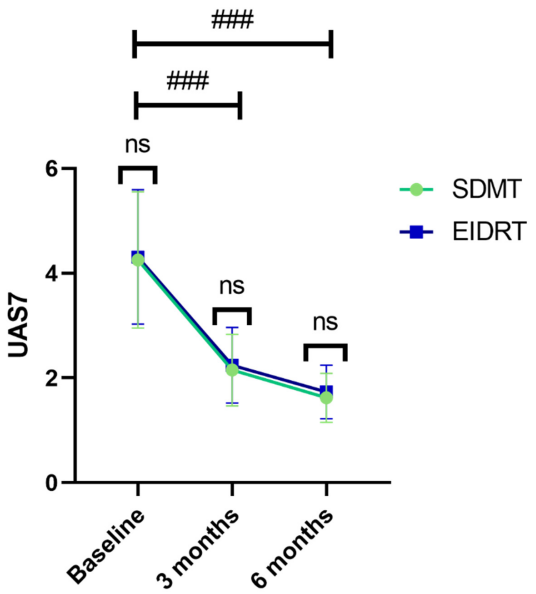

Figure 1. Comparison of UAS7 scores between the two groups. ns: no significant difference; ###, Bonferroni-corrected P<0.001, compared to baseline within the group. Abbreviations: SDMT, standard dose maintenance therapy; EIDRT, extended interval dose reduction therapy; UAS7, urticaria activity score over 7 days.

(14.81 ± 0.48; t=20.000, Bonferroni-corrected P<0.001) and 6 months (15.58 ± 0.21; t=35.745, Bonferroni-corrected P<0.001). Similarly, in the EIDRT group, the UCT score increased significantly from baseline (13.26 ± 0.63) to 3 months (14.75 ± 0.54; t=21.095, Bonferroni-corrected P<0.001) and 6 months (15.54 ± 0.22; t=40.137, Bonferroni-corrected P<0.001).

CU-QoL

As shown in **Table 4**, no significant between-group differences were observed at baseline (P=0.485), 3 months (P=0.103), or 6 months (P=0.112). In the SDMT group, the CU-QOL score decreased notably from baseline (53.42 ± 6.17) to 3 months (36.15 ± 4.45; t=24.869, Bonferroni - corrected P < 0.001) and 6 months (25.67 ± 1.21; t=48.347, Bonferroni - corrected P < 0.001). Similarly, in the EIDRT group, the CU-QoL score was much higher than it was at the baseline (52.89 ± 5.94) and markedly increased after 3 (37.08 ± 4.68; t=24.560, Bonferroni-corrected P<0.001) and 6 months (25.94 ± 1.53; t=51.613, Bonferroni-corrected P<0.001).

DLQI

As shown in **Table 5**, no significant between-group differences were observed at baseline (P=0.836), 3 months (P=0.317), or 6 months (P=0.313). Within-group analyses demonstrated significant improvements in both groups over time. In the SDMT group, the DLQI score decreased significantly from baseline (5.42 ± 1.56) to 3 months (2.75 ± 0.84; t=16.508, Bonferroni-corrected P<0.001) and 6 months (1.63 ± 0.47; t=25.482, Bonferroni-corrected P<0.001). Similarly, in the EIDRT group, the DLQI score increased significantly from baseline (5.38 ± 1.62) to 3 months (2.86 ± 0.91; t=15.932, Bonferroni-corrected P<0.001) and 6 months (1.69 ± 0.52; t=25.477, Bonferroni-corrected P<0.001).

Time to discontinuation and relapse rate

Time to treatment discontinuation and relapse outcomes are summarized in **Table 6**. Patients in the EIDRT group had a significantly longer time to treatment discontinuation (10.27 ± 1.23 months) compared to that in SDMT group (9.82 ± 1.18 months) (t=2.997, P=0.003). Within 6 months after omalizumab discontinuation, the relapse rate was significantly lower in the EIDRT group than in the SDMT group (11.59% vs. 23.33%; P=0.012).

Pharmacoeconomic analysis

The pharmacoeconomic benefit of the EIDRT strategy compared to SDMT is presented in **Figure 2**. Specifically, patients in the EIDRT group received significantly fewer omalizumab injections during the treatment period than those in the SDMT group (8.21 ± 0.76 vs. 9.82 ± 1.25; P < 0.001). In addition, the number of outpatient visits was significantly lower in the EIDRT group compared to the SDMT group (9.08 ± 1.37 vs. 11.35 ± 1.42 visits; t=13.008, P < 0.001). These findings indicated reduced medical resource utilization in the EIDRT group, resulting in reduced medical cost during the treatment course.

Multivariate logistic regression analysis

Multivariate logistic regression for relapse within 6 months after discontinuation is shown in **Table 7**. EIDRT was identified as an independent protective factor against relapse (OR=

Table 3. Comparison of UCT scores between the two groups

Data	SDMT group (n=120)	EIDRT group (n=138)	t	P
Baseline	13.32 ± 0.66	13.26 ± 0.63	0.766	0.444
3 months	14.81 ± 0.48###	14.75 ± 0.54###	1.044	0.297
6 months	15.58 ± 0.21###	15.54 ± 0.22###	1.584	0.114

Abbreviations: SDMT, standard dose maintenance therapy; EIDRT, extended interval dose reduction therapy; UCT, urticaria control test; ###, Bonferroni-corrected P<0.001, compared to baseline within the group.

Table 4. Comparison of CU-QoL scores between the two groups

Data	SDMT group (n=120)	EIDRT group (n=138)	t	P
Baseline	53.42 ± 6.17	52.89 ± 5.94	0.700	0.485
3 months	36.15 ± 4.45###	37.08 ± 4.68###	1.637	0.103
6 months	25.67 ± 1.21###	25.94 ± 1.53###	1.596	0.112

Abbreviations: SDMT, standard dose maintenance therapy; EIDRT, extended interval dose reduction therapy; CU-QoL, chronic urticaria quality of life questionnaire; ###, Bonferroni-corrected P<0.001, compared to baseline within the group.

Table 5. Comparison of DLQI scores between the two groups

Data	SDMT group (n=120)	EIDRT group (n=138)	t	P
Baseline	5.42 ± 1.56	5.38 ± 1.62	0.207	0.836
3 months	2.75 ± 0.84###	2.86 ± 0.91###	1.002	0.317
6 months	1.63 ± 0.47###	1.69 ± 0.52###	1.011	0.313

Abbreviations: SDMT, standard dose maintenance therapy; EIDRT, extended interval dose reduction therapy; DLQI, dermatology life quality index; ###, Bonferroni-corrected P<0.001, compared to baseline within the group.

Table 6. Comparison of time to discontinuation and relapse rate between the two groups

Data	SDMT group (n=120)	EIDRT group (n=138)	t/χ^2	P
Time to discontinuation (months)	9.82 ± 1.18	10.27 ± 1.23	2.997	0.003
Relapse rate within 6 months after discontinuation [n (%)]	28 (23.33%)	16 (11.59%)	6.253	0.012

Abbreviations: SDMT, standard dose maintenance therapy; EIDRT, extended interval dose reduction therapy.

0.373, 95% CI: 0.189-0.739, P=0.005). Longer disease duration (OR=1.063, 95% CI: 1.014-1.115, P=0.011) and the presence of concomitant angioedema (OR=2.399, 95% CI: 1.330-4.329, P=0.004) were identified as independent risk factors for relapse. Baseline serum total IgE level was not significantly associated with relapse risk (P=0.693).

Discussion

The present study compared the effects of two omalizumab dose-reduction strategies for CSU patients during the disease control period: SDMT and EIDRT. Although the two groups were comparable at baseline and showed similar clinical data, significant differences were observed in treatment discontinuation time and recurrence outcomes.

Patients in the EIDRT group experienced a markedly delayed time to treatment discontinuation, consistent with previous reports. For instance, Kucharczyk et al. demonstrated in a retrospective study that, compared to a fixed intermittent discontinuation regimen, a personalized, progressively extended dosing-interval strategy was associated with a decreased recurrence risk [20]. This may be attributable to the gradual adaptation of mast cells and basophils to decreasing levels of free IgE and thereby reducing rebound activation. In this manner, there can be a long elimination after the treatment [21, 22].

The EIDRT group demonstrated a lower recurrence rate at six months after treatment cessation, indicating that gradual dose-interval extension is more advantageous for long-term

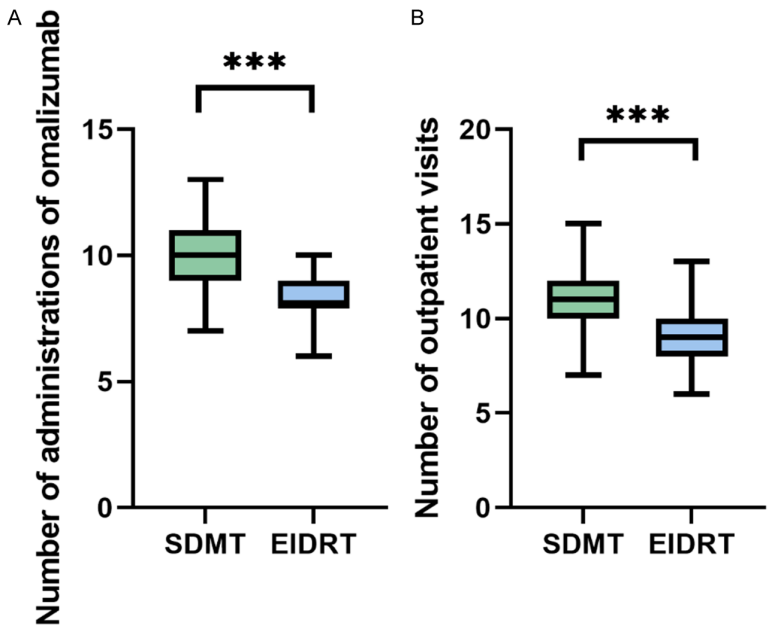

Figure 2. Comparison of pharmacoeconomic outcomes between the two groups. A. Number of administrations of omalizumab; B. Number of outpatient visits[a]. ***P<0.001, compared to the SDMT group. Abbreviations: SDMT, standard dose maintenance therapy; EIDRT, extended interval dose reduction therapy. a, including follow-up during treatment and seeking medical attention for symptom recurrence.

remission than abrupt discontinuation. Similar findings were reported by Salman et al. in their study, in which patients who discontinued omalizumab through progressive interval extension had a higher likelihood of maintaining remission [23]. Mechanistically, EIDRT may confer prolonged immune modulation by extending overall drug exposure, thereby sustaining IgE blockade at FcεRI, reducing downstream immune activation, and suppressing *de novo* IgE production by B cells [3]. In contrast, abrupt discontinuation in SDMT may prematurely terminate these immunomodulatory effects and contribute to earlier relapse [22, 24]. Consistently, our regression analysis identified EIDRT as an independent protective factor against disease recurrence.

Two independent risk factors identified by regression analysis in this study included longer disease duration and the presence of angioedema. This is consistent with previous studies indicating that patients with a more longstanding or severe disease phenotype-particularly those with angioedema-are more prone to relapse and may require closer monitoring and individualized tapering strategies [22, 24]. Notably, baseline total IgE levels were not predictive of relapse after treatment discontinuation when adjusted for other clinical variables. Although this appears counterintuitive given the IgE-targeting mechanism of omalizumab, it aligns with prior studies demonstrating that baseline total IgE is not significantly associated with treatment response or relapse risk in CSU [22, 24]. Several explanations may account for this observation. First, the therapeutic efficacy of omalizumab is more closely related to IgE functionality, FcεRI expression, and effector-cell sensitivity rather than absolute circulating IgE concentrations. Second, changes in IgE during treatment, including the formation of omalizumab - IgE complexes, may be more relevant to relapse risk than static pre-treatment levels. Third, CSU is a heterogenous disease comprising multiple endotypes, including autoimmune- and coagulation-driven pathways that are not primarily IgE-mediated, thereby limiting the predictive value of total IgE alone. Collectively, these findings suggest that clinical features such as disease duration and angioedema are more reliable predictors of relapse following omalizumab discontinuation than baseline total IgE.

Pharmacoeconomically, EIDRT demonstrated advantages in drug-related cost, which is consistent with previous reports. For instance, Matsubara et al. reported that although the introduction of omalizumab initially increased direct drug costs, dose reduction and prolonged dosing intervals substantially alleviated the long-term economic burden of disease [13]. Our findings support this conclusion by providing real-world evidence from a Chinese clinical setting. Given the approximately 26-day half-life of omalizumab [7, 30], extending dosing intervals allows sustained disease control with reduced cumulative drug consumption. Additionally, fewer clinic visits indirectly result in reduced costs, including travel expenses and

Table 7. Multivariate logistic regression analysis of risk factors affecting the recurrence in patients with CSU during disease control phase

Data	Coefficient	Std Error	Wald Stat	P	OR	OR CI Lower	OR CI Upper
EIDRT	-0.985	0.347	8.057	0.005	0.373	0.189	0.739
Duration of disease	0.061	0.024	6.469	0.011	1.063	1.014	1.115
Concomitant angioedema	0.875	0.301	8.451	0.004	2.399	1.330	4.329
Baseline total IgE level	0.045	0.114	0.156	0.693	1.046	0.839	1.307

Abbreviations: CSU, chronic spontaneous urticaria; OR, odds ratio; CI, confidence interval; EIDRT, extended interval dose reduction therapy; IgE, immunoglobulin E.

productivity loss, which may further enhance treatment adherence and quality of life [25, 26]. These economic benefits are particularly relevant in healthcare systems with limited resources, underscoring the value of EIDRT as a cost-effective and resource-efficient strategy for long-term CSU management which reduces the number of physician visits [27-29].

Conclusion

Compared to SDMT, the EIDRT strategy offers potential advantages for patients with CSU during the disease control phase. EIDRT is associated with a longer time to treatment discontinuation, a lower relapse rate after discontinuation, and fewer omalizumab administrations and outpatient visits, which may translate into improved pharmacoeconomic outcome. However, given the retrospective design of this study, further prospective and long-term studies are warranted to determine the optimal tapering schedules and to confirm the efficacy and safety of EIDRT across broader patient populations before it can be widely recommended for clinical practice.

Disclosure of conflict of interest

None.

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