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Clinical Impacts of Omalizumab on the Psychiatric Comorbidities of Chronic Spontaneous Urticaria: A Systematic Review and Meta-Analysis

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INTRODUCTION

Individuals with chronic spontaneous urticaria (CSU) experience significant sleep disturbances and are at risk of anxiety and depression.[1] There is strong evidence supporting the use of omalizumab in the management of CSU.[2] Clinical impacts of omalizumab on the cutaneous symptoms of CSU have been widely investigated, but its impact on the psychiatric comorbidities of CSU remains unclear.[3] The objective of this systematic review and meta-analysis is to determine the clinical impacts of omalizumab on depression, anxiety, and sleep in patients with CSU.

Our study protocol was pre-registered on PROSPERO (CRD42021272707). Medline, Embase, and CENTRAL were searched from inception to April 20th, 2022, using the keywords "urticaria" and "anxiety"/"depression"/"sleep". Of 200 records, seven studies totaling 1,398 patients were included (71% female, age range of means 44.6 to 46.4 years). All studies were of fair or good quality and low risk of bias. Standardized mean difference (SMD) combined disparate scales, with 0.2, 0.5, and 0.8 representing small, moderate, and large SMDs, respectively.[4]

Across three studies totaling 124 patients with CSU, treatment with omalizumab was associated with a large decrease in depression scores (SMD=1.07, 95%CI 0.68-1.46, $P<0.001$) from baseline (Figure 1). Patients on omalizumab demonstrated a large, clinically meaningful reduction in depressive symptoms (17.5% reduction in Beck Depression Inventory), irrespective of their cutaneous response. In one randomized controlled trial (RCT) of 68 patients with CSU, patients receiving omalizumab were significantly more likely to no longer meet the clinical criteria for depression at 28 weeks (OR 5.55, 95%CI 1.7-18.2, $P=0.005$) compared to placebo.

Across two studies totaling 257 patients with CSU, treatment with omalizumab was associated with a large decrease in anxiety scores (SMD=1.00, 95% CI 0.72-1.27, $P<0.001$) from baseline. Across three RCTs totaling 975 patients with CSU, treatment with omalizumab resulted in a moderate improvement in sleep quality at 12 weeks (SMD=0.43, 95% CI 0.34-0.53, $P=0.001$) compared to placebo. Of note, CSU patients on 300 mg of omalizumab every 4 weeks had the best response (test for subgroup differences: $P=0.06$, $I^2=65.1\%$).

The association between CSU and psychiatric comorbidities is likely multifactorial. In addition to increased counts and degranulation of mast cells and basophils in CSU, patients with depression also demonstrate increased TNF-α and interleukin-6 levels.[5] Omalizumab binds to free IgE to inhibit mast cell degranulation and prevent the release of pro-inflammatory cytokines, including TNF-α and interleukin-6.[1] This reduction in pro-inflammatory cytokines, along with a reduction in cutaneous symptoms, likely contributed to the improvement of psychiatric comorbidities in patients with CSU treated with omalizumab.[3] The alleviation of psychiatric comorbidities of CSU by omalizumab, independent of the patient's cutaneous response, further supports this. This review is limited by the paucity of randomized, placebo-controlled studies, and further controlled studies are needed to support its use for managing the psychiatric comorbidities of CSU.

In conclusion, this review lends further support to the use of omalizumab in the management of moderate-to-severe CSU. Patients with CSU receiving omalizumab reported markedly improved symptoms of depression, anxiety, and sleep disturbances, and were more likely to have resolution of CSU-associated depression. Furthermore, omalizumab was found to be effective in reducing the psychiatric impacts of CSU on patients, independent of their cutaneous response. Thus, clinicians may wish to consider the use of omalizumab as an effective treatment not only for the cutaneous symptoms of CSU, but also for the psychiatric comorbidities resulting from this disease.

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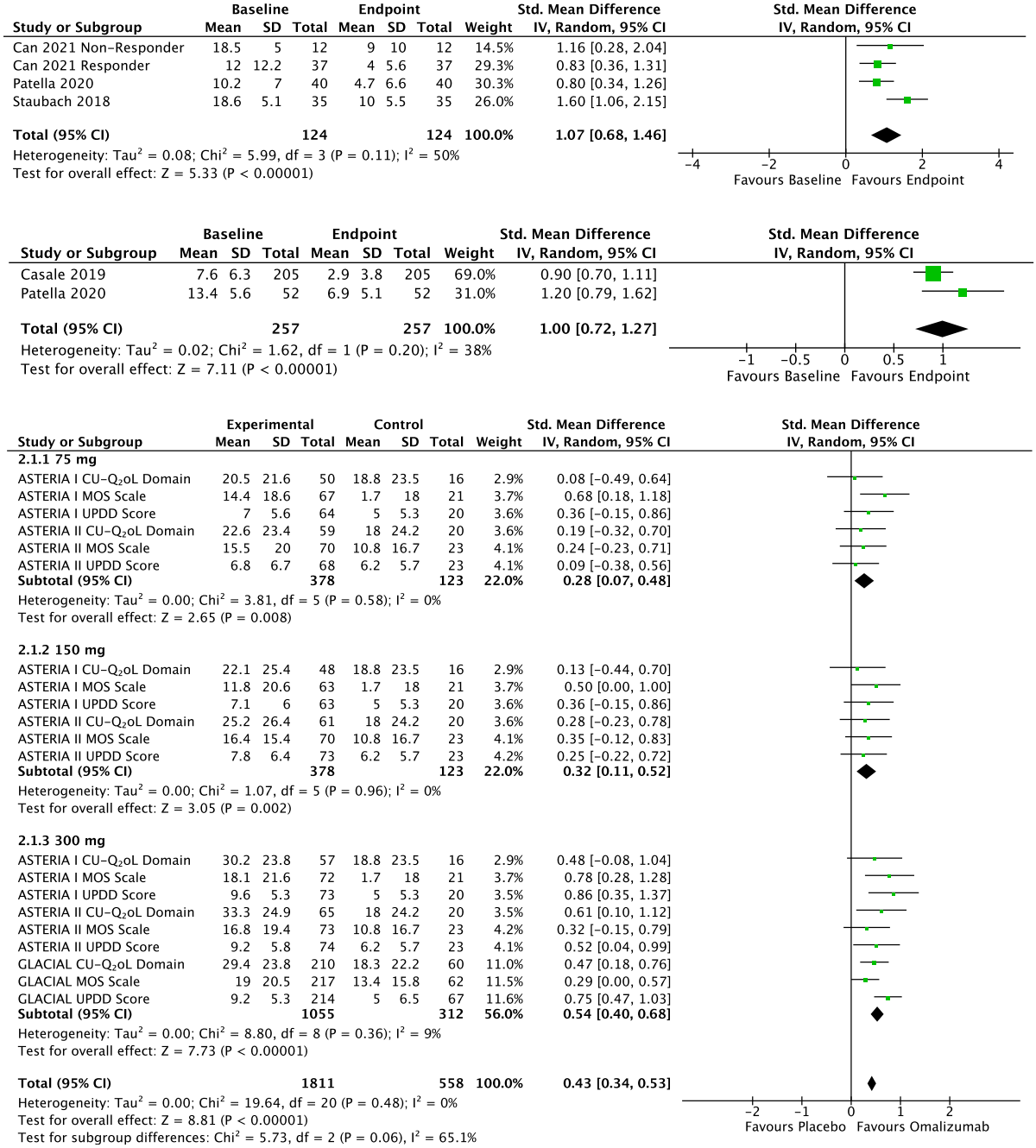
FIGURE 1. Forest plot showing the improvement in depression (top panel), anxiety (middle panel), and sleep disturbance (bottom panel, various doses) scores across studies in patients receiving omalizumab compared to baseline or placebo at study endpoint.



DISCLOSURES

The authors have no conflicts of interest to declare.

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