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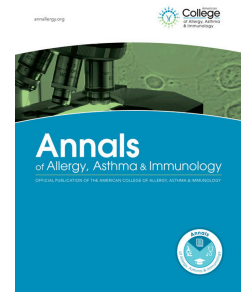
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Running head: Angioedema and quality of life in CSU

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Chronic spontaneous urticaria (CSU) symptoms are wheals in a number of cases accompanied by recurrent angioedema. The proportion of CSU patients manifesting both wheals and angioedema and those reporting only one type of symptoms is different - a similar number of patients experience both symptoms or wheals only, whereas 1–13% experience angioedema only^{1,2}. Symptoms of CSU have a detrimental influence on patients' quality of life. Additionally, the coexistence between angioedema symptoms and wheals is related to prolonged disease duration². According to the recent guidelines, the CU-Q2oL questionnaire, the only chronic urticaria-specific device is designed to assess the quality of life in patients with CSU³. The Polish validated version of CU-Q2oL was developed⁴. As the quality of life is a general term, disease-specific questionnaires allow more precise analyses of different aspects of the quality of life. The Urticaria Activity Score (UAS) is a tool designed to assess urticaria activity³. Clinical experience shows that symptoms of angioedema, especially in a specific location result in fear in patients, which probably adversely influences the quality of life. Therefore we decided to investigate the quality of life in CSU patients, especially in terms of the influence of coexisting angioedema. Moreover, we aimed to assess the relations between detailed domains of the quality of life by analyzing subscales of the urticaria-focused questionnaire.

In total, 79 CSU subjects (51 females and 28 males, median age: 42 years; range 18–58) were enrolled. Symptoms of recurrent angioedema coexisting with wheals were found in 27 patients (U-Ae group), contrary to 52 patients with urticarial wheals only (U group). The exclusion criteria were other somatic or psychiatric diseases. In both groups disease duration time was analyzed. All subjects were requested to complete the Polish version of the CU-Q2oL questionnaire. It consists of 23 questions in six subscales: *Itching*, *Swelling/Mental*

status, *Functioning*, *Sleep*, *Eating/Limits* and *Embarrassment*. Answers to the items are presented on a five-point Likert scale. The UAS was used for the analysis of disease activity. This tool calculates the number of wheals and the intensity of pruritus. A recommended seven-day monitoring period was added up – UAS7. We used Kruskal-Wallis, U Mann-Whitney and Spearman tests for statistical analysis (Statsoft INC., Statistica 12.0). The study protocol was approved by the Bioethics Committee of the Medical University of Silesia in Katowice, Poland.

We did not notice any statistically significant difference between analyzed groups in disease duration time (U-18.4±16.5 months; U-Ae-19.8±17.3 months). We observed a marked impairment in the quality of life in CSU. The impairment was statistically significantly greater in *Itching* and *Embarrassment* subscales as compared to other CU-Q2oL subscales. Additionally, we showed that the occurrence of angioedema was a significant predictor of impaired quality of life in Polish patients, especially in the *Embarrassment* subscale and in the *Swelling/Mental status* subscale with no influence on disease intensity assessed with UAS7 (Table 1). When analyzing inter-domain relations, we observed a statistically significant ($p<0.05$) relationship between *Itching* and *Swelling/Mental status* subscales ($R = 0.35$) as well as between *Itching* and *Sleep* subscales ($R = 0.32$). The *Swelling/Mental status* subscale is related to *Functioning* ($R = 0.33$), *Sleep* ($R = 0.33$) and *Eating/Limits* ($R = 0.29$) subscales. The *Functioning* subscale is related to *Sleep* ($R = 0.44$) and *Eating/Limits* ($R = 0.36$) subscales. The *Sleep* subscale is additionally related to the *Eating/Limits* subscale ($R = 0.32$).

Previous researches assessed that 30%-50% of CSU patients are affected by coexisting angioedema⁵. It is suspected that angioedema plays a crucial role in CSU, affecting economic aspects and producing direct costs². Recent studies have demonstrated that psychological stress and emotional disturbances are relatively common in patients with CSU^{2,6,7}. Ozkan et al.⁸ proved that even 60% of chronic urticaria patients had psychiatric disturbances and their

quality of life was markedly impaired. In the case of angioedema, an additional impact of this symptom is poorly analysed. Patients with hereditary angioedema noticed that an angioedema attack causes symptoms of depression and anxiety but, on the other hand, feelings of depression and anxiety may initiate this attack⁹. Due to the above facts we tried to analyse precisely the influence of angioedema in CSU on the quality of life with the analysis of its detailed aspects. In our study we noticed that manifestation of angioedema impaired the quality of life, particularly in the domains related to embarrassment and obviously swelling. The number of other studies on this phenomenon is extremely insufficient. For instance, Choi et al.¹⁰ found a significant association between coexisting angioedema and poor scores in the symptom domain of CU-Q2oL and UAS. In our study the occurrence of angioedema symptoms adversely influenced the quality of life, which is consistent with the Korean results. Contrary to their study, we did not observe differences in the UAS values when angioedema was considered. We believe it is not surprising as UAS is dedicated to pruritus and the assessment of wheals and these symptoms are not directly associated with angioedema. In the Korean study the symptom domain seemed to be most impaired. However, marked impairment observed in other quality of life domains also demonstrated that CSU patients do not suffer only due to the occurrence of physical symptoms but also due to the impairment in their emotional well-being and in daily or social activities¹⁰. In our study we used a relatively new questionnaire and we proved more precisely which aspects of the quality of life are particularly impaired in CSU patients. This questionnaire allows for a detailed analysis of the quality of life and its particular aspects. We observed a number of relations between CU-Q2oL subscales, which shows in detail the specificity of the impairment in the quality of life in CSU. We are among the first to bring such novel data. In our opinion it is necessary to identify CSU patients with coexisting angioedema as they are more likely to have markedly impaired quality of life. Some patients are not aware of the differences between wheals and

76 angioedema and therefore this problem should be investigated and explained when taking
77 medical history and preparing indications for patients.

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Tab.1. Comparison of CU-Q₂oL subscales values, total quality of life score (Total) and Urticaria Activity Score seven day assessment (UAS7) in chronic spontaneous urticaria patients without angioedema (U) and with recurrent angioedema symptoms (U-Ae) (*p* – statistical significance)

	U			U-Ae			<i>p</i>
	Median	Min.	Max.	Median	Min.	Max.	
Itching	75.0	12.5	100	62.5	12.5	100	0.48
Swelling/ Mental status	40.0	5.0	70.0	50.0	20.0	80.0	0.003
Functioning	43.75	0.00	91.67	41.67	0.00	91.67	0.81
Sleep	37.5	0.00	100	40.62	12.5	100	0.92
Eating/ Limits	31.25	0.00	93.75	28.12	0.00	68.75	0.63
Embarrassment	75.00	0.00	100	68.75	0.00	100	0.04
Total	40.0	17.0	67.0	38.0	18.0	67.0	0.74
UAS	16.0	8.00	28.0	18.0	6.00	31.0	0.17