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Overweight and obesity may play a role in the pathogenesis of chronic spontaneous urticaria

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Summary

Background. Chronic spontaneous urticaria (CSU) is one of the commonest diseases in allergological and dermatological practice. It constitutes an interdisciplinary problem, and its pathogenesis is not always easily determined. It has been suggested that metabolic syndrome and hyperlipidaemia are more frequent in patients with CSU, but the influence of overweight and obesity on the development of CSU has not been thoroughly investigated.

Aim. To assess the association between body parameters and the development of CSU.

Methods. The study enrolled 85 patients with CSU, who were divided into three subgroups: patients whose only symptoms were weals, patients whose only symptom was angio-oedema, and patients with urticaria and accompanying angio-oedema. Mean weight, height, body mass index (BMI), body surface area, disease duration and age of disease onset were recorded

Results. There was a statistically significant association between CSU and heavier weight, higher BMI, greater affected body surface area and older age at disease onset. Subjects with higher BMI values had a tendency towards longer disease duration. There were no statistically significant differences between the three subgroups.

Conclusions. Our results suggest that CSU, especially if of long duration, may be associated with overweight and obesity, while increased body mass can result in later onset of urticaria symptoms. Further analyses to confirm the presented results and possible association between obesity and CSU occurrence are needed.

Introduction

Chronic spontaneous urticaria (CSU) is one of the commonest skin diseases in allergological and dermatological practice. It constitutes an interdisciplinary clinical problem, and its background is not always easily determined. CSU significantly reduces patients' quality of life. The intensity and nature of the signs and symptoms as well as their location may be variable. CSU is a heterogeneous syndrome, the primary symptom of which is a pink to red weal characterized by oedema, which appears quickly and usually disappears within 24 h without leaving marks. The disease is usually accompanied by pruritus and may also be accompanied by angio-oedema.

The healthy range for body mass index (BMI) (weight in kg divided by height in m^2) is 18.5–24.9, while BMI > 25 is considered overweight and BMI > 30 is considered obese.[4] In Europe, obesity has reached epidemic proportions. Obesity is related to skin disorders, and both obesity and urticaria are more frequent in women.[1] It is suggested that metabolic syndrome and hyperlipidaemia are more frequent in

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patients with CSU, but the influence of overweight and obesity on the development of CSU has not been thoroughly investigated.[1–4]

The results of previous research indicate that excessive body weight may be a potential risk factor for the development of allergic diseases,[3–9] but no research has to date defined an association between obesity and CSU. We performed a study to assess the relation between the development of CSU symptoms and the patients' body parameters.

Methods

We enrolled 85 consecutive patients with CSU (59 women and 26 men; mean age 48 years; range 21–77 years) into the study. CSU was diagnosed on the basis of an analysis of the entire clinical picture, and coexistence of other diseases was excluded (thyroid abnormality was excluded based on laboratory findings).

The patients were divided into three subgroups: patients whose only symptom was weals, patients whose only symptom was angio-oedema, and patients with urticaria and an accompanying angio-oedema. Mean body weight, body height, BMI, body surface area (BSA), age of disease onset and duration of disease were calculated for the whole group and for each subgroup separately.

Statistical analysis

For statistical analyses, we used ANOVA and Spearman tests with Statistica software (v12; StatSoft Inc., Tulsa, OK, USA). $P = 0.05$ was considered statistically significant.

Results

A statistically significant association was found between older age at disease onset and heavier weight, higher BMI and greater BSA involvement (Table 1). It is also worth highlighting that patients with higher BMI values had a trend ($P = 0.06$) towards longer disease duration (Table 1). No statistically significant differences in BMI and BSA values were determined between the studied subgroups (Fig. 1a,b).

Discussion

Many aetiological factors have already been associated with CSU, but the disease aetiology remains unrecognized in the majority of cases. Several theories about the pathogenesis of that disease have been advanced. An inflammatory condition can constitute significant factors that may contribute to the development of CSU. Even though CSU is not usually a life-threatening condition, its treatment may be complicated and difficult, which has a significant influence on patients' quality of life and constitutes a considerable socioeconomic burden.

According to the results presented by Lapi *et al.*, the risk of developing CSU is related to numerous factors.[10] The relationship between obesity and various diseases

Table 1 Association between age of disease onset and body parameters, and between disease duration time and body parameters in patients with chronic spontaneous urticaria.

	Age at disease onset		Disease duration	
Parameter	*R**	*P*	*R**	*P*
Weight	0.33	0.001	0.15	0.20
Height	−0.18	0.12	−0.04	0.70
BMI	0.48	< 0.001	0.21	0.06
BSA	0.23	0.04	0.09	0.44

BMI, body mass index; BSA, body surface area. *Spearman *R*.

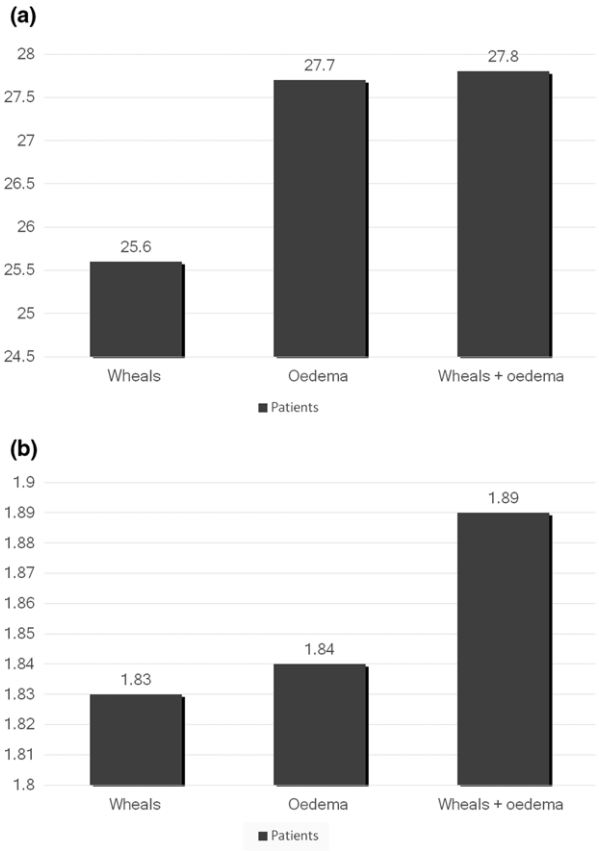


Figure 1 (a) Body mass index (BMI; kg/m^2) values and (b) body surface area (BSA; m^2) values in three examined subgroups of patients with chronic spontaneous urticaria. $P > 0.05$.

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such as arterial hypertension, diabetes and joint degeneration is obvious, but the relationship between obesity and allergic diseases has not yet been fully investigated.[11] The connection between CSU and obesity is especially intriguing, and may suggest pathogenic involvement of factors such as adipokine-induced inflammation. Patients with metabolic syndrome have elevated levels of inflammatory markers such as interleukin (IL)-1, IL-6, tumour necrosis factor and C-reactive protein (CRP).[12] Earlier studies also revealed elevated levels of inflammatory parameters and coagulation factors in patients with metabolic syndrome and CSU.[5–8] The literature data suggest that plasma levels of prothrombin 1 and 2, D-dimers and CRP may be possible markers of CSU severity. Moreover, the frequency of metabolic syndrome development was significantly higher in patients with CSU than in healthy subjects.[9]

Detailed research into fatty tissue has shown unambiguously that it is an active endocrine organ synthesizing numerous biologically active proteins of significant diversity in terms of structure and role, referred to as adipokines. The biological functions fulfilled by adipokines in the human body have not been fully elucidated, but some may play a role in inducing beneficial metabolic processes in the body, whereas others may be directly involved in the development of complications related to obesity, such as type 2 diabetes or atherosclerosis.[13] Since the discovery of the influence of adipokines on the immune system and inflammatory conditions, the relationship between obesity and autoimmune disorders has been emphasized.[14,15] The action of adipokines may be targeted directly to human mast cells, which play a role in endothelial inflammation,[16] for example. Intensification of endothelial inflammation is proportional to progression of the atherosclerotic process.[17] Proinflammatory factors such as C3a and C5a complement proteins, cytokines, monocyte chemoattractant protein-1 or low-density lipoprotein particles activate mast cells gathered in the atherosclerotic plaque.[18] Activation of those cells may also influence the development of CSU. The level of tryptase produced by mast cells and the number of fat cells are significantly elevated in obese patients and in mice fed on a fat-rich diet.[19,20] The described mechanisms could potentially lead to the coexistence of obesity and CSU.

Obesity is characterized by a chronic, systemic, often asymptomatic, inflammatory condition,[15] and may result in a decreased immune tolerance to antigens, therefore increasing the risk of allergies and other diseases with immune aetiology.[21,22] As indicated by our study, excessive fatty tissue may exert a certain protective action in CSU because people with higher BMI developed urticaria signs and symptoms later than those with a healthy BMI. We postulate that an inflammatory condition of mild intensity might protect the body, maintaining the immune system in a state of 'readiness'. However once this protection threshold is broken, the disease course seems to be more severe in obese patients. Ye *et al.*[9] obtained similar results, and reported that metabolic syndrome development was an independent predictor of an uncontrolled course of CSU. Hyperlipidaemia characterized by high blood levels of lipids, including cholesterol and triglycerides, is involved in inflammatory processes, which are related to an increased risk of atherosclerosis development. CSU is thought to carry a higher risk of hyperlipidaemia development, and some authors have suggested that the occurrence of urticaria symptoms should prompt investigations for elevated lipid parameters.[1] Moreover, according to Stauber *et al.*,[23] diabetes and obesity are risk factors for recurrent angioneurotic oedema with a severe course. Older age is associated with a higher risk of autoimmune disturbances, and CSU frequently coexists with autoimmunity, particularly with autoimmune thyroid disorders.[24,25] Additionally in older people, there is a change in the balance between the amount of muscular and fatty tissue.

Thorough clinical examination, supplemented with an individually selected panel of diagnostic tests, constitutes the basis for initiating effective therapy for CSU. However, it often proves impossible to determine the cause of urticaria symptoms, so symptomatic treatment based on modern antihistamine therapy should be initiated, which may need to be supplemented with alternative therapies. Moreover, it is necessary to apply a holistic approach towards treating the patient and if applicable, to address the problem of obesity, which affects an increasingly large group of people.

Conclusion

To our knowledge, this is the first study to investigate possible associations between CSU and overweight/obesity. Our results suggest that CSU, especially if of long duration, may be associated with overweight and obesity, whereas increased body mass can result in later onset of urticaria symptoms. Further studies are warranted to confirm the presented results and explain the relationship between obesity and CSU.

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What's already known about this topic?

• It is suggested that metabolic syndrome and hyperlipidaemia are more frequent in patients with CSU, but the influence of overweight and obesity on the development of this disease has not been deeply investigated.

What does this study add?

• We performed study aimed at determining the influence of obesity on CSU, which is the first such study, to our knowledge.
• The results suggest that overweight and obesity may be associated with CSU, especially with long-lasting CSU.
• Increased body mass can result in later onset of CSU symptoms.

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