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Original Research

Assessment of plasma levels of S100A8, S100A9, and S100A12 in patients with Chronic Spontaneous Uritcaria

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ABSTRACT:

Background: Chronic spontaneous uritcaria (CSU) is characterized by the spontaneous appearance of transient itchy wheals, angioedema or both, for at least 6 weeks. The present study was conducted to assess plasma levels of S100A8, S100A9, and S100A12 in patients with chronic spontaneous uritcaria. **Materials & Methods:** 56 patients with CSU were enrolled. Plasma levels of S100A8, S100A9, and S100A12 were assessed using enzyme linked immunosorbent assay (ELISA) kit. **Results:** The mean S100A8 level in group I was 1215.6 pg/ml and in group II was 2104.6 pg/ml, S100A9 level was 406.2 pg/ml in group I and 815.2 pg/ml in group II, S100A12 level was 1924.6 pg/ml in group I and 2146.8 pg/ml in group II. The difference was significant (P< 0.05). **Conclusion:** Plasma level of S100A8, S100A9, and S100A12 were elevated in CSU patients than those of healthy controls.

Key words: Chronic spontaneous uritcaria , Plasma, angioedema

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INTRODUCTION

Chronic spontaneous uritcaria (CSU) is characterized by the spontaneous appearance of transient itchy wheals, angioedema or both, for at least 6 weeks.[1] While it affects 0.5%–1% of the population, it not only has negative visual impact on patients, but also decreases the quality of life. CSU is an inflammatory disease, probably caused by an interactive combination of immune, genetic, and environmental factors, including infections. Various changes in levels of immune-inflammatory, coagulation/fibrinolytic, hormonal, and metabolic markers have been reported in CSU patients.[2]

Urticaria lasting greater than 6 weeks is divided into 2 general groups; namely, inducible or spontaneous. Inducible urticarias are, perhaps, more accurately described as intermittent urticarias because the frequency is dependent on the particular stimulus. In this category are physical urticarias e.g., cold urticaria and dermatographism. Others include local heat urticaria, generalized heat urticaria (more commonly called cholinergic urticaria), solar urticaria, and aquagenic urticaria. One inducible physical urticaria that differs from all of these is delayed pressure urticaria.[3]

S100 family consists of a serial of EF-hand calcium (Ca^{2+})-binding proteins, with more than 20 distinguished proteins.[4] It is reported that S100A8, S100A9, and S100A12 play important roles in the pathogenesis of immunological disorders in the human body. They are involved in the development of autoimmune-associated diseases, such as psoriasis, rheumatoid arthritis, and systemic lupus erythematosus.[5]

The present study was conducted to assess plasma levels of S100A8, S100A9, and S100A12 in patients with chronic spontaneous uritcaria.

MATERIALS & METHODS

The present study was conducted among 56 patients with CSU. All patients were informed regarding the study and their consent was obtained. Equal number of healthy subjects were also recruited. CSU was diagnosed according to the EAACI/GA[2] LEN/EDF/WAO guidelines.

Data such as name, age, gender etc. was recorded. A thorough clinical examination was performed in all patients. Group I had CSU patients and group II had healthy subjects. Plasma levels of S100A8, S100A9, and S100A12 were assessed using enzyme linked immunosorbent assay (ELISA) kit. Thermo MK3 microplate reader 490 nm was used to measure the optical density values. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Total- 56		
Gender	**Males**	**Females**
Number	30	26

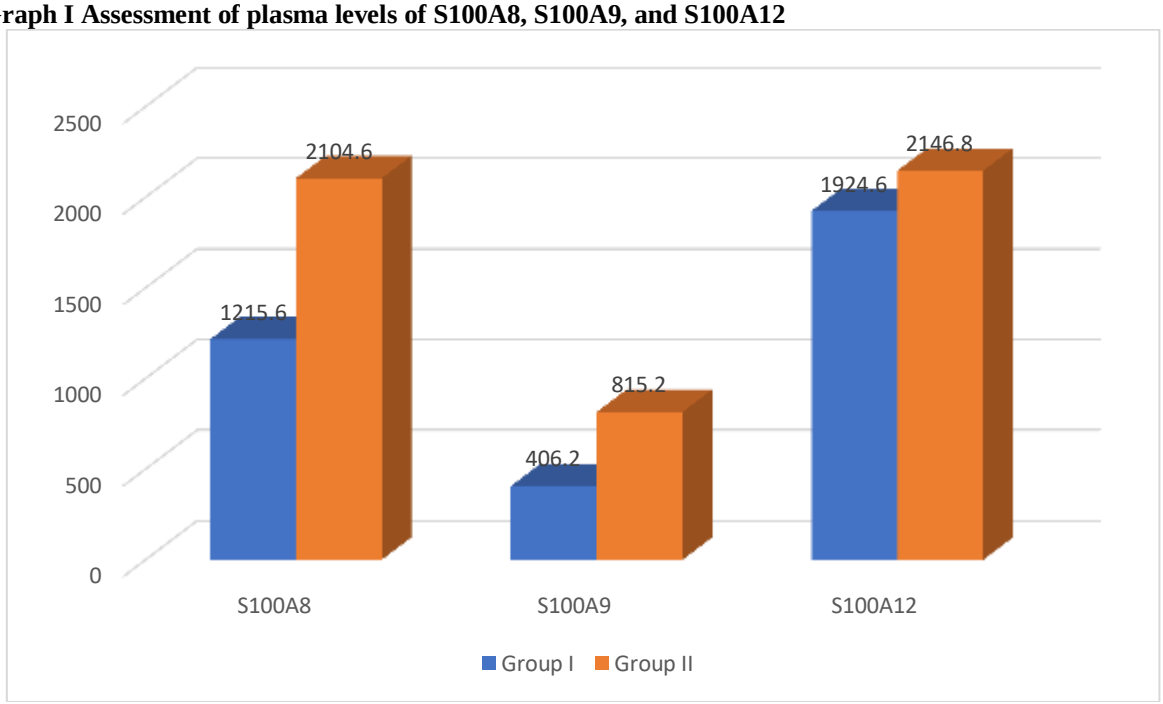
Table I shows that out of 56 patients, males were 30 and females were 26.

Table II Assessment of plasma levels of S100A8, S100A9, and S100A12

Parameters	Group I	Group II	P value
S100A8	1215.6	2104.6	0.001
S100A9	406.2	815.2	0.01
S100A12	1924.6	2146.8	0.02

Table II, graph I shows that mean S100A8 level in group I was 1215.6 pg/ml and in group II was 2104.6 pg/ml, S100A9 level was 406.2 pg/ml in group I and 815.2 pg/ml in group II, S100A12 level was 1924.6 pg/ml in group I and 2146.8 pg/ml in group II. The difference was significant (P< 0.05).

Graph I Assessment of plasma levels of S100A8, S100A9, and S100A12



DISCUSSION

Urticaria that is present for greater than 6 weeks is arbitrarily considered to be “chronic” based on the observations that acute, self-limited episodes of urticaria tend to subside in 1–3 weeks, and that by assuming a cut off at 6 weeks, the likelihood that some exogenous cause of the pathogenic process is very low and thus differs from causes of acute urticaria. Acute urticaria is typically caused by an identifiable agent such as an allergic reaction to a food or drug, or associated with viral illnesses as is often the case in children. Conversely, an exogenous cause for the chronic circumstance is virtually never found.[6] S100A8, S100A9, and S100A12 are predominant cytoplasmic proteins of neutrophils and are produced by various cells, playing important role in innate

immunity and the inflammatory process.[7] There is evidence that they were involved in many autoimmune-associated diseases including psoriasis, rheumatoid arthritis, atopic dermatitis, and so on. However, there are no available data regarding behavior of S100A8, S100A9, and S100A12 in patients with CSU.[8] This study was performed to investigate S100A8, S100A9, and S100A12 levels in plasma of CSU patients and to compare with that of healthy controls.

In present study, out of 56 patients, males were 30 and females were 26. Zhou et al[9] in their study the levels of plasma S100A8, S100A9, and S100A12 were measured in 51 CSU patients and 20 healthy controls using enzyme linked immunosorbent assay kits. The values in the patient group and that of the healthy controls were statistically compared. The plasma levels of S100A8, S100A9, and S100A12 were significantly higher in CSU patients than those in controls. Interestingly, the level of S100A12 was significantly correlated with S100A8 and S100A9 in CSU patients ($P < 0.05$ and $P < 0.001$, respectively). In addition, S100A8, S100A9, and S100A12 were all significantly inversely correlated with blood basophil percentage.

We found that mean S100A8 level in group I was 1215.6 pg/ml and in group II was 2104.6 pg/ml, S100A9 level was 406.2 pg/ml in group I and 815.2 pg/ml in group II, S100A12 level was 1924.6 pg/ml in group I and 2146.8 pg/ml in group II. The exact pathogenic role of S100A8, S100A9, and S100A12 in the development of CSU is still unknown. We propose that these three S100 proteins are involved in the pathogenesis of CSU in several ways. Firstly, these three S100 proteins bind to and activate responses by two widely expressed but divergent receptors, namely, toll-like receptor 4 (TLR4) and the receptor for advanced glycation end-products (RAGE).[10] The engagement of these two receptors by S100 proteins is linked to an array of signaling pathways, notably NF-κB and mitogen-activated protein kinases; the induction of p38 signaling was known to trigger the release of proinflammatory cytokines including interleukin (IL)-6, tumor necrosis factor (TNF)-α, and IL-1β through the action of NF-κB. On the other hand, it is increasingly clear that chronic urticaria is characterized by a systemic proinflammatory state. Chronic urticaria patients were found to show increased levels of a series of cytokines including TNF-α, IL-1, IL-6, and IL-10. Recent evidence suggests that these three S100 proteins were associated with IL-1.[11] A recent report indicated that the epithelial cells could produce IL-1 and IL-1 was involved in the expression of S100A8/A9 in a human epidermal keratinocyte cell line (HaCaT). In another study, the investigators observed that S100A12 was closely linked to IL-1 expression. IL-1 is an important key cytokine related to inflammatory diseases. IL-1 evokes immune responses and induces skin lesions in urticaria and other allergy-related diseases including asthma, atopic dermatitis, and contact dermatitis.[12]

CONCLUSION

Authors found that plasma level of S100A8, S100A9, and S100A12 were elevated in CSU patients than those of healthy controls.

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