

RESEARCH ARTICLE

An approach to urticaria in the elderly patients

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Abstract

The guidelines for the management of urticaria in adults and children have been published in outstanding position papers. By contrast, the onset of urticaria in the elderly has not yet had a clear definition. In order to approach diagnosis and treatment in a population of elderly patients, we have performed an epidemiological study on a population of elderly people observed in the Immuno Allergology Unit in Bari University Hospital. The patients underwent skin prick test for food allergy and laboratory and instrumental tests. From the data it resulted that 49% of cases have had urticaria because of adverse drug reactions (ADRs), 16% of cases were positive to food, while in 21% of cases systemic and metabolic diseases (SMDs) have been diagnosed. If we consider the young controls, urticaria for ADR was present in 48% of cases; however, in 28% it was possible to make the diagnosis of food allergy, 12% cases had a SMD. Our results show that the main cause of urticaria in the elderly is related to drug assumption because of the high number of drugs taken, followed by internal pathologies correlated to the typical immune and metabolic changes of the elderly. Furthermore, from the observation of our data it was possible to give guidelines for the treatment of urticaria in geriatric age.

Keywords: Old people, systemic and metabolic disease, food allergy, comorbidities, adverse drug reaction

Introduction

Urticaria is described as one of the most common dermatological diseases with a prevalence ranging between 0.5% and 1% in the general population and with an higher incidence in women than men. According to the current guidelines, Chronic Urticaria (CU) is characterized by the appearance of wheals and/or angioedema persisting for more than 6 weeks.⁽¹⁾ Urticaria is an extremely disabling syndrome, which limits the normal activities of daily living, even in response to severe anxiety disorders linked to the sudden onset of symptoms.⁽²⁾ Urticaria has not only an allergic etiology, but may also result from internal pathologies, including bacterial, viral and parasitic diseases, cancer, diabetes, autoimmune diseases⁽³⁾ and physical factors. In addition, there are hereditary forms such as hereditary angioedema etc.

There are several studies in the literature investigating the prevalence and suggesting guidelines for the diagnosis and treatment of urticaria in adults⁽⁴⁾ and children.

However, few studies have examined the prevalence of urticaria in elderly people and its possible

etiopathogenesis. In addition, there are no specific guidelines for the diagnosis and treatment of this syndrome in elderly patients at the moment. The aims of our study are:

1. To assess the prevalence of urticaria in elderly subjects admitted to an Immuno Allergology Unit (IAU)
2. To explore its etiopathogenesis
3. To propose diagnostic and therapeutic procedures for old patients.

Materials and methods

One hundred and ninety-three patients who were observed in the IAU of Bari University Hospital complained the onset of urticaria/angioedema episodes. Among these, 67 were males and 126 were females; the mean age was 73 years (ranging from 65 to 91). Family and personal history were taken, paying special attention to allergic diseases, particular emphasis was dedicated to atopy and any adverse reaction to drugs and foods. Two

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hundred subjects were considered as control group: of them 69 were males and 131 females (mean age 34, ranging from 17 to 64). They were received at the same IAU for problems of urticaria and/or angioedema. The patients underwent blood tests (blood count, blood glucose, total protein and serum electrophoresis, liver function, direct and indirect bilirubin, renal function, serum electrolytes, thyroid function and autoantibody pattern, viral markers, total cholesterol, high-density lipoprotein, low-density lipoprotein cholesterol, triglycerides, uric acid, erythrocyte sedimentation rate, C reactive protein, C3-C4, rheumatoid test, Waaler Rose, tumor markers, prostate-specific antigen in males, urine analysis with urine culture if necessary and parasitological examination of stool) and skin prick test for food allergens. All the patients were requested cardiology consultation with electrocardiogram, clinical breast and pelvic examinations in women, urological visit for men, breath test for *Helicobacter Pylori* (HP) and oral panoramic radiograph for the detection of dental infectious foci.

Results

Considering all old patients, in 49% of cases we could diagnose adverse drug reactions (ADRs); 16% had an immunoglobulin E (IgE) - mediated food allergy; 21% had systemic and metabolic disorders; in 5% cases it was possible to diagnose a cancer (breast and prostate), 3% had an intestinal infestation with parasites; in 1% of cases dental

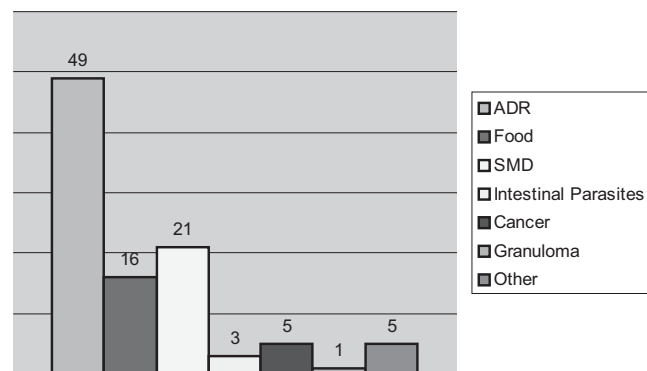


Figure 1. Incidence of urticaria in elderly people.

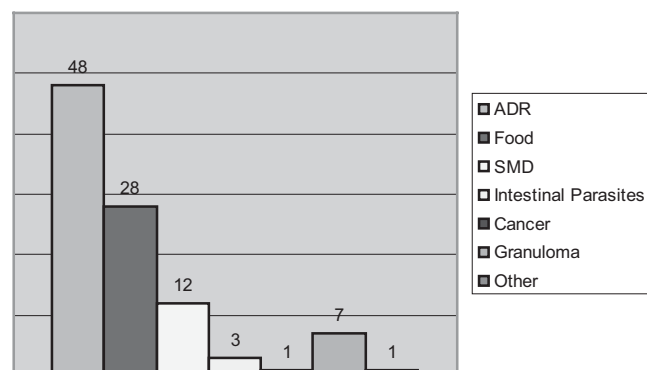


Figure 2. Incidence of urticaria in young people.

granuloma was radiographically diagnosed (Figure 1). With regard to the ADR it is important to outline that the symptoms appeared after taking the suspected drug with complete disappearance after the suspension in 93% of cases. It should be outlined that the patients were taking angiotensin-converting enzyme (ACE) inhibitors in cases of urticaria that did not remit even after the discontinuation of the drug. If we consider the young controls, ADRs were responsible in 48% of cases. We observed the complete remission in 99% of subjects after the suspension of the offending drug. At the same time it was possible to diagnose food allergy in 28%; 12% had SMDs; only 1% had cancer; 3% had infestation of intestinal parasites; in 7% it was possible to diagnose foci of tooth or tonsil (Figure 2).

With particular regard to the SMD, 30 of the 193 subjects suffered from diabetes; 22 of the 193 subjects suffered from dysthyroidism (12 patients with both diseases), thus confirming the association between more than one metabolic disease and, in 9 cases, there were also other diseases like dental granuloma, cancer or intestinal parasites etc.

If we consider the two groups of patients with regard to the incidence of urticaria, there is no statistically meaningful difference ($p = n.s.$). However, in the old people SMD is associated to urticaria, while in young people there is a meaningful difference: $p < 0.05$. By analysing the possible correlation between comorbidity and CU in our elderly population, the presence of two or more concomitant diseases results in increased risk of urticaria. In addition, subjects with comorbidities have a major risk of ADR because of the intake of many drugs. Thus considering the incidence of urticaria in patients with ADR, it is confirmed that the comorbidity increases the risk factor for urticaria in the elderly.

Discussion

Our results show that the main cause of urticaria in the elderly in comparison with young people is the comorbidities; our hypothesis is that the elderly generally have three or more diseases and take many drugs, with the risk of adverse reactions that are also correlated with autoimmune diseases, neoplasms, metabolic and skin changes, typical of advanced age.⁽⁵⁻⁷⁾ In young subjects the presence of urticaria is commonly correlated with IgE-mediated food allergy.⁽⁸⁾

Considering the high incidence of diseases such as diabetes, dysthyroidism, autoimmune diseases and malignancies in the geriatric age, it is therefore important to stress the possibility that other underlying diseases could be masked by urticaria, or that urticaria itself could be the first clinical manifestation of such diseases. From the data it can be highlighted that the elderly population suffer from multiple diseases and that the treatment with more than one drug predisposes to ADR. The risk is increased when there are two or more underlying diseases.

With regard to ADR, it seems that the impact of urticaria is comparable in juvenile and geriatric age. However, the meaningful correlation between urticaria and ADR in elderly people treated with ACE-inhibitors must be emphasized. Urticaria is strictly correlated to the degranulation of mast cells and to the increase of mediators such as bradykinin, that is responsible for angioedema induced by many drugs like antihypertensive drugs.^(9,10) This event is particularly important in geriatric age because of the typical old age polypharmacy, that exposes this population to the phenomenon of ADR and because of the problems of pharmacokinetic and pharmacodynamic interactions between different active molecules.⁽¹¹⁾ The cause of this increased susceptibility is undoubtedly due to both progressive depletion of the functions of metabolism, to the increased sensitivity of the immune system to different stimuli, to the changes and also to the multiple diseases affecting old people.⁽¹²⁾ The gradual deterioration of equipment and systems, the comorbidity and the polypharmacy make the treatment of urticaria very difficult in geriatric age. In fact, the range of therapeutic possibilities and also the dosages should be reduced and subjected to a more accurate assessment. From the therapeutic point of view, the indiscriminate use of antihistamines and corticosteroids should be carefully avoided. For this purpose it should be remembered that the gold standard treatment of urticaria is the use of second-generation antihistamines, characterized by greater efficiency and duration of action; by contrast, side effects appear to be lower than the antiH1 of first generation.^(13,14) If the symptoms persist for more than 2 weeks in the young adult, dosages of these drugs can be increased up to four times more than the baseline dose to achieve remission from disease and a prolongation of clinical wellness. If the resolution of the picture is not achieved after further 1–4 weeks, it would be useful to change antihistamine or to associate leukotriene modifiers. The lack of improvement in symptoms requires a more aggressive treatment, causing worse side effects. Among the drugs used for the treatment of more resistant urticaria, several studies have shown excellent results with cyclosporine, which shows inhibitory effects on the degranulation of mast cell and basophils.⁽¹⁵⁾ As the elderly population increases worldwide, it becomes imperative to draw guidelines and therapeutic strategies for this population that requires particular attention in the management of doses and the time of administration because of drug interactions, because of the possible negative effect on pre-existing conditions and because of the increased metabolic and immune modification in geriatric age.⁽¹⁶⁾

In particular, the dosages of antihistamines should be limited to prevent the risk of falls due to excessive sleepiness or kinetic instability. In case of treatment with steroids, they should be administered as briefly

as possible, and with continuous control of blood pressure and measurement of glucose level, given the high prevalence of hypertension and diabetes in the elderly population, with much less reactions occurring with steroids. In our experience in the chronic treatment and in the prevention of exacerbations in case of resistance it is at first necessary to remove the cause and do not exceed two or three times from the baseline value of the recommended antihistamine dosage. Old people should avoid the first-generation antihistamines because of the typical anticholinergic effects of this class of drugs, badly tolerated and responsible for the worsening of constipation and urinary retention, that is very frequent in geriatric patients, as well as further impairment of cardiovascular problems with tachycardia and possible cognitive worsening in patients with dementia.

Declaration of interest

The authors report no conflict of interest.

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