

Acute Urticaria: Clinical Aspects and Therapeutic Responsiveness

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Although acute urticaria is common, its eliciting factors, clinical course and therapeutic responsiveness have not been intensively investigated. We have therefore prospectively studied all patients with acute urticaria attending the department of dermatology ($n=72$) and a rural dermatology office ($n=37$) during the course of 1 year. After a standardized history and physical examination, patients were randomized into treatment with either loratadine (10 mg/day for 3 days) or prednisolone (50 mg/day for 3 days). All patients were followed up until complete remission.

Most patients suffered from moderate (42%) to severe (40%) disease. Possible eliciting factors were identified in less than 50% of the cases. Associated upper respiratory tract infections were found most commonly (39.5%), followed by possibly eliciting drugs, mostly analgesics (9.2%) and suspected food intolerance (0.9%). The course of the disease was self-limited in all cases, the longest episode lasting for 3 weeks. Both treatment regimens were effective in controlling whealing, but in corticosteroid-treated patients, symptoms ceased earlier, with complete remission occurring within 3 days of treatment in 93.8%, compared to 65.9% of patients treated with loratadine ($p<0.001$). Acute urticaria is thus frequently idiopathic and only rarely associated with IgE-mediated events. It is, however, largely self-limited, with prompt response to symptomatic treatment. **Key words:** upper respiratory tract infection; drug intolerance; anti-histamines; corticosteroids.

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Acute urticaria is defined as a short, self-limited period of whealing lasting for a few days up to a few weeks. The disease is common, affecting more than 12% of the population at least once in their lifetime (1, 2). Drug reactions, food allergy and infections are regarded as possible causes (3–6), but the prevalence and relevance of each of these factors are not well known. Also, hardly any data are available on the natural course of the disease and on the number of cases proceeding to chronic urticaria, which has been estimated to range at about 10% (7, 8). Furthermore the effect of antihistamine versus corticosteroid treatment has not been investigated so far. In order to address these questions, we designed a prospective study regarding causes and treatment responsiveness in patients seen over the course of 1 year.

PATIENTS AND METHODS

All patients with newly developed and untreated acute urticaria attending the off-hour service of the department of dermatology ($n=72$) and one dermatological practice in the vicinity of Berlin ($n=37$) within 1 year (Dec. 1993–Nov. 1994) were included in this prospective study. (There was a predominance of female (59%) and young to middle-aged patients (37% were younger than 25 years and 77% younger than 40 years), mean age 31.4 years, SD: 13.7 years, range

5–86 years with only one pre-school child and one senior citizen; corrected for these two extreme values the age ranged between 11 and 66 years.)

A standardized history was taken at first presentation on the basis of a questionnaire, and a brief physical examination was then performed. Questions referred to the duration and intensity of cutaneous and systemic symptoms, associated activities, intake of drugs (within 24 h before onset) and food (within 2 h before onset), associated acute infectious diseases, other diseases, known allergies and former episodes of urticaria. Severity of clinical symptoms was classified as mild (less than 10% of body area affected, in 18% of patients), moderate (10–50% of body area affected, in 42% of patients), or severe (> 50% of body area affected and/or systemic symptoms, in 40% of patients, coexisting systemic symptoms: mild shortness of breath 7.3%, dizziness 2.7%, headache 1.8%, nausea 1.8%, diarrhoea 0.9%).

None of the patients required emergency i.v. drug treatment. Wheals were mostly red (88%) and in 80% larger than 1 cm in diameter. Six percent of patients showed exclusively pinpoint sized wheals.

Unless contraindicated (possible pregnancy, allergy against loratadine), all patients were treated with loratadine until remission of symptoms (10 mg/day, $n=44$) during the first 6 months of the study. This regimen was changed to an initial treatment with prednisolone (50 mg/day for 3 days), followed by loratadine treatment (10 mg/day) until remission of symptoms during the second 6 months of the study ($n=65$). This simple design was chosen since blinded randomization appeared too complicated for logistic reasons, in particular with regard to the shifting off-hour staff and different emergency rooms. When symptoms persisted beyond the first 3 days of treatment, loratadine (10 mg/day) was given to all patients until total clearance of symptoms.

All patients were followed up for 8 weeks by the same physician, who also verified the original history taken at the first presentation. A prolonged follow-up had been planned in case of incomplete remission at that time. Drug intolerance was considered likely if drugs were taken within 24 h before onset of symptoms. Drugs taken regularly over longer periods of time were allowed to be continued. These drugs were not considered to be a likely cause of the urticaria when remission of whealing was observed in spite of continuous intake. Food intolerance was only regarded as a likely cause in patients reacting with urticaria within 2 h after ingestion of suspected foods. Foods which were tolerated after remission of symptoms were subsequently rejected as a possible eliciting factor.

The chi square test was used for statistical analysis.

RESULTS

Table I summarizes the possible triggering factors of acute urticaria. A strikingly high prevalence (39.5%) of associated upper respiratory tract infections was observed (generally a common cold, pneumonia was not seen).

Table I. Possible eliciting factors of acute urticaria based on patient's history and information gathered during follow-up

Suspected cause	Percentage of patients
Upper respiratory tract infection	39.5
Drug intolerance	9.2
Food intolerance	0.9

Table II. Follow-up of patients with acute urticaria after initial treatment with loratadine ($n=44$) or prednisolone ($n=65$) for 3 days

All patients were then treated with loratadine (10 mg/d) until remission.

Cessation of whealing within:	Loratadine (10mg/d)	Prednisolone (50 mg/d, for 3 days)
3 days	65.9%	93.8%*
7 days	15.9%	3.1%
14 days	15.9%	1.5%
21 days	2.3%	1.5%
>21 days	0%	0%

* $p < 0.001$.

Possible drug reactions were infrequent (9.2%) and were in all but one case associated with upper respiratory tract infections. Implicated drugs included aspirin (4 ×), other analgesics (5 ×) and sulfonamide (1 ×). 20.2% of the patients were taking other drugs on a regular basis, but these could be excluded as a possible cause since remission occurred in all cases despite continued treatment.

Sixty-three per cent of the patients had consumed some food 2 h before the onset of urticaria. Food allergy was suspected only in one 58-year-old patient, who had reacted repeatedly in the past within 15 min after the ingestion of buttercream filled cakes. In the other patients, food intolerance appeared unlikely, since the ingested foods were either part of the daily diet or were tolerated on reexposure. None of these patients had experienced any signs of food intolerance before. The overall prevalence of type I allergy (allergic rhinitis and allergic asthma) was 22%, based on patient's history. Thirteen patients (12%) reported preceding solitary episodes of acute urticaria between the previous 6 months and 10 years. In 2 of these patients hives had been related to aspirin intake, in one patient urticaria had followed the sting of a wasp, in the other patients the cause had remained unclear.

All patients were included in one of the two treatment groups following the criteria described in the methods section. Since patients with potential pregnancy had to be excluded from loratadine therapy, more women were treated with prednisolone (43 females/23 males) than with loratadine (21 females/23 males), but no statistically relevant differences were seen regarding age and severity of urticaria in the two treatment arms (32 ± 1.7 years in the prednisolone group versus 30 ± 2.1 years in the loratadine group and 43% moderate and 37% severe cases in the prednisolone group, versus 41% moderate and 43% severe cases in the loratadine group). The results of the different treatment regimens are summarized in Table II. Both treatments proved to be effective, with cessation of symptoms within 3 days in the majority of patients, although patients improved more rapidly after treatment with prednisolone ($p < 0.001$). None of the patients developed chronic urticaria. Side-effects were not observed in either treatment group.

DISCUSSION

The present study is in agreement with previously published data regarding a higher prevalence of females and young to middle-aged persons in acute urticaria (6, 7, 9). In addition,

it provides new data regarding eliciting factors, clinical course and responsiveness to treatment.

Regarding possible etiologic factors, this study underlines the potential importance of upper respiratory tract infections (39.5%) as an underlying cause of acute urticaria. A high prevalence (28%) of infections (mostly acute respiratory) has been previously observed by Kauppinen et al. in a retrospective study (10) of 40 children with acute urticaria. An even higher association was noted by Aoki et al. (11) in a follow-up study of 50 adults with acute urticaria, with 31 patients having noted signs suggestive of acute infection before or shortly after onset of urticaria. In a retrospective study of infants, Legrain et al. (12) suspected mainly viral infections and/or drugs in 50% as eliciting cause of acute urticaria in the subgroup older than 6 months of age ($n=28$). These observations are in agreement with our findings, where drugs were incriminated as the second most frequent cause (9.2%) and the combination infection and/or drugs had a frequency of 48.7%. Since in all but one case, these drugs (mostly aspirin and analgesics) were taken for upper respiratory tract infections, it cannot be determined with certainty which of the two factors, infection or drug, was the eliciting cause of urticaria. Furthermore, urticarial reactions against aspirin and other non-steroidal analgesics are of a pseudoallergic nature (13), with no reliable diagnostic measure available except for provocation tests. For safety reasons, however, it did not seem justified to perform such tests, since the suspected drug could easily be avoided or substituted by a non-crossreactive substance.

Regarding the frequency of food intolerance in urticaria, Legrain et al. (12) found a high prevalence in infants younger than 6 months of age (10 of 12 children, mainly cow's milk allergy), while infections hardly played any eliciting role (1 of 12 children only) in this age group. In older children with urticaria (6 months to 16 years), Kauppinen et al. (10) observed only a 15% prevalence of food intolerance and in adult patients, foods could not be incriminated in a single case of the 50 patients followed by Aoki et al. (11). In our study, which also includes mainly adult patients, food allergy appeared also to be of minor importance as an eliciting factor of acute urticaria. Furthermore, the prevalence of atopy in our patients (22%) was similar to the 30% prevalence of atopy found in a healthy Berlin population (age group 15–35 years) (14). Based on the present findings and the more recent studies on acute urticaria, type I allergy thus appears to play a less important role in the etiology of acute urticaria than suspected in older reports (1–3). In addition, acute urticaria mostly represents a solitary and self-limited episode of whealing. Its eliciting causes can therefore not be sought among foods or drugs taken regularly or frequently, while acute infections or a transient drug intake would fit into the picture. Since none of our patients developed chronic urticaria, earlier estimations of about 10% (7, 8) of cases proceeding from acute to chronic urticaria appear much too high. Thus, due to the lack of simple diagnostic tests and the generally benign, self-limited course of the disease, an extensive search for the eliciting factor does not appear justified in most of the cases of acute urticaria.

For symptomatic treatment of acute urticaria, both antihistamines or a short course of corticosteroids are in use but so far, no hard data are available on the comparative value of these treatments. In the present study, both prednisolone and loratadine proved to be highly effective in controlling whealing

and pruritus, but a significantly higher number of patients were free of symptoms after 3 days of treatment in the prednisolone-treated group. The reasons for this finding must remain speculative. The most likely explanation relates to the multifold actions of corticosteroids on various immune and inflammatory aspects of urticarial reactions (15). Although it was recently shown that loratadine has functions beyond those of H1 receptor blockade, such as inhibition of basophil histamine release (16) or cytokine release from mast cells (17), these effects are not as pronounced as those of corticosteroids. On the other hand, antihistamines are very well tolerated, with hardly any potential adverse events compared to corticosteroids, and they should be chosen when prolonged treatment is necessary. Still, the short, low-dose course of corticosteroids employed in this study hardly involves any risk of side-effects and may be considered an effective therapeutic choice in acute urticaria.

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