Urticaria and Its Update Management

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Abstract

Urticaria is a skin lesion consisting of a wheal and flare reaction, localized intracutaneous edema is surrounded by an area of redness with pruritus. Angio-oedema has some pathogenic mechanisms as urticaria but is in the deep dermis, subcutaneous tissue and swelling is the major manifestation. Urticaria / angio-oedema is considered acute if the condition lasts less than 6 weeks and chronic if lasting beyond 6 weeks. Update management of urticaria depends on the correct evaluation of clinical patterns and causes where these can be identified. Urticaria has a profound impact on the quality of life and effective treatment is required. The recommended first line treatment are non sedating H1 antihistamines. For different urticaria subtypes and in view of individual variation in the course of the disease and response to treatment, additional or alternative therapies may be required. Update treatment is presented based on the literature review available at the time of preparation. As many of the recommendations relate to the use of drugs, it is particularly important that clinicians should be familiar with dosing and site effects of treatment in the contest of managing urticaria. 

Key words: Urticaria, update management.

Introduction

Urticaria is defined as a skin lesion consisting of a wheal and flare reaction in which localized intracutaneous edema is surrounded by an area of erythema that is pruritic. Incidence rate for acute urticaria are similar for men and women but chronic urticaria occurs more frequently in women(60%). No racial

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Urticaria affects 15-20% of the general population at sometime during their lifetime. 

Urticaria(Hives)

Angioedema
variation is noted. Urticaria can occur in any age group although chronic urticaria is more common in the 4th and 5th decades.²

Clinically urticaria classified as³:

Ordinary urticaria
- Acute (up to 6 weeks of continuous activity)
- Chronic (6 weeks or more of continuous activity)
- Episodic (acute intermittent or recurrent activity)

Physical urticaria (reproducibly induced by the same physical stimulus)
- Mechanical
  - Delayed pressure urticaria
  - Symptomatic dermographism
  - Vibratory angio-edema
- Thermal
  - Cholinergic urticaria
  - Cold contact urticaria
  - Localized heat urticaria

Others:
- Aquagenic urticaria
- Solar urticaria
- Exercise induced anaphylaxis
- Angio edema with wheels
- Angio edema associated with ACE inhibitors
- Angio edema without wheels
- Idiopathic
- Drug induced
- CI esterase inhibitor deficiency
- Contact urticaria (contact with allergens or chemicals)
- Urticular vasculitis (defined by vasculitis on skin biopsy)
- Autoinflammatory syndromes
- Hereditary
- Cryopyrin associated periodic syndromes
- Acquired
- Schnitzel syndrome

According to etiology urticaria classified as⁴:

- Idiopathic
- Immunological
- Autoimmune
- Allergic
- Immune complex
- Complement dependent (CI esterase inhibitor deficiency)
- Nonimmunological
- Direct mast cell releasing agents (opioids)

Aspirin, NSAIDS and dietary pseudoallergens

ACE inhibitors

Management

General measures: Non specific aggravating factors, such as overheating stress, alcohol and drugs (aspirin, codeine) should be minimized. NSAIDS should be avoided in aspirin sensitive patient. ACE inhibitors should be avoided in patients with angioedema without wheals. Oestrogen should be avoided in HAE. Cooling antipruritic lotions such as calamine or 1% menthol in aqueous cream can be soothing.³ Cool compresses ice pack may provide temporary relief.⁴

Specific treatment

Acute urticaria: Non sedating 2nd generation antihistamine: Loratadine⁴ or Cetirizine⁵ once daily. In non responsive patients: Prednisolone 2x20 mg/day for 4 days⁶ or Prednisolone 50 mg /day for 3 days⁷ or H2 blocker, single dose for 5 days.⁸⁹

For severe reactions (anaphylaxis): 0.3 ml dose of 1:1000 dilution of epinephrine is administered every 10 to 20 minutes as needed. In young children, a half strength dilution is used. Oct. Adjunctive therapy includes intramuscular antihistamine (diphenhydramine 25 mg iv or im or hydroxyzine 50 mg im² with systemic corticosteroid (250 mg hydrocortisone or methyl prednisolone iv every 6 hours for 2 to 4 doses).⁹

Chronic urticaria: The mainstay for treating chronic urticaria is non sedating 2nd generation antihistamines (Cetirizine, Desloratadine, Loratadine, Azelastine, Ebastine, Fexofenadine, Levocetirizine, Micolastine)¹⁰¹¹ used as once daily or may increase doses if necessary up to four fold.

In case of non responsive patients:
Combination therapy: Non sedating 2nd generation antihistamine and cyclosporine A¹²¹³ / non sedating 2nd generation antihistamine and montelukast¹⁴¹⁵ / non sedating 2nd generation antihistamine and cemetidine¹⁶¹⁷¹⁄₂ non sedating 2nd generation antihistamine and stanazol¹⁸¹⁹ / non sedating 2nd generation antihistamine and zafirlukast.²²

Monotherapy: Tricyclic antidepressants
(doxipen)23,24 / Ketotifen25 / Hydroxychloroquine27 / Dapsone28 / Sulfasalazine29 / Methotrexate30 / Corticosteroid31 / Azathioprine32 / Oxatomide33 / Nifedipine34 / Montelukast35 / Warfarin36 / Interferon37 / Plasmapheresis38 / Immunoglobulin39 / UV light therapy.40

Angioedema

Hereditary Angioedema:41

Type I and II (decrease C4, C1q, C2, normal C1-E1):
- Concentrates or Fresh Frozen plasma
- Stannazol
- Anti fibrinolytic tranexamic acid

Type III (Normal complement, normal C1-E1):
- Danazol

Acquired Cesterase inhibitor deficiency (Type I, II, Idiopathic):
- Tranexamic acid 0.5 to 3.0 g/m/day
- Danazol
- Immunosuppressive therapy
- Stanozol
- Systemic corticosteroids
- Plasmapheresis

Physical Urticaria:
- Dermatographism: Cetirizine32 / Ketotifen33
- Pressure urticaria: Cetirizine34
- Non responsive patients: Montelukast with Loratadine35 / Dapsone36 / IVIG37
- Cold urticaria38:
  - Primary: Dosepsin / Cyproheptadine / Acrivastine / Cetirizine / Cetirizine with Zafirlukast / Ketotifen / Desensitization
  - Familial cold urticaria: Stannazol
- Solar urticaria: Cetirizine39 / Fexofenadine27 / Loratadine9

In non responsive patients: Plasmapheresis / Plasmapheresis + PUVA / Photopheresis
- Plasma exchange / IVIG / Hydroxychloroquine
- Adrenergic urticaria: Propranolol40 10 mg 4 times daily
- Cholinergic urticaria: Cetirizine48

In non responsive patients: Ketotifen33 / Danazol39
- Exercise induced urticaria: H1 + H2 antihistamines / Epinephrine
- Visceral angioedema: H1 antihistamines
- Aquagenic urticaria: Antihistamine / PUVA and prevention by pretreatment of the skin with petrolatum.

Conclusion
The quality of life in urticaria is affected severely and management of the disease should therefore be prompt and in close co-operation between patient and physician. Due to high variability of disease severity, an individual approach is necessary for each patient. In the majority of patients, symptomatic pharmacological treatment is possible with new generation antihistamines, with a very low adverse effect profile and good patient compliance. In non responding patients, higher dosages (up to four fold) and alternative medication should be tried.

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