Review Article

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-edema has same pathogenic mechanisms as urticaria but is in the deep dermis, subcutaneous tissue and swelling is the major manifestation. Urticaria / angio-edema 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.

Indroduction

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.[1]

Urticaria results from the release of histamine, bradykinin, leukotriene C4, prostaglandin D2 and other vasoactive substances from mast cells and basophils in the dermis.[2]

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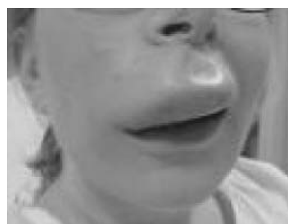
Incidence rate for acute urticaria are similar for men and women but chronic urticaria occurs more frequently in women(60%). No racial

Urticaria(Hives)



Angioedema

Urticaria affects 15-20% of the general population at sometime during their lifetime.[1]

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 as[3]:

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 wheals
Angio edema associated with ACE inhibitors
Angio edema without wheals
- Idopathic
- Drug induced
- C1 esterase inhibitor deficiency

Contact urticaria(contact with allergens or chemicals)
Urticarial vasculitis(defined by vasculitis on skin biopsy)
Autoinflammatory syndromes
- Hereditary
  - Cryopyrin associated periodic syndromes
- Acquired
  - Schintzer syndrome

According to etiology urticaria classified as[3]:
- Idiopathic
- Immunological
  - Autoimmune
  - Allergic
  - Immune complex
  - Complement dependent(C1 esterase inhibitor deficiency)
- Nonimmunological
  - Direct mast cell releasing agents(opiates)
  - 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 with urticaria. 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 aquous cream can be soothing.[3] Cool compresses ice pack may provide temporary relief.[1]

Specific treatment

Acute urticaria: Non sedating 2nd generation antihistamine:Loratadine4 or Cetirizine5 once daily. In non responsive patients: Prednisolone 2×20 mg/day for 4 days[6] or Prednisolone 50 mg /day for 3 days4 or H2 bloker, single dose for 5 days.[7,8,9]

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 used10. Adjunctive therapy includes intramuscular antihistamine (diphenhydramine 25mg iv or im or hyrdroxyzine 50mg im[2] with systemic corticosteroid (250mg hydrocortisione or methyl prednisolone iv every 6 hours for 2 to 4 doses).[10]

Chronic urticaria: The mainstay for treating chronic urticaria is non sedating 2nd generation antihistamines (Cetirizine, Desloratadine, Loratadine, Azelastine, Ebastine, Fexofenadine, Levocetirizine, Mezolastine)[11-12] used as once daily or may increase doses if necessary upto four fold.

In case of non responsive patients:

Combination therapy: Non sedating 2nd generation antihistamine and cyclosporineA[13]/ non sedating 2nd generation antihistamine and montelokast[14-16]/ non sedating 2nd generation antihistamine and cemetidine[17-20]/ nonsedating 2nd generation antihistamine and stanazol[21]/ nonsedating 2nd generation antihistamine and zafirlukast.[22]

Monotherapy: Tricyclic antidepressants

(doxipen)[23-25]/ Ketotifen[26]/ Hydroxy chloroquine[27]/ Dapsone[10]/ Sulfasalazine[10]/ Methotrexate[10]/ Corticosteriod[10]/ Azathiprine[10]/ Oxatomide[28]/ Nifedifine[29]/ Montelukast[30]/ Warfarin[31]/ Interferon[10]/ Plasmapheresis[10]/ Immunoglobulin[10]/ UV light therapy.[10]

Angio Edema

Hereditary Angioedema[10]:

Type I and II (decreaseC4,C1,C1q,C2, normal C1-E1):

Concentrates or Fresh Frogen plasma
Stanazol
Anti fibrinolytic tranexamic acid

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

Danazol

Acquired C1esterase inhibitor deficiency(Type I, II, Idiopathic)[3,10]:

Tranexamic acid 0.05 to 3.0 gm/day
Danazol
Immunosuppressive therapy
Stanozol
Systemic corticosteroids
Plasmapheresis

Physical Urticaria:

Dermatographism: Cetirizine[32]/ Ketotifen[33]
Pressure urticaria: Cetirizine[34]

Non responsive patients: Montelukast with Loratadine[35]/ Dapsone[10]/IVIG[10]

Cold urticaria[10]:

Primary: Doxepin/ Cyproheptadine/ Acrivastine/Cetirizine/Cetirizine with Zafirlukast/Ketotifen/Desensitization

Familial cold urticaria: Stanazol

Solar urticaria : Cetirizine[36]/ Fexofenadine[37]/ Loratadine[3]

In non responsive patients[3]: Plasmapheresis/ Plasmapheresis+PUVA/ Photopheresis/ Plasma exchange/ IVIG/ Hydroxychloroquine

Adrenergic urticaria:Propranolol[10] 10 mg 4 times daily

Cholinergic urticaria: Cetirizine[38]

In non responsive patients: Ketotifen[33]/ Danazol[39]

Exercise induced urticaria[10]: H1+H2 antihistamines/ Epinephrine

Vibratory angioedema[10]: H1 antihistamines

Aquagenic urticaria[10] : 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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