Frequency of Cholinergic Urticaria among University Students in Cairo and its Impact on Quality of Life

Thesis

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Amr Mohamed Swidan

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List of Abbreviations

Abb.	Full term
AD	Atopic dermatitis
AGH	Acquired generalized hypohidrosis
ASA	Addition to aspirin
CBC	Complete blood count
CHRM3	Cells express cholinergic receptor muscarin 3
CIU	Chronic idiopathic urticaria
CU	Cholinergic urticaria
cu-Q2oL	Chronic urticaria quality of life questionnaire
DLQI	Dermatology Life Quality Index
ESR	Erythrocyte sedimentation rate
FDEIA	Food-dependent exercise-induced anaphylaxis
GI	Gastrointestinal
H1RAs	H1 receptor antagonist

INTRODUCTION

Cholinergic urticaria is a physical type of urticaria caused by an increase in core body temperature after exercise, intake of spicy foods, or exposure to stress. Lesions appear as itchy, numerous, small, 1 to 5mm papules or wheals that last for a few minutes to an hour ***(Krupa Shankar et al., 2010).***

Cholinergic urticaria (CU) is a rare condition, but its incidence might be higher than that expected by general physicians. Chrolinergic urticaria is clinically characterized by pinpoint-sized, highly pruritic wheals. Although the symptoms subside rapidly, commonly within one hour, CU may significantly impair the quality of life, especially sporting and sexual activities ***(Poon et al., 1999).***

After the morphological and functional analyses of sweat glands in CU patients ***Tong et al. (1997)***, found the involvement of acetylcholine receptor for sweating. The sweat glands receive sympathetic innervations but express muscarinic acetylcholine receptors, which are normally expressed on parasympathetic nervous systems; therefore, acetylcholine is considered to be a central signal mediator for the secretion of sweat. subcutaneous injection of cholinergic agents induces sweating and the development of numerous pin-point hives in patients with CU, and symptoms of CU are inhibited by prior atropinization of the skin ***(Horikawa et al., 2009).***

Cholinergic urticaria is not a homogeneous disease, its classification is necessary for the clinical use. however, few attempts have been performed to classify CU in the literature, and there is no solid consensus on the categorization. ***Horikawa et al. (2009)*** observed that a strong hypersensitivity to sweat was not observed in all CU patients and assumed other factors other than sweat hypersensitivity are also involved in the pathogenesis of CU.

A few studies addressed the prevalence of cholinergic urticaria,a german study done by ***Zuberbier et al. (1994),*** showed that the overall prevalence of cholinergic whealing was 11.2% with most of the affected persons being older than 20 years.

In another Indian study the overall prevalence was 4%. although the disorder occurs in both sexes, it seems to be more common in males than in females. Cholinergic urticaria usually first develops in people aged 10-30 years, with an average age at onset of 16 years and a mean age of 22 years ***(Godse et al., 2013).***

No studies have looked on the frequency of cholinergic urticaria in Egypt.

AIM OF THE WORK

To assess the frequency of cholinergic urticaria among medical students at Ain Shams university and its impact on quality of life.

1. CHRONIC URTICARIA

1.1. Definition:

Urticaria is characterized by hives or wheals, which are edematous and pruritic. In angioedema, the swelling is deeper than wheals and may affect mucosal surfaces. Urticaria is not a single disease but a reaction pattern that represents cutaneous mast cell degranulation, with the condition being defined as chronic if it persists for longer than 6 weeks ***(Azkur, 2016)***.

1.2. Classification and Etiology of urticaria

1.2.1. "Allergic" urticaria

Other than certain reactions to medication, the allergic cause of urticaria is easily recognized by the afflicted individual. In general, urticaria follows less than 30 minutes after ingestion of contact with the sensitizing agent (food, insect, etc.). Skin tests can be very useful in confirming the diagnosis of allergy.

1.2.2. "Non allergic" urticaria

- Physical urticaria

Diverse physical stimuli (heat, exercise, the sun, cold, pressure and vibration) may provoke urticaria. This kind of urticaria is called "physical", and very often occurs rapidly

(several minutes) after a physical stimulus, except in certain cases of pressure urticaria which can occur later.

Late-onset pressure urticaria (belt, bras, hands of a manual labourer, etc.) is particular, because it is often chronic, difficult to treat and characterized by lesions that are warm rather than itchy. This "inflammatory" urticaria may also be precipitated by the ingestion of "irritant" foods.

- "Pseudo-allergic" urticaria

Several substance labeled as "non-specific histamine liberators" (foods, hormones, medications, etc.) can provoke urticaria. Among these agents, the classics are: codeine, morphine, several antibiotics, radio-contrast products used in radiology, the curares (general anaesthesia) and dextran. Finally, numerous foods (strawberries, fermented products, honey, etc.) in addition to aspirin (ASA) and other anti-inflammatories can provoke a "pseudo-allergic" urticaria, quite rapidly in predisposed subjects. Unfortunately, in all these cases, allergy tests are unreliable.

- "Secondary" urticaria

Sometimes, urticaria is associated with an auto-immune disease, a hypocomplementemia, thyroid disease, cancer, or an infection (parasites, helicobacter pylori, etc.). Obviously, these pathologies need to be eliminated.

- "Reflex" urticaria

Recent studies of several hormones (gastrin, neurohormones) suggest that there is a link between these substances, mastocytes and the skin. It seems, therefore, that several "external irritants" (emotional, food, etc.) could cause urticaria (that is often called "idiopathic").

- Hereditary angioneurotic angioedema and acquired deficiencies in the inhibitor of C1 esterase. These very rare conditions are associated with a non-itchy angioedema in particular that may also manifest internally ***(Guérin Dorval, 2016)*** **- The Association of Allergists and Immunologists of Québec).**

1.3. Signs and symptoms

Urticarial lesions are transient in nature, with individual wheals typically lasting for less than 24 hours. Pruritus is the most common associated symptom of chronic urticaria.

Lesions typically can be described as follows:

- Primary lesions are edematous, erythematous papules or plaques with a pale center (wheal) and surrounding erythema (flare).
- Lesions may be pale to red (depending on background skin color)
- Lesions can be localized or generalized

- Lesions may be round, oval, annular, arcuate, serpiginous, or generalized
- Lesions resolve without post-inflammatory pigmentary changes or scaling

(Frigas et al., 2009)

1.4. Urticaria severity assessment

Visual analogue scales can be used to record and compare the degree of itch.

The activity of chronic urticaria can be assessed using the UAS7 scoring system. The daily weal/itch scores are added up for 7 days; the maximum score is 42, (table1.1).

Table (1.1): Urticaria severity assessment

Score	Weals/24 hours	Itch
0	None	None
1	<20	Mild
2	20-50	Moderate
3	>50	Intense

(Daudén et al., 2011)

1.5. Possible allergy-based etiology

The main three factors in cholinergic urticaria patients are:

An increased incidence in patients with), a marked sensitivity in some patients with anaphylactic and anaphylactoid reactions, and an immediate reactivity in some patients, suggest an allergic basis for cholinergic urticaria ***(Montgomery, 2015)***.