

AUTOLOGOUS WHOLE BLOOD VERSUS AUTOLOGOUS SERUM INJECTIONS IN PATIENTS WITH CHRONIC URTICARIA

Thesis

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By

Marwa Ali Elzamk
(M.B., B.Ch.)

Supervised by

Prof. Mohamed Abdel-Naem Sallam
*Professor of Dermatology, Venereology and Andrology,
Faculty of Medicine, Ain Shams University*

Dr. Mahmoud Abdel-Rahim Abdallah
*Assistant Professor of Dermatology, Venereology and Andrology,
Faculty of Medicine, Ain Shams University*

**Faculty of Medicine,
Ain Shams University**

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تأثير حقن الدم الكامل أو حقن مصل الدم المستمد من المريض نفسه على مرضى الشرى المزمن

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تحت إشراف

أ.د. محمد عبد النعيم سلام

أستاذ الأمراض الجلدية والتناسلية

كلية الطب - جامعة عين شمس

د. محمود عبد الرحيم عبد الله

أستاذ مساعد الأمراض الجلدية والتناسلية

كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

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10.0. SUMMARY



Chronic urticaria (CU) is defined as the recurrent occurrence of short lived wheals with or without angioedema three times or more per week for more than six weeks. It has been estimated that 0.1 % of the general population is suffering from CU but the real prevalence probably exceeds this figure.

Chronic urticaria may appear at any age although it occurs more frequently in adults and affects more women than men.

The aetiology of CU is heterogeneous. Autoimmune chronic urticaria nearly constitutes 30 -50 %. If no aetiological factors are found in spite of extensive investigations the diagnosis is chronic idiopathic urticaria.

Autoimmune chronic urticaria is characterized by presence of antibodies in the serum of the patient, these antibodies react with α -chain of the high affinity IgE receptors (Fc ϵ RI α) or with the IgE itself, leading to histamine release, they are pathogenic antibodies and belong to IgG1 and IgG3 subclasses.

The diagnosis of CU is based primarily on the patient history and clinical examination which usually adequate to establish a diagnosis of chronic urticaria and further investigations may not be

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

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ABBREVIATIONS

| | |
|---------------|--|
| AAE | : Acquired angioedema |
| Abs | : Antibodies |
| ACE inhibitor | : Angiotensin converting enzyme inhibitor |
| ACU | : Acquired cold urticaria |
| Ag | : Antigen |
| ASI | : Autologous serum injection |
| ASST | : Autologous serum skin test |
| AWB | : Autologous whole blood |
| B.C. | : Before Christ |
| CAU | : Chronic autoimmune urticaria |
| CBC | : Complete blood cell count |
| CIU | : Chronic idiopathic urticaria |
| CNS | : Central nervous system |
| CU | : Chronic urticaria |
| CYP | : Cytochrome P450 enzyme |
| DPU | : Delayed pressure urticaria |
| ESR | : Erythrocyte sedimentation rate |
| FCεRI | : High affinity IgE receptor |
| GM-CSF | : Granulocyte-macrophage colony-stimulating factor |
| h | : Hour |
| H. pylori | : Helicobacter pylori |
| HAE | : Hereditary angioedema |
| HIV | : Human immunodeficiency virus |
| IDDM | : Insulin dependant diabetes mellitus |
| IgE | : Immunoglobulin E |
| IgG | : Immunoglobulin G |
| IgM | : Immunoglobulin M |
| IL | : Interleukin |
| IVIG | : Intravenous immunoglobulin |
| LTRAs | : Leukotriene receptor antagonists |
| M/F | : Male/female |
| MC | : Mast cell |
| NB-UVB | : Narrow band ultraviolet B |
| NSAIDs | : Non-steroidal anti-inflammatory drugs |
| NSAH | : Non sedating antihistamine |
| PAF | : Platelet-activating factor |
| PG | : Prostaglandin |
| PUPPP | : Pruritic urticarial papules and plaques of pregnancy |

| | |
|--------------|---|
| RAST | : Radio-allergosorbent test |
| SA | : Spontaneous angioedema |
| SD | : Standard deviation |
| Th1 | : T helper-1 |
| Th2 | : T helper-2 |
| TNF α | : Tumour necrosis factor-alpha |
| TSS | : Total severity score |
| UEMS | : European Union of Medical Specialists |
| UV | : Ultraviolet |
| Vs | : Versus |

INTRODUCTION

Chronic urticaria (CU) is defined as the recurrent occurrence of short lived wheals with or without angioedema three times or more per week for more than six weeks. It has been estimated that 0.1% of the general population is suffering from this disease but the real prevalence probably exceeds this figure (**Greaves, 2000**).

CU may appear at any age although it occurs more frequently in adults and affects more women than men (**Sibbald et al., 1991**).

The aetiology of CU is heterogeneous. **Grattan et al. (2002)** reported that 35% of chronic urticaria cases were physical urticarias. Autoimmune urticaria nearly constitutes 20-35%. Other less common cause is urticarial vasculitis. If no aetiological factors are found inspite of extensive investigations the diagnosis is chronic idiopathic urticaria.

The simplest screening method to identify autoimmune urticaria is autologous serum skin test (ASST) in which intradermal injection of autologous serum in these patients leads to wheal and flare response indicating the presence of circulating histamine releasing factors (**Sabroe et al., 1999a**).

The basic treatments of chronic autoimmune urticaria are antihistamines and systemic steroids, but response is often incomplete (**Greaves, 1981**).

Staubach et al. (2006) suggested that repeated intramuscular injections of autologous whole blood to patients with chronic autoimmune urticaria gave benefit to ASST +ve patients.

Also **Bajaj et al. (2008)** suggested that repeated intramuscular injections of autologous serum to patients with CU gave more benefit to ASST +ve patients. To the best of our knowledge no body has compared serum with blood injection.

AIM OF THE STUDY

Aim of the study is to evaluate the efficacy of autologous whole blood versus autologous serum therapy in patients with chronic autoimmune urticaria.



1.0.0. DEFINITION AND CLASSIFICATION OF URTICARIA



1.1.0. Definition and history of urticaria

1.1.1. Definition

Urticaria is characterized by the rapid appearance of wheals and/or angioedema (**Zuberbier and Maurer, 2007**).

It is described as an eruption of pruritic transient (<24 hours), well demarcated superficial erythematous or pale swelling of the dermis (**Greaves, 1995**).

1.1.2. History of urticaria

Urticaria, commonly called 'hives,' has a long and rich history in documented medicine dating back at least to the 10th century B.C. when it was called 'Feng Yin Zheng' in China. Many cultures have described urticaria in some capacity and the disorder has had many names. In the 4th century B.C., Hippocrates noted the similarities between urticaria, contact with stinging nettles, and insect bites and called the condition 'cnidosis' (nettle rash). William Cullen was probably the first to use the term urticaria in 1769 (**Poonawalla and Kelly, 2009**).

1.2.0. Classification of urticaria

The clinical manifestations of different urticaria subtypes vary considerably. Also, it is important to note that in one patient two or more different subtypes of urticaria can coexist. Table (1.1) presents a

classification for clinical use. Physical urticarias, although of a chronic nature, are grouped separately, since they depend on the presence of their eliciting physical factors, whereas in acute and chronic urticaria wheals arise spontaneously without specific external physical stimuli (Zuberbier and Maurer, 2007).

Table 1.1: *Classification of urticaria (Zuberbier and Maurer, 2007)*

| Group/Subgroup | Characteristics |
|---|---|
| <i>Spontaneous urticaria</i> | <i>Definition</i> |
| Acute urticaria | Spontaneous wheals < 6 weeks |
| Chronic urticaria | Spontaneous wheals > 6 weeks |
| <i>Physical urticaria</i> | <i>Eliciting factors</i> |
| Acquired cold urticaria | Cold air/water/wind/food/objects |
| Delayed pressure urticaria | Vertical pressure (wheals arising with a 3–8 h latency) |
| Heat urticaria | Localized heat |
| Solar urticaria | UV and/or visible light |
| Dermographic urticaria/urticaria factitia | Mechanical shearing forces (wheals arising after 1–5 min) |
| Vibratory urticaria/ angioedema | Vibratory forces, e.g. pneumatic hammer |
| <i>Other urticaria disorders</i> | |
| Aquagenic urticaria | Water |
| Cholinergic urticaria | Increase of body temperature |
| Contact urticaria | Contact with urticariogenic substance |
| Exercise-induced anaphylaxis/urticaria | Physical exercise |

UV: ultraviolet

1.2.1. *Spontaneous urticaria*

1.2.1.1. *Acute urticaria*

Acute urticaria is defined as recurrent occurrence of short lived wheals for <6 weeks. The individual lesions typically resolve in <24 hours, occur more commonly in the pediatric population, and are often associated with atopy. Between 20% and 30% of patients with acute urticaria progress to chronic or recurrent urticaria. Etiologic data suggest that acute urticaria is idiopathic in about 50% of patients, due

to upper respiratory tract infections in 40%, to drugs in 9%, and to foods in 1%. Food allergies probably contribute more often than is reflected in these data, but are under-represented because patients often self-diagnose and then avoid the offending agent (**Grattan and Black, 2003**).

1.2.1.2. Chronic urticaria

Chronic urticaria (CU) has been defined as the daily or almost daily occurrence of wheals for more than 6 weeks (**Zuberbier et al., 2009**).

Chronic urticaria is frustrating for both physicians and patients, it might be caused by a variety of causes; however the majority of cases have been considered idiopathic (**Vonakis and Saini, 2008**).

1.2.2. Physical urticaria

1.2.2.1. Dermographic urticaria factitia

Dermographic urticaria is defined by whealing induced by shearing forces on the skin. Dermographic urticaria is the most frequent form of physical urticaria, affecting mainly young adults and has a mean duration of 6.5 years (**Zuberbier and Maurer, 2007**).

1.2.2.2. Delayed pressure urticaria (DPU)

Delayed pressure urticaria can interfere severely with the quality of life. The typical lesions in this type of urticaria are deep, painful swellings developing 4–8 h after exposure to a vertical static pressure, persisting for 8–48 h, especially on the palms and soles. In DPU, men are two times more frequently affected than women. The average age of onset is 30 years; the mean duration is 6–9 years. Since pressure is the force per area, it is important to advise the patient that simple measures, such as avoiding sharp edges or using gel-filled soles in the shoes, can be helpful and effective in avoiding the outset of symptoms (**Zuberbier and Maurer, 2007**).