The Open Conferences Proceedings Journal

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The Open Conferences Proceedings, Volume 4, 2013

ISSN: 2210-2892
DOI: 10.2174/2210289220130513001

Article Type: Research Article

Received: March 20, 2013
Revised: April 22, 2013
Accepted: April 27, 2013

Provisional PDF Publication Date: May 13, 2013

Evaluation of Wet Cupping Treatment in Patients with Chronic Urticaria and Angioedema

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Running title: Treatment of chronic urticaria and angioedema

Keywords: Angioedema, Chronic urticaria, CRP, ESR, Traditional medicine, Wet cupping

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Abstract

Urticaria is a kind of skin rash that sometimes caused by allergic reactions. Acute viral infection, stress, pressure, exercise and sunlight are some other causes of urticaria. However, chronic urticaria and angioedema could be either idiopathic or caused by autoimmune reaction. They last more than six weeks and could even persist for a very long time. It is thought that the level of C-reactive protein CRP increases and the level of Erythrocyte sedimentation rate (ESR) decreases in patients with chronic urticaria.

Thirty four patients with chronic or recurrent urticaria were selected for the treatment with wet cupping. Six of them, because of having a history of recent infection/cold urticaria, were eliminated and the remaining 28 were chosen for this study. ESR and CRP were measured in these patients aged 21-59, comprising 12 females and 16 males, ranged from 5-24 mm/h for ESR with a median 11 mm/h and 3.3-31.2 mg/L with a median of 11.95 mg/L for CRP before and after phlebotomy (250-450mL) which was performed as a control for wet cupping therapy. Three weeks after phlebotomy, wet cupping was performed on the back of these patients between two shoulders and the levels of ESR and CRP were measured again three weeks after wet cupping. The changes were observed in the level of CRP and ESR after phlebotomy being negligible. However, the level of CRP with a median 11.95 before wet cupping dramatically dropped to 1.1 after wet cupping. The level ESR also with a median 11 before wet cupping rose to 15.5 after wet cupping therapy. The clear correlation between the urticaria/angioedema and the rise of CRP was observed as was anticipated. No recurrence has been observed on twenty five of these patients and three of them are still recovering from the lesions.

Introduction

Acute urticaria is a kind of skin rash, caused by allergic reactions and the cause can be indentified in most cases. It usually lasts less than six weeks. Acute viral infection, stress, pressure, exercise and sunlight are some other causes of acute urticaria [1]. In contrast, Chronic Urticaria (CU) lasts longer than six weeks and sometimes could become a life time disease [2]. CU patients should be examined for an autoimmune origin and associated diseases [3]. The Central Nervous System (CNS) plays a role in the pathophysiology of urticaria in general, particularly in CU [4]. In fact, irrespective of the cause, what all kind of urticaria has in common is the release of histamine in the peripheral tissues, the cutaneous mast cell, which can degranulate in response to many different causes [1]. Such a peripheral upset in turn, alters the hypothalamic functions of the histaminergic, serotoninergic and other monoamine neurotransmitter systems. Hypothalamic dysfunction may also upset peripheral vascular function initiating antigenic insult. Therefore stress could initiate the event and as the histaminergic system is ascending, thus anxiety and depression may also have a physiological basis [5]. On the other hand, a different approach has shown basophil responsiveness and signal transduction with abnormal responsiveness in half of the patients that does not necessarily correlate with the presence of autoimmunity [6-9]. However, this abnormal responsiveness normalizes as patients' symptoms remit [10]. Cutaneous and systemic disorders of urticaria have some common features which can be clinically diagnosed. The wheal like lesions of pinpoint size and up to a few inches in diameter can be seen in both the disorders that have been caused by leakage of inflammatory mediators including histamine from cutaneous mast cells or in the case of urticarial vasculitis from eosinophils of deeper blood vessels [11]. Acute urticaria is common in children and adults, a self-limiting condition that is related to food or drug allergic, infections, temperature and sunlight as it was discussed earlier. CU has no obvious causes; it is very rare in children and mainly seen in adults. The typical wheals of acute urticaria have different sizes and shapes and random distribution on the skin surface, pale or erythematous in colour. They last maximum 36 hours and leave no mark behind [12]. The only systemic disorder having a clear association with CU and angioedema is Hashimoto's disease. Garves is also associated with CU and angioedema but it is less common than Hashimoto's disease [13, 14]. Antithyroglobulin antibody, antimicrosomal antibody or both found in 27% of CU and 19% of angioedema patients have abnormal thyroid functions. However, the existence of these abnormal thyroid functions does not prove the pathogenicity but a parallel underlying autoimmune disease [14].

In over 40% of the patients, CU has an autoimmune origin caused by presence of autoantibodies to FcεRIα or to IgE itself [14]. UC can be devastating, affecting patient's daily life activities and work. The cutaneous lesions may be very itchy, stinging and might have a big impact on sleeping and patient's confidence in social life. Clinical diagnosis of physical urticaria would be straight forward and the patients would be explained and informed of the trigger/s such as rubbing, pressure, temperature and ultraviolet light [15-17]. Angioedema can also be caused by allergic and nonallergic reaction, the wheals are clinically identifiable as they are originated from the deeper blood vessels are more painful and may leave marks behind as they heal unlike cutaneous wheals and lesions [18]. Angioedema and urticaria are the same disease with the same pathophysiology and mechanism but occurring at a different skin depth. Angioedema is pale or skin colored associated with pain or tenderness but not with pruritus. It takes time in healing and often appears on the face or the extremities [10, 18].

Perhaps the most effective treatment has been and will be the identification of the causal factor/s which stands as a daunting task. In 20-30% of both urticaria; acute and chronic, causal factors can be identified and if practical can be removed/avoided [19]. The use of aspirin, alcohol and non-steroidal anti-inflammatory drugs can worsen the disease. The remaining 70-80% is usually treated with H1-/ H2-Receptor antagonists or sometime Combined H1- and H2-Receptor antagonists [20, 21].

Antihistamine drugs were introduced to the market in early 50s after many research and clinical trials. Acute urticaria is treated with H_1 blocker such as loratadine, desloratadine, fexofenadine and cetirizine [22, 23]. These are second-generation of the nonsedating antihistamine and are taken once a day. . They certainly ease pruritus and decrease the severity of the wheals in urticaria and mild CU [24]. If not effective then the higher doses of antihistamines are administrated whereas the effects go beyond the blockade of histamine receptors and that may have been the case for the efficacy of older antihistamines. A new nonsedating antihistamine, mizolastine, has shown to be effective for CU [25-27].

As it has mentioned above, the mast cells in the skins and tissues release histamine and other pro-inflammatory substances in response to the binding of IgE antibodies to high-affinity cell surface receptors. A large number of patients with chronic urticaria develop autoantibodies directed at the receptor FcεRI located on skin mast cells. Hypothetically, if these cells are physiologically removed from the skin, the recovery of the irritation should follow soon. Therefore, the wet cupping was performed on the patient with 60-40 small skin incision.

Wet cupping therapy

Wet cupping is a process in which a vacuum is used to bring up the blood to the surface of the skin at different points on the body with incisions in order to remove that blood which has been brought up just beneath the surface of the skin. The wet cupping should only be administered by a physician or a cupping therapist and it should be carried out aseptically [28, 29].

Cupping therapy has been around for thousands of years [30]. It is hard to say when and where it took place for the first time, however, the historical evidence points to ancient Egyptians as the first nation who practiced cupping therapy systematically. The oldest medical textbook *Ebers Papyrus* thought to be written approximately in 1550 BC describes the story of wet cupping as a mean to remove foreign matter from body. Hippocrates and Galen were also the ones who practiced wet cupping extensively [31]. In contrast, Erasistratus did not practice wet cupping but used fasting for almost every disease as there were two schools of thought those days; starve the pathogen by fasting or drain it by bleeding. Ancient Persians are also thought to practice wet cupping. They also believed in the four elements of Air, Wind, Fire and Water as described in Avesta (559 BC), very similar to the Greek's four temperaments of Sanguine (Warm and Moist), Choleric (Hot and Dry), Melancholic (Cold and Dry) and Phlegmatic (Cold and Wet) [32, 33]. The cupping therapy has also been used for thousands of years in China perhaps Ancient Chinese were the first to introduce cupping, even though this has not been documented [30]. Wet cupping, Phlebotomy and leaches were further developed by Middle

Eastern healers and were well documented particularly by Persian physician and philosopher Avicenna (980-1037 AD) [34] who in his study used wet cupping to treat Chronic Urticaria (CU).

Case Histories and Patient's Examinations

Thirty four patients with chronic or recurrent urticaria/angioedema were treated in a single clinic in Tehran, Iran, with wet cupping in which 28 of these patients aged 19-59 were chosen for this study and the rest 6 having a history of recent infection or cold urticaria, were therefore eliminated. Ice cube test was performed on all the patients to eliminate cold urticaria and those who showed positive results were not included in this study [35, 36]. To eliminate atopic urticaria, an epicutaneous allergy skin test was performed against dairy products, dust mite, nuts, fish, and some other local foods and delicacy and those with positive results were excluded. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured in these patients to confirm and control inflammation [37]; 12 females and 16 males, ranged from 5-24 mm/h for ESR with a median 11 mm/h and 3.3-31.2 mg/L with a median of 11.95 mg/L for CRP before and after phlebotomy (250-450) (phlebotomy was performed as a control to see if the reduction of CRP has resulted from the changes in the volume/concentration of the blood). Three weeks after phlebotomy (to allow recovery), wet cupping was performed on the back and between two shoulders of these patients. Wet cupping was exceptionally performed on the face of patient number 18 as well as his back. The levels of ESR and CRP were measured again three weeks after wet cupping. The wet cupping procedure was carried out for all the patients on June 2012.

The procedure was explained to the patients and consent was obtained from them. Measures were taken to eliminate those patients who were anaemic or were likely to become after phlebotomy. Fluids were given to the patients, they were asked to stay in the clinic for an hour or so and their blood pressure was monitored.

The patients, chosen for this study, were treatment resistant. Depending on the stage of their disease, they were all treated with both sedative and non-sedative antihistamine on and off. Most of these patients were also treated with hydrocortisone 0.05% or/and 0.1% to alleviate pruritus (Table 1).

Table 1: Summary of the patient's history and symptoms

Patient No.	Age/ Sex	Symptoms	Family history	First Seen
1	35/M	Recurrent diffuse hives and angioedema of the legs pruritus	family history of allergies to certain foods	05/2012
2	59/M	Life time history of hives and pruritus	Not known	03/2010
3	29/M	Two years history of hives on the face and angioedema on the legs	Not known	04/2011
4	22/F	Skin rash extremities and face, chest and back	No family history	2/2012
5	42/M	Hives on abdomen and thighs with itchy bumps.	No family history	03/2009
6	36/M	Recurrent hives and angioedema of the legs	Not known	02/2012
7	33/M	Hives on the face, neck, and on the nose with itchy bumps and angioedema on the legs.	No family history	05/2011
8	49/F	Hives on abdomen area and legs	Not known	10/2011
9	56/F	Skin rash of extremities and face, chest and abdomen	Family history	3/2012
10	43/F	Recurrent hives on the face and angioedema of the legs	Family history of idiopathic urticaria	04/2012
11	36/F	Hives on the face, neck, and on the nose	No family history	07/2011
12	43/F	Hives on the face legs	Family history	05/2010
13	51/M	Skin rash and bumps on extremities and face	Not known	12/2011
14	57/M	Hives on the face, abdomen and chest	No family history	04/2011
15	23/M	Edema of the lower limbs and lesions on thigh caused by scratching.	No family history	03/2012
16	41/M	Hives on face, neck and on thigh	Not known	03/2012
17	35/F	Recurrence hives on the face and angioedema on the thigh and abdomen	Not known	01/2011
18	52/M	Skin rash on extremities, face and nose with itchy bumps	No family history	2/2011
19	55/F	hives on abdomen and thighs	Not known	03/2011
20	19/M	edema of the lower limbs with skin lesions	Not known	03/2012
21	49/F	hives and pruritus on abdomen and thigh	Not known	02/2012
22	35/M	hives on the face and angioedema on the legs	Not known	02/2012
23	46/F	skin rash on extremities, face, abdomen and thigh	Not known	01/2012
24	30/F	hives on abdomen and thighs	Not known	01/2012
25	32/M	Recurrent diffuse hives and angioedema of the legs	Not known	01/2012
26	36/F	Hives on the face, neck, and on the nose	Family history	03/2012
27	22/F	hives on face and neck	Not known	03/2011
28	51/M	Recurrent hives on the face and neck	Not known	10/2011

Results

Table 2 shows the changes in the level of CRP and ESR after phlebotomy which was performed as a control three weeks before wet cupping therapy and the changes were observed in the level of CRP with a median 1.1 and the level of ESR with a median 15.5 after wet cupping therapy.

Table 2: Summary of the patient's blood test before and after phlebotomy and wet cupping therapy

Patient No.	Age/ Sex	Before phlebotomy		After phlebotomy		After wet cupping therapy		Volume of blood taken
		CRP (mg/L)	ESR (mm/h)	CRP (mg/L)	ESR (mm/h)	CRP (mg/L)	ESR (mm/h)	
1	35/M	3.3	23	3.1	23	0.6	21	250 mL
2	59/M	3.5	7	3.7	9	0.5	15	250 mL
3	29/M	4.2	9	4.1	9	0.3	11	250 mL
4	22/F	5.0	15	5.0	15	0.7	15	250 mL
5	42/M	6.1	5	6.3	7	0.7	8	450 mL
6	36/M	6.5	17	6.7	17	0.7	17	250 mL
7	33/M	7.5	24	7.2	21	1.1	20	250 mL
8	49/F	7.6	5	7.3	7	0.7	16	250 mL
9	56/F	8.2	7	8.4	7	0.7	8	250 mL
10	43/F	9.5	11	9.5	11	1.3	17	250 mL
11	36/F	11.4	22	11.6	23	2.2	23	250 mL
12	43/F	11.5	23	11.4	23	0.8	23	250 mL
13	51/M	11.7	15	11.1	14	0.3	18	250 mL
14	57/M	11.7	8	10.8	9	0.9	12	250 mL
15	23/M	12.2	11	12.1	11	1.3	13	250 mL
16	41/M	12.3	17	18.5	17	1.1	21	250 mL
17	35/F	13.1	8	13.1	7	1.3	11	250 mL
18	52/M	15.0	6	13.0	7	1.7	13	450 mL
19	55/F	15.3	6	15.6	9	1.1	11	250 mL
20	19/M	15.5	12	15.5	13	1.1	15	250 mL
21	49/F	15.5	23	15.7	21	1.2	22	250 mL
22	35/M	17.6	11	17.4	12	1.4	17	250 mL
23	46/F	17.7	8	13.2	8	1.5	18	250 mL
24	30/F	21.5	11	21.1	12	2.3	13	250 mL
25	32/M	23.2	22	23.8	21	2.1	20	250 mL
26	36/F	26.6	9	26.6	7	1.9	13	250 mL
27	22/F	27.5	7	22.5	7	3.2	12	250 mL
28	51/M	31.2	21	31.2	19	1.8	23	450 mL

Discussion

As it can be seen in table 2, the changes were observed in the level of CRP and ESR after phlebotomy was negligible. However, the level of CRP with a median 11.95 before wet cupping, dramatically dropped to1.1 after wet cupping. The level of ESR also with a similar median 11 before wet cupping rose to 15.5 after wet cupping therapy. The clear correlation between the urticaria/angioedema and the rise of CRP was observed as was anticipated. Unlike other researchers, we were not able to establish a link between the severity and the level of CRP or ESR and the reason behind this may be the complex nature of the disease and underlying systemic disease. However, we have clearly confirmed the relationship between the drop of CRP and alleviation of the CU/angioedema symptoms by wet cupping therapy followed by blood tests. As it has been mentioned in the method, we will recommend this therapy only by a trained physician and will not definitely endorse wet cupping therapy on the face. The urticaria/angioedema symptoms of twenty five of the patients have been alleviated with no recurrence and three of them are still recovering from the lesions.

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