

The Role of Bloodletting and Cupping in Severe Acute Urticaria and Angioedema as Skin Emergencies in Persian Medicine

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Objectives: Some dermatological diseases can be life-threatening. Urticaria and angioedema are common reasons for patients to seek treatment at an emergency department. Severe, generalized urticaria and angioedema can endanger patients' lives by involving the airways and causing anaphylactic shock. The humor-based Persian Medicine (PM) concepts of *Shara* and *Mashara*, referring to two kinds of skin lesions, have similarities to urticaria and angioedema, respectively. This article aims to provide scientific evidence regarding the application of PM as an early intervention strategy in the emergency management of urticaria and angioedema.

Methods: This was a narrative review of PM studies identified by searching medical databases using search terms related to these diseases, as well as risk-associated keywords such as "fatal", "death", "life-threatening", "emergency", "cupping", and "bloodletting". Data were then compared, interpreted, and analyzed.

Results: PM scholars consider the human body as a unified whole and believe in an inner power (Nature) which stems from the body. When the presence of excessive hot substances cause an imbalance of bodily humors, Nature directs their heated vapors sharply toward the skin, thus causing *Shara* and *Mashara*. If there is a high risk of inflammation spreading to vital organs under severe conditions, urgent manual interventions are crucial.

Conclusion: In serious conditions of urticaria and angioedema, *Fasd* or bloodletting and *Hijama* can be effective in speeding up the control of lesions and reducing morbidity and mortality. Consequently, the development of integrated Persian and conventional medicines may provide new therapeutic pathways for skin emergencies.

Keywords: urticaria, angioedema, emergencies, persian medicine

INTRODUCTION

According to the World Health Organization, an emergency patient is someone whose health is threatened if not treated promptly [1, 2]. When acute injuries or illnesses from exacerbations of chronic diseases are life-threatening, immediate care is needed [3]. In dermatology, the rapid diagnosis of potentially life-threatening skin conditions is important in order to avoid serious complications. Progressive edema, scaly erythematous skin eruptions, large and infectious blisters, extensive petechiae

and purpura, and the co-occurrence of skin lesions with fever, severe pain, or a disruption in vital signs may indicate the presence of serious conditions such as angioedema, anaphylactic shock, Stevens-Johnson syndrome, or Rocky Mountain spotted fever [4-7]. In these situations, prompt medical attention and resolution in the emergency department is crucial [1, 2].

In total, 8-20% of patients admitted to the emergency department present with dermatologic manifestations [4, 8]. Urticaria typically presents as sudden erythematous, raised, and pruritic lesions caused by the release of inflammatory mediators includ-

ing histamine from mast cells. In 50% of cases, urticaria is accompanied by angioedema. Although these skin conditions are usually self-limiting, mucocutaneous airway inflammation can be life-threatening in itself, or might contribute to anaphylactic shock [4, 6, 8]. Recent studies have reported that urticaria and angioedema are among the most common dermatological reasons patients are admitted to emergency rooms [1, 2, 9, 10]. In emergency cases, airway patency must be ensured. Intravenous epinephrine or corticosteroids, followed by antihistamines, are recommended as initial treatments [4, 9].

High medical costs, uncertain insurance, and limited access to ambulances all emphasize the need to increase pre-hospital expertise in the management of medical emergencies conditions including severe urticaria and angioedema, especially in lower- and middle-income countries [3, 11].

Traditional and Complementary Medicine (TCM), also known as non-conventional medicine, has emerged as an important part of healthcare systems in almost all countries, and the demand for these services is increasing [12]. Acute and chronic illnesses have been treated by Persian Medicine (PM) scholars for thousands of years [13-15]. PM is a holistic medicine that believes in the immense complexity of the whole body and its various organs [16]. Before molecular aspects in medicine came to the fore, the humoral theory was the dominant paradigm of medicine in the civilized world. In PM, the term *Tabiat* (Nature) refers to an innate power in the body which keeps it healthy. This resourceful force tries to restore health when the quantity or quality of the body's humors change. The physician in PM serves Nature, and tries to restore the patient's health. Lifestyle modification, medications, and manual interventions are the methods by which physicians reinforce *Tabiat* [13, 17-19].

PM scholars have described inflammatory dermatologic diseases which appear closely compatible with some skin rashes described in conventional medicine. In particular, the symptoms and causes of *Shara* and *Mashara* are very similar to that of urticaria and angioedema, respectively [20, 21]. In severe, life-threatening urticaria and angioedema, PM physicians use manual methods like *Fasd* (bloodletting) and *Hijama* (wet cupping) to help Nature expel hot substances from the blood and alleviate symptoms [22, 23]. To date, no studies have examined the role of TCM and PM in controlling serious dermatologic conditions. This study aimed to review and compare the measures taken in PM and conventional medicine used to prevent and treat emergency cases of urticaria and angioedema.

MATERIALS AND METHODS

This narrative review incorporated specialized books and articles describing the emergency treatment of urticaria and angioedema. First, the valid and primary sources of PM were examined. These included *Al-Havi* (865-925 AD), *Kāmil al-Sinaā al Tibbiya* (930-994 AD), *Hidayat al-Muta Allimin fi al-Tibb* (?-983 AD), *Qanun fi al-Teb* (980-1037 AD), *Zakhireye Kharazmshahi* and *Al-Aghraz al-Tebbie va al-Mabahes al-Alayieh* (1136-1040 AD), *Sharh al-Asbab val-Alamat* (1409-1449 AD), *Kholaseh al-Tajareb* (1456-1507 AD), *Mofarrah al-Ghoolob* (17th and early 18th centuries AD), *Kholaseh al-Hekmat* (1670-1747 AD), *Tebe Akbari* (late 17th and early 18th centuries AD), *Moalejat-e Aghili* (1670-1747 AD), *Eksir Azam* and *Qarabadin-e Azam* (?-1902 AD). We scanned these sources for information related to *Shara* and *Mashara*, and searched for terms indicative of the dangerous nature of these diseases, such as “killer”, “fatal”, “death”, “urgency”, “organ corruption”, “*Fasd*” and “*Hijama*”. We then performed a literature search of reputable databases and search engines such as PubMed, Google Scholar, ScienceDirect, SID, and Up-to-Date using relevant keywords, including “angioedema”, “urticaria”, “anaphylaxis”, “emergency department”, “emergency room”, “cupping” and “bloodletting”. We excluded unpublished thesis data, as well as studies where abstract or full-text articles were not available. Studies published in languages other than English and Persian were also excluded.

In total, 25 main PM books written in Arabic or Persian and published between the 9th and 19th centuries were identified. Our initial search of relevant medical databases further identified more than 1200 articles published between 1990 and 2021. With the application of initial restrictions based on selected keywords, the number of eligible studies decreased. Two reviewers met and deliberated to finalize the selection of suitable studies through consensus. In total, 46 papers and 13 books were selected for this review. The collected data were then compared and examined from the perspectives of PM and conventional medicine. The process of article selection is featured in Fig. 1.

RESULTS

1. Clinical manifestations of emergent conditions

1) The perspective of Persian Medicine

Oram and *Bosur* refer to swelling and rashes of varying sizes

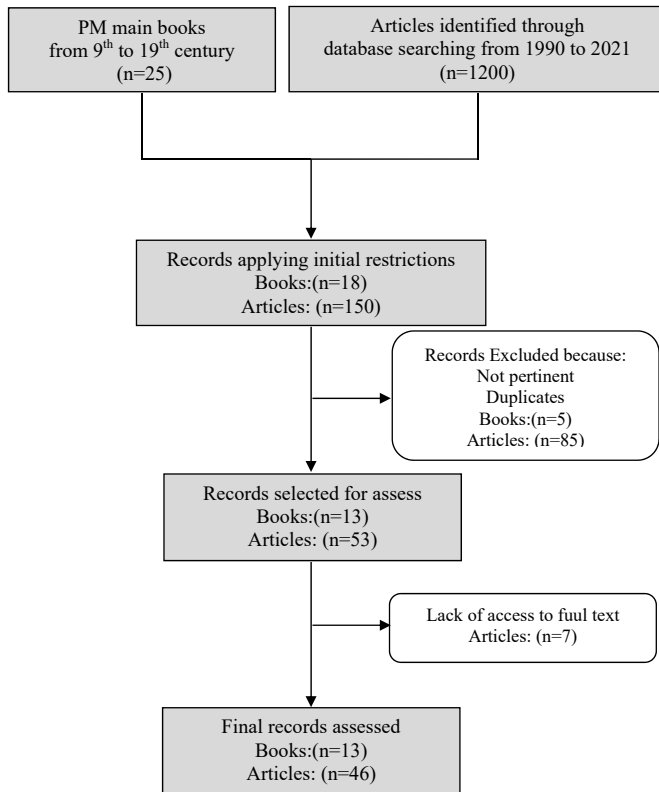


Figure 1. Flow chart showing the process of selecting the relevant documents.

caused by the accumulation of bodily waste products under the skin. Erythematous, pruritis, painful, and purulent lesions occur in the presence of inflammatory and hot substances. In cases where the lesions are left untreated, serious complications might develop which require emergency treatment [13-15, 22-27]. The skin lesions *Shara* and *Mashara* are highly similar to, and compatible with, urticaria and angioedema, respectively [20, 21]. *Shara* manifests as acute, swollen, erythematous, pruritic, painfu, non-localized rashes of different sizes. If left untreated, the disease can cause abscesses and skin damage. Restlessness, fainting, fever, fatigue, nausea, and discoloration of the lips and limbs are also present in severe cases [13, 23, 25, 26]. *Mashara* presents as very hot, painful, and pruritic swelling with a burning sensation that affects the face and forehead, particularly the regions around the eyes and nose. It is usually accompanied by restlessness, thirst, and fever. Severe *Mashara* can spread to the throat and airways, causing shortness of breath. It can be fatal if there is cardiac involvement [13-15, 22-27].

(1) The importance of the skin in the excreting of waste substances to produce inflammatory lesions

PM maintains that a large portion of ingested food goes

through multiple stages of digestion in the stomach, liver, vessels, and tissues to form normal humor. The remainder is turned into waste or unusable substances, and excreted in the form of feces, urine, sweat, nasal and lung secretions, menstrual blood, or imperceptibly through skin pores [13, 26]. PM scholars believe that the heart, brain, liver, and stomach play a more important role in health and disease than the skin. On the other hand, the skin is a vitally important excretory organ. When other pathways of the body are disrupted or large amounts of unhealthy waste are produced, Nature (as a wise force in the body) directs the extra substances to non-principal organs like the skin in order to protect more critical organs. Accumulation of these waste products generates swelling in the form of *Oram* and *Bosur* [13, 18, 28, 29]. In *Shara* and *Mashara*, the production of hot substances and their vapors in the body is increased. When they move quickly towards the skin for the purposes of excretion, pruritic, raised lesions can occur. In critical situations, if the amount of hot extra substances in the blood is too high, the lesions spread from the skin and mucosa to vital organs, which can be life-threatening [22, 23, 25].

2) The perspective of conventional medicine

Urticaria is one of the most common allergic skin diseases, with a prevalence of nearly 20% in the general population. Urticarial lesions or wheals present as extremely pruritic, circumscribed, elevated, and erythematous plaques of varying sizes. Although urticaria is often self-limiting, it sometimes leads patients to seek treatment in the emergency room [4, 30, 31]. Acute urticaria is the most common skin disease treated in the emergency room [9, 32]. Also, patients with chronic urticaria may be referred to the emergency department if they experience disease exacerbation [9].

Excoriations of the skin in severe acute urticaria may result from vigorous scratching [33]. Chronic urticaria may be accompanied by systemic symptoms such as fatigue, headache, flushing, joint swelling and pain, nausea, abdominal pain, palpitations, and wheezing. Urticaria in this subgroup is more severe and longer-lasting, and often association with anxiety and depression [33, 34]. Cutaneous small-vessel vasculitis as well as renal, musculoskeletal and pulmonary involvement can accompany these systemic symptoms in patients with long-lasting, painful urticaria [35, 36]. Exacerbation of symptoms at night may contribute to restlessness. Patients may therefore present at the emergency department seeking faster alleviation of their symptoms.

Angioedema accompanies urticaria in 50% of cases, and presents as sudden and severe erythema or swelling in areas with loose connective tissue, such as the face, lips, mouth, throat, larynx, uvula, extremities, genitalia, and the bowel wall. It is typically characterized by pain to a greater extent than itching [37]. Angioedema is typically self-limiting, but can also be life-threatening. Bowel wall edema may cause abdominal pain, nausea, vomiting, and diarrhea, while airway obstruction in severe cases may cause dyspnea and hypoxemia [4]. In both urticaria and angioedema, mast cells, granulocytes, and monocytes activate the inflammatory cascade and release mediators such as histamine, platelet-activating factor (PAF) and cytokines [37, 38]. The sudden systemic release of inflammatory mediators may cause an acute and life-threatening anaphylactic reaction. Hypotension, loss of consciousness, diarrhea, vomiting, abdominal cramps, laryngeal edema, and bronchospasm are some of its typical features. The early recognition and treatment of anaphylaxis is therefore crucial [39]. The similarities between the clinical manifestations and complications of *Shara* and *Mashara* compared to urticaria and angioedema, respectively, are outlined in Table 1.

2. Therapeutic approach

It is essential that physicians are able to distinguish the benign forms of urticaria and angioedema from potentially severe and life-threatening conditions, particularly when first visiting a newly admitted patient [7]. In emergency rooms as well as outpatient clinics, a combined interventional approach drawing from both conventional and complementary medicine could assist recovery and improve survival in affected patients [40, 41].

1) The perspective of Persian Medicine

According to the principles of patient management defined by PM, the physician helps Nature to balance itself in order to improve a patient's lifestyle, including optimal sleep, movement and rest, evacuation and retention, psychological and mental reactions, as well as nutrition. Medications and manual interventions (*Amal-e-yadavi*) such as phlebotomy and cupping are applied in subsequent stages. Depending on the severity of the disease and the patient's condition, the order of treatment may change [13].

Table 1. The similarities of *Shara* and *Mashara* with urticaria and angioedema

	Urticaria	<i>Shara</i>	Angioedema	<i>Mashara</i>
Signs and symptoms	Transient, circumscribed, raised, and erythematous plaques in variable size with the itchy or burning sensation	Sudden, swollen, erythematous, and itchy rashes of different size	Sudden and severe erythema or swelling	Very hot and pruritus swelling
Affected site	The superficial layer of the skin	The skin	Deep in the skin of the face, hands, and genital area	On the face and forehead, especially around the eyes and nose
Pain incidence	Pain due to scratching and trauma to the skin if severe itching persists or the possibility of urticarial vasculitis	Pain due to itching	More pain than itching	Painful
Pathogenesis	Sudden systemic release of inflammatory mediators	Sudden moves of hot blood and its vapors towards the skin and mucosa	Sudden systemic release of inflammatory mediators especially in head and neck	Sudden moves of hot blood and its vapors towards the skin and mucosa especially of the head and neck
Complications	Anxiety and depression, fatigue, headache, joint pain and swelling, hot flashes, nausea and abdominal pain, palpitations, wheezing, and fever	Restlessness, fainting, fever, fatigue, nausea, and discoloration of the lips and limbs	Abdominal pain, nausea, vomiting, and diarrhea in gut wall edema Dyspnea or hypoxemia in airway obstruction and the risk of anaphylactic shock	Restlessness, thirst, and fever Shortness of breath Death if involved the heart

(1) The importance of nature deviating during emergency conditions

In severe cases of inflammatory skin lesions, including acute, progressive *Shara* and *Mashara*, should rusk to assist Nature when there is a risk of redistribution of inflammation and swelling from the skin and mucosa to the vital organs. In these situations, various non-pharmacological therapies such as *Fasd* (bloodletting, phlebotomy) and *Hijama* (wet cupping) can be performed [23, 42]. *Fasd* is a manual intervention that treats diseases through the removal of small amounts of blood in order to rid the body of abnormal humors and waste products. Based on the patient's condition, some blood is drawn by making a small incision with a sterile blade in different veins of the body [43, 44]. Cupping is another intervention used to purify the connective tissue of the skin by creating suction. In *Hijama* (wet cupping), a small amount of blood is removed through fine scratches on the skin made by a sterile blade after cupping is performed on a specific area of the body [44-47].

In PM, manual interventions are used during two phases: first, to prevent harm to patients during acute attacks, and second, before the onset of these attacks, in order to prevent disease relapse [15, 44, 46]. In life-threatening cases of *Mashara* and *Shara*, phlebotomy is often the first line of treatment aimed at reducing the risk of spreading the inflammation throughout the body, especially to the cardiovascular and respiratory systems. *Fasd* thus creates a new path for causative agents and waste products to be expelled from the body. Nature therefore stops guiding substances to vital organs and notices where the substances can exit the body via the vessels. Veins on the elbow surface, e.g. the median cubital and basilic veins, are among those chosen for incision in cases of severe *Shara*. Incision into these veins allows unhealthy blood to be removed from the whole body, especially the liver.

In *Mashara*, phlebotomy is performed on the head and neck veins, including the cephalic vein. In certain cases, more delicate vessels around the nose or sublingual veins are alternative choices. If the patient's condition is not suitable for performing phlebotomy, *Hijama* (wet cupping) is used to reduce blood volume and divert Nature. Both procedures should be performed by a specialist under medical supervision [14, 22, 23, 25, 44, 48, 49]. Table 2 presents the recommended locations for *Fasd* and *Hijama* in severe forms of *Shara* and *Mashara*.

2) The perspective of conventional medicine

Various pharmacological treatments are often prescribed on

Table 2. Recommended places for *Fasd* and *Hijamat* in severe *Shara* and *Mashara*

Disease	Phlebotomy veins	<i>Hijama</i> places
<i>Shara</i> (Urticaria)	Median cubital vein Basilica vein	Depending on the location of lesions
<i>Mashara</i> (Angioedema)	Cephalic vein Nasofrontal vein Angular vein Sublingual vein	Legs

an outpatient basis to prevent mast cell mediator release and provide symptomatic relief. These include first and second-generation H1-antihistamines, H2-antihistamines, leukotriene receptor antagonists, immunosuppressive agents, and glucocorticoids [37, 38]. In severe and generalized urticaria and angioedema, when there is a risk of anaphylaxis, patients should be assessed and treated promptly to prevent life-threatening respiratory and cardiovascular complications. Epinephrine injection, immediate intubation in cases of impending airway obstruction, oxygen administration, intravenous fluids, antihistamines, and glucocorticoids are the mainstay of treatment in critical cases [50, 51].

DISCUSSION

Although some skin conditions are self-limiting and can be treated on an outpatient basis, others can be life-threatening, and require immediate care [4, 52]. Severe urticaria and angioedema increase the risk of anaphylaxis, which requires hospitalization and urgent care [52]. Differentiating mundane skin ailments from serious and life-threatening conditions such as severe urticaria and angioedema require immediate treatment, and can be challenging for physicians to manage [4, 9].

A signification proportion of patients across the world are turning to TCM as a cost-effective form of treatment [12, 45]. Numerous studies have shown the important role of these therapies in the treatment of various diseases [53-56]. In contrast, very few studies have explored the role of TCM, especially PM, in the prevention and treatment of life-threatening diseases that need immediate care [40, 41]. Meng et al. found that, although Traditional Chinese medicine is widely recognized as effective in treating chronic diseases, some TCM therapies like blowing air to the ear, nose insufflating therapy, acupuncture, and moxibustion are potent in many acute and urgent medical conditions [40]. In PM, Nature as an innate power controls all aspects

of the body [18, 57]. Deviating Nature by phlebotomy and wet cupping, two common manual interventions used in PM, plays an important role in protecting the principal organs of the body by purifying the blood [46, 58, 59].

Eghbalian et al. described the role of saphenous vein phlebotomy and wet cupping performed on the back of legs in the treatment of epilepsy from the perspective of PM. The authors also noted that emergency bloodletting in patients with epilepsy may be performed based on the patient's condition [46]. In a similar fashion, Atyabi et al. studied the role of wet cupping and phlebotomy in alleviating various causes of headaches in PM. The researchers believed that *Fasd* and *Hijama* were cost-effective methods that could control headaches by reducing blood or deviating Nature [58]. Indeed, bloodletting and cupping have been widely used around the world for centuries to treat diseases outside the context of PM [43, 60, 61]. A systematic review and meta-analysis conducted by Xiao et al. examined the effects of cupping therapy on urticaria and the possible mechanisms which underlie its therapeutic efficacy. The authors concluded that wet cupping may be as effective as treatment with antihistamines in patients with chronic urticaria. The addition of wet cupping to acupuncture or antihistamine therapies might also increase their effectiveness. Cupping with several mechanisms may control urticaria. A Reduction in plasma IgE levels, cell transmitter release, and vascular permeability, as well as improved functioning of the immune system, are some of the mechanisms whereby cupping could help relieve urticaria [61].

Ma et al. conducted a randomized control trial in 2020 and reported that bloodletting therapy can be an effective complementary treatment in chronic urticaria [62].

Although the mechanism of bloodletting is yet not clear in conventional medicine, draining the body's heat or excess energy, imbalance the Qi-Blood circulation, and cleaning the channels and collaterals are possible bloodletting roles in Traditional Chinese Medicine (TCM) [43].

Apart from many studies on the importance of bloodletting and cupping in the treatment of diseases, no studies have yet published on skin emergencies and the effect of these manual interventions in Persian Medicine.

This novel study described *Shara* and *Mashara* two inflammatory skin lesions in PM which resemble urticaria and angioedema. In severe and life-threatening situations, *Fasd* and *Hijama* can help expel hot excessive substances promptly as early interventions to avoid potentially serious sequelae.

CONCLUSIONS

It is worth mentioning that PM manual therapies may have great potential for being applied as immediate interventions under urgent conditions of urticaria and angioedema to increase the survival and recovery rate in patients.

Future experimental and clinical efforts could be spent on PM research and then applied in emergency medicine.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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