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Ting Ye, Weiping Tu & Gaosi Xu

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## STATE OF THE ART REVIEW

# Hot bath for the treatment of chronic renal failure

Ting Ye<sup>1,2</sup>, Weiping Tu<sup>1</sup>, and Gaosi Xu<sup>1</sup>

<sup>1</sup>Department of Nephrology, Second Affiliated Hospital, Nanchang University, Nanchang, PR China and <sup>2</sup>Medical Center of Graduate School, Nanchang University, Nanchang, PR China

## Abstract

**Background:** Dialysis and its complications were debated recently. There was lack of an adjuvant renal replacement method to reduce the complications of patients with chronic renal failure and dialysis itself. **Materials and methods:** In this article, we reviewed the role of thermal sweating in treating of the patients with chronic renal failure, and the role of traditional Chinese medicine in the therapy of chronic kidney diseases. **Results:** Thermal sweating can reduce interdialytic weight gain and improve the patients' blood pressure; Chinese herbal medicine can promote the excretion of uremic toxicities and relieve the skin disorders of these patients. **Conclusions:** Traditional Chinese medicine-mediated hot bath could be one of the adjuvant renal replacement methods.

## Keywords

Chronic renal failure, chronic kidney disease, dialysis, traditional Chinese medicine

## History

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## Introduction

Although dialysis has been considered as a life-saving treatment in the setting of end-stage renal diseases (ESRD), there were considerable doubt concerns between the benefits of relieving advanced uremia and the inherent dangers relating to dialysis therapy itself.<sup>1</sup> Newly finished randomized controlled trial indicated that there was no significant difference in the frequencies of adverse events (cardiovascular events, infection, or complications of dialysis), or in quality-of-life measures between the earlier start group and the later start group.<sup>2</sup> Despite the wide-accepted adoption of this life-saving therapy, dialysis treatment was redolent with dangers, many of which were only recently starting to be appreciated.<sup>3</sup> Therefore, decreasing dialysis frequency and seeking for alternative renal replacement methods is not equal to the old wine in a new bottle.

The major skin disorders in ESRD are xerosis, pruritus, hyperpigmentation, perforating and calcifying manifestations, and bullous diseases. Nearly 50–100% of the ESRD patients present with at least one skin lesion.<sup>4</sup> Sometimes these symptoms can be the first clear sign of chronic kidney diseases (CKD).<sup>5</sup> Severe pruritus not only affects the quality of life in patients with chronic renal failure (CRF), but is also associated with poor prognosis in these subjects.<sup>6</sup> Although medications including antihistamine drugs, activated carbon, cholestyramine, nicergoline, opioid antagonists, a leukotriene inhibitor, erythropoietin, heparin, lidocaine, thalidomide,

and fatty acids are reported effective in uremic pruritus, no specific, effective treatment is currently available for uremic pruritus.<sup>7</sup>

Traditional Chinese herbalists have been treating patients with CRF for thousands of years. The formulas used usually include diuretics combined with herbs with the role of reducing inflammation and protecting the kidney.<sup>8</sup> Warm-water bath or sauna improved the quality of life in patients with congestive heart failure (CHF) by permitting an increase in daily activities and improving appetite, sleep quality, and general well-being.<sup>9</sup> Based on the above-mentioned evidences, this mini review article attempts to discuss the possible roles of traditional Chinese medicines (TCMs)-mediated hot bath in treating the complications of patients with CRF, and offers an adjuvant alternative renal replacement method to this era when dialysis is widely debated.<sup>1–3,10,11</sup>

## Hot bath for the treatment of CRF

Sauna bathing decreased systolic blood pressure without affecting heart rate, resulting in significant decrease in plasma epinephrine and norepinephrine. Therefore, it might be an effective adjunctive therapy for chronic systolic CHF.<sup>9,12</sup> After one to two hours' sauna bath, the patient's body weight decreased by 1.5–2 kg.<sup>13</sup> Sweat fluid mainly contains sodium chloride, potassium, nitrogen metabolites such as urea, ammonia, uric acid, and creatinine.<sup>14</sup> Urea is the major nitrogen-containing metabolic product of protein catabolism, accounting for about 75% of the nonprotein nitrogen eventually excreted. The mean sweat fluid urea concentration could reach 5.5 to 50 times the serum concentration; therefore, urea excretion via sweating is important when the renal function is impaired.<sup>15</sup>

Address correspondence to Gaosi Xu, Department of Nephrology, Second Affiliated Hospital, Nanchang University, No. 1, Minde Road, Nanchang 330006, PR China. Tel.: +86(0)791 86270383; Fax: +86(0)791 86270383; E-mail: xugaosi@gmail.com

The presence of a high concentration of urea in sweat fluid suggested an alternative transport mechanism to clear the blood urea across the eccrine sweat gland. In normal subjects, thermal sweating is considered to be an ineffective mean for elimination of urea and uric acid, since the diminution in urinary output. However, for oliguric, especially anuretic patients with CRF, the decrease in uric acid excretion is insignificant. The 24-hour urinary urea excretion in summer was as much as one-quarter of the quantity in winter in uremic patients, indicating the compensatory urea excretion in sweat gland fluid, which was verified by that the sweat fluid creatinine level was the highest in anuretic uremic subjects.<sup>15</sup>

A 30-minute hot water bath every day was as effective as a two-hour sauna bath three times a week. Sweat rates in sauna and hot water baths were 21 and 33 mL/min, respectively.<sup>13</sup> Urea clearance in hot (42 °C) water baths were higher than in sauna baths, which were 56 and 40 mL/min, respectively. Calculated losses of urea and potassium in sweat fluid were 43 and 12 mmol/h compared with 117 and 20 mmol/h by hemodialysis. These findings indicated that hot bath can be used as a valuable adjunct to chronic intermittent hemodialysis.

Potassium is the major intracellular cation, which is about 30 times the concentration in serum. Potassium secretion is partially controlled by the aldosterone, but other mechanisms such as potassium permeability of the sweat gland ductal wall may also influence its sweat concentration.<sup>16,17</sup> The concentrations of urea and potassium in sweat fluid were even higher than that in serum from volunteers, as described in Table 1 (adapted from Huang et al.).<sup>18</sup> In normal subjects, sweat fluid urea concentration had been shown to be age-related, and can reach to above 65 mmol/L in older people.<sup>19</sup> However, the excretion of uric acid in sweat fluid was only about 178.5 µmol/day, and such an excretion amount was significantly lower than 1.5–4.5 mmol/day via urine.<sup>18</sup>

Urea level in sweat fluid had been found to increase severalfold after exercise.<sup>20</sup> The volume of fluid lost by sweating was also highly variable, depending on physical activity and environmental temperature. The amount of sweat normally is about 100 mL/day, but during heavy exercise or in very hot weather, fluid loss from sweating can increase up to 2 liters/hour.<sup>21</sup>

Although sauna bathing causes occasionally various acute, transient cardiovascular, and hormonal changes, very few acute myocardial infarctions and sudden deaths occur in saunas, therefore, it is well tolerated by most adults and children.<sup>22</sup> These findings initiated the hypothesis that eccrine sweat fluid assumes a natural alternative route for the excretion of urea and creatinine.

Table 1. Concentrations of each analyte in sweat, urine and serum from subjects (mmol/L).

|            | Sweat         | Urine         | Serum         |
|------------|---------------|---------------|---------------|
| Uric acid  | 0.025 ± 0.007 | 3.7 ± 1.3     | 0.389 ± 0.064 |
| Urea       | 22.2 ± 8.0    | 392.7 ± 137.8 | 6.2 ± 0.9     |
| Creatinine | 0.031 ± 0.017 | 21.5 ± 7.4    | 0.102 ± 0.025 |
| Sodium     | 66.3 ± 46.0   | 109.9 ± 84.1  | 140.5 ± 2.2   |
| Chloride   | 59.4 ± 30.4   | 102.8 ± 37.0  | 98.9 ± 6.7    |
| Potassium  | 9.0 ± 4.8     | 69.2 ± 27.7   | 4.8 ± 0.8     |

Note: Values are expressed as mean ± SD.

When in sauna bath, there is an approximate 40% decrease in peripheral resistance, which accounts for increased peripheral circulation.<sup>23</sup> Sweat gland is in similarity with the convoluted tubules of the nephron. Sweat K<sup>+</sup> concentration was significantly higher in patients with CRF than in healthy controls, while the concentrations of Na<sup>+</sup> and Cl<sup>-</sup> were similar.<sup>24</sup> Although the pathogenesis involved with the cutaneous manifestations was not clear in the patients with CRF, urea concentration in the sweat fluid was found to be present at a much higher concentration than the serum level. Therefore, the possibility of using thermal induction as an alternative way to hemodialysis was considered. The presence of such a high level of urea in the sweat fluid suggested a selective transport mechanism across the eccrine sweat gland to clear the blood of urea.<sup>15,25</sup>

### Specific symptoms of CRF that can be relieved by hot baths

Hot bath can reduce mean interdialytic weight gain and improve blood pressure and potassium/urea balance in patients with ESRD. Therefore, hot bath can increase the sufficiency of dialysis and reduce the fluctuation of blood pressure and cardiovascular events in peridialysis period.<sup>26</sup> Sauna (hot bath) had positive effects on 24-hour systolic and mean blood pressure in patients with untreated hypertension. Sauna bath reduced total vascular resistance, with positive effects lasting up to 120 minutes after heat exposure.<sup>27</sup> There were statistically significant reductions in systolic blood pressures, plasma epinephrine levels and less hospitalization, and significant improvements in left ventricular ejection fraction, exercise tolerance, peak respiratory flow, as well as anaerobic threshold during the following year than those in the non-sauna group.<sup>12</sup> Sauna baths are used as a method of depuration protocols because they increase sweating, which might increase the excretion of impurities, such as uremic toxicity, excrescent water, and heavy metals.

### The role of TCMs in the treatment of CRF

TCMs can delay the progression of CRF by ameliorating the podocyte injury, nephrotoxicity of proteinuria, hyperactivity of renin–angiotensin–aldosterone system, cytokines over-expression, tubular epithelial myofibroblast transdifferentiation, and hyperlipidemia.<sup>28</sup> TCMs significantly relieved symptom severity of dermatitis and was reported as well tolerated.<sup>29</sup> A number of studies have shown the usefulness of TCMs in the treatment of every skin disorder, such as psoriasis and atopic dermatitis, and thus it is worthwhile for dermatologists throughout the West to gain some familiarity with this method.<sup>30,31</sup> However, well-designed, multicentered, randomized, and controlled trials are needed to make further conclusions.

TCMs can ameliorate glomerulosclerosis and renal interstitial fibrosis during the progression of CRF by improving glomerular hemodynamics turbulence, podocyte injury, transforming growth factor (TGF)-beta overexpression, hyperlipidemia, macrophage infiltration, and tubular epithelial myofibroblast transdifferentiation.<sup>32</sup> For the patients with CKD stage 3, TCMs can improve estimated glomerular filtration rate (eGFR) and hemoglobin with lower side

effects.<sup>33</sup> TCM Hachimi-jio-gan played a protective role in the progression of CRF through the decline in uremic toxins, elevation of antioxidative enzyme activity such as superoxide dismutase and catalase, and amelioration of histopathological lesions in the kidney.<sup>34</sup>

Cumulative evidence suggests that some TCMs, including Astragalus and a mixture of Astragalus plus Angelica, Ligusticum, Triptolide, and Rhubarb, show benefits in slowing the progression of CKD.<sup>35,36</sup> Tanshinone IIA, an active component of *Salvia miltiorrhiza*, successfully suppressed increases in urinary protein excretion in CKD rats.<sup>37</sup> By remethylation of TGF- $\beta$ 1 promoter and then the TGF- $\beta$ 1 be transcribed and translated normally, Uremic Clearance Granules (Niaoduoqing Keli in Chinese) was proved to be able to reduce serum creatinine, blood urea nitrogen, and homocysteine in adenine-induced CRF rats.<sup>38</sup> A combination of two Chinese herbs, *Astragalus membnaceus* var. *mongolicus* and *Angelica sinensis*, displayed renoprotective effects by suppression of extracellular matrix deposition, upregulation of vascular endothelial growth factor (VEGF), and reducing the loss of capillaries.<sup>39</sup>

All the same, TCMs therapies were criticized for their lack of standardization and lack of toxicological studies and well-designed clinical trials.<sup>40</sup> Large-scale, multi-centered, randomized controlled trials should be further performed to verify the effects of TCMs on the progress of patients with CRF.

### Herbal medications benefit for dermatological manifestations

Herbal treatments have been used successfully in treating dermatologic disorders for thousands of years in Europe and Asia.<sup>41</sup> During the last 15 to 20 years, complementary and alternative medicine (CAM) has become increasingly popular in the United States. Topical herbal supplements in cosmetics have become some of the most frequently used alternative therapies. Among the numerous botanical ingredients, Ginkgo biloba, ginseng, silymarin, soy, and tea tree oil had been proven effective in treating dermatological problems.<sup>42</sup>

The herbs were found to effectively reduce inflammatory acne lesions through mechanisms related to sebaceous glands, *Propionibacterium acnes*, and reactive oxygen species (ROS).<sup>43</sup> The herbal topical medication (QoolSkin) reduced the Psoriasis Area and Severity Index (PASI) by 32.0% and the Beer-Sheva Psoriasis Severity Score (BPSS) by 37.8% in patients with chronic plaque psoriasis.<sup>44</sup> Poison oak and related hypersensitivity dermatitides had been successfully treated with herbal medicines *Grindelia* spp.<sup>45</sup> CAM, especially herbal medicine were used in more than one-third of outpatients with general dermatologic conditions. More than 45% of these patients used CAM to treat their dermatologic condition.<sup>46</sup> TCMs alleviated the reduction or deletion of accessory structure, such as hair follicle and sweat gland.<sup>47</sup> Physicians in general, however, should be aware of potential adverse reactions related to the use of certain herbal remedies.

### TCMs-mediated hot bath for the treatment of CRF

The overall prevalence of skin disorders in patients with CKD was reported between 79% and 100%.<sup>48</sup> Patients receiving

dialysis had a higher prevalence of pruritus than those with conservative therapy, confirming that dialysis itself may precipitate pruritus.<sup>49</sup> The pathogenesis of pruritus is correlated with hyperparathyroidism, hypervitaminosis A, iron deficiency anemia, and elevated serum magnesium, phosphate, aluminum, histamine, etc.<sup>50</sup> By activating of proteinase-activated receptor 2, serine protease has been shown to be involved in itch induction.<sup>51</sup> The treatment options including antihistamines, serotonin antagonists, ondansetron, activated charcoal and cholestyramine, retinoids, capsaicin, cryotherapy, keratolytic drugs, UV phototherapy, etc.<sup>52</sup> However, the therapeutic effects of pruritus are variable.<sup>7</sup>

The sweat gland is a tubular structure consisting of a deep-coiled portion for secreting sweat fluid and a duct to the surface of skin. Sweat fluid concentrations are determined by solutes secretion and the subsequent absorption. Therefore, the sweat solute concentrations are influenced by the fluid flow rate.<sup>53</sup> It is easy to understand that uric acid excretion and clearance are increased at high rates of urine flow.<sup>54</sup> Changes in the structure of skin underlying the epidermis, such as increased extensibility, elastin fragmentation, atrophy of sebaceous and sudoriferous glands can cause dehydration, which is correlated with decreased sweating.<sup>55</sup> Although dry skin in ESRD is associated with reduced stratum corneum glycerol levels, permeability barrier and the ultrastructure appears to not be impaired in these patients.<sup>56</sup>

By adding some decoction of Chinese medicine into warm water for bath, mediated bath is a traditional external treatment of CRF. The heat effect and absorption of active components of Chinese herbal medicine are the major reason for the curative effects.<sup>57</sup> The components of TCMs for mediated bath are built according to the differentiation of symptoms and signs. TCMs with the function of promoting blood circulation such as rhizoma Chuanxiong and radix Angelicae are formulated for bath with three to four times as large as those for oral administration.<sup>58</sup> Ligustici Chuanxiong Rhizoma ether extracts exhibited an effect on the skin permeability of moderately lipophilic compounds owing to their accumulative property.<sup>59</sup>

Hot baths appear to be a safe way to reduce interdialytic weight gain in selected hemodialysis patients. However, published recommendations suggested that persons with aortic stenosis, unstable angina, severe orthostatic hypotension, or any history of recent myocardial infarction avoid hot bath therapy.<sup>60,61</sup>

In conclusions, TCMs-mediated hot bath can dehydrate and clear uremic toxins by skin eccrine sweating in patients with chronic renal failure, decrease their skin complications and frequencies of adverse events (cardiovascular events, infection, or complications of dialysis). Therefore, it offers an adjuvant alternative renal replacement method for these subjects to reduce the frequency of dialysis due to its complications.

### Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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