

# Acupuncture of the Five Shu Acupoints in spleen meridian to lower blood uric acid level

Bao-Guo Sun, Jun Meng, Ting Xiang, Ze-Xiong Chen, Shi-Jun Zhang

First Affiliated Hospital of Sun Yat-sen University, Guangzhou 510080, China

Corresponding to: Bao-Guo Sun, physician. First Affiliated Hospital of Sun Yat-sen University, No 58 Zhong Shan road II, Guangzhou 510080, China.

Email: sunbaoguo666@126.com.

**Background:** Based on the principle of “spleen governing transportation and transformation”, we have found that acupuncture of the Five Shu Acupoints in spleen meridian can remarkably lower the blood uric acid levels in patients with primary hyperuricemia.

**Objective:** To explore the clinical efficacy of the acupuncture of the Five Shu Acupoints in spleen meridian in reducing the blood uric acid level and its relevant mechanism

**Methods:** A total of 32 patients with primary hyperuricemia were enrolled in this study. They were allowed to have free access to diets. The initial treatment for the concomitant diseases (but not including the therapy that might affect uric acid metabolism) was kept unchanged. The observation was formally initiated at 8:00 am on day 1. Acupuncture was not performed within the 48 hours, and only the 24-hour urine volume was recorded. The urine uric acid concentration and urinary creatinine concentration were measured from 25 to 48 hours. On the 46th hour, venous blood samples were collected to detect blood uric acid and creatinine concentrations. After the 48th hour, the patients received acupuncture of the Five Shu Acupoints in spleen meridian each morning. Once Qi was encountered, retain the needle for 30 min. The acupuncture was performed once daily for ten consecutive days. The 24-hour urine volume was recorded daily, and the fasting indicators were detected on the morning of the 11th day.

**Results:** After the acupuncture, the blood uric acid level significantly decreased in patients with increased production (overproduction) of uric acid, decreased excretion (underexcretion) of uric acid, and mixed type (all  $P < 0.01$ ). In the underexcretion type, the urine uric acid concentration significantly increased after the treatment ( $P < 0.01$ ). After the acupuncture, the fraction excretion of uric acid (FEUA) significantly increased in the underexcretion type and mixed type ( $P < 0.01$ ) and decreased in the overproduction type ( $P < 0.01$ ). After the acupuncture, the serum uric acid concentration decreased by 16.32-18.29% whereas the 24-hour urine volume increased by 24.22-29.32%.

**Conclusions:** Acupuncture of the Five Shu Acupoints in spleen meridian can lower the blood uric acid levels by promoting uric acid excretion and increasing urine volume.

**Keywords:** Acupuncture; spleen meridian; Five Shu Acupoints; hyperuricemia



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The primary hyperuricemia is an unexplained hyperuricemia caused by a variety of factors including genetic background, age, and environment. Causes of hyperuricemia can be classified into three functional types: increased production of uric acid (overproduction type), decreased excretion of uric acid (underexcretion type), and mixed type. Clinically it may

manifest as increased blood uric acid level, but may remain asymptomatic in some patients. It is often detected when the patients are presented due to gout attacks, metabolic diseases, and/or cardiovascular and cerebrovascular diseases. High blood uric acid level is closely correlated with metabolic syndrome and cardiovascular diseases (1-4),

**Table 1** The concomitant diseases

	Hypertension	Type 2 diabetes	Hypercholesterolemia	Hypertriglyceridemia
Hypertension	20	10	15	11
Type 2 diabetes	10	15	10	9
Hypercholesterolemia	15	14	16	12
Hypertriglyceridemia	10	14	11	20

Note: this two dimensional table displays the number of enrolled patients with these concomitant diseases.

which has aroused great attention in recent years. The mainstream treatment for this disease remains the drugs capable of promoting uric acid excretion and inhibiting uric acid synthesis. Typically long-term medication is required (5,6). Acupuncture has found to be an effective treatment for acute gout (7), while its role in lowering blood uric acid remains unclear. Metabolic disorder of uric acid is a manifestation of the body's poor absorption and excretion of substances. Based on the principle of "spleen governing transportation and transformation", hyperuricemia is a manifestation of the dysfunction of spleen in transportation, which results in the poor functioning of the meridians and Qi. A proper adjustment of the meridians and Qi will facilitate the recovery of the spleen's function in governing transportation and transformation. According to the Nine Needles and Twelve Source in Ling Shu, the meridians and Qi originate from the limb extremities and spread along the Five Shu Acupoints (Jing, Xing, Shu, Jing, and He) towards heart, during which their activities gradually increase. Thus, we found that acupuncture of the Five Shu Acupoints in spleen meridian can dredge the spleen meridians and Qi and thus lower the blood uric acid level, without being affected by the patients' inherent lifestyles.

In our current study, all the patients signed the informed consents, and the study was approved by the Institutional Review Board of the First Affiliated Hospital of Sun Yat-sen University.

## Subjects and methods

### General data

A total of 32 eligible patients were obtained in our cohort. These patients were inpatients in our department from January 2013 to October 2013. There were 20 men and 12 women, aged (64.35±12.35) years, with a body weight of (68.33±12.41) kg and disease course of (10.87±8.66) years. *Table 1* summarizes the concomitant diseases.

## Methods

### Inclusion and exclusion criteria

Inclusion criteria: (I) Met the diagnostic criteria for hyperuricemia (8): when fed with normal-purine diets, the patients had a fasting serum uric acid level of >420 μmol/L (7 mg/dL) (for men) or >357 μmol/L (6 mg/dL) (for women) on two separate days; (II) Aged 18-80 years; and (III) Signed the informed consents.

Exclusion criteria: (I) Secondary hyperuricemia; (II) With a bleeding tendency: prothrombin time (PT) >17 s, platelet <50×10<sup>9</sup>/L, and/or hemophilia; (III) Pregnant or lactating women; accompanied with severe diseases in cardiovascular system, liver, kidney, or hematopoietic system; with psychopath/psychosis; and/or with malignant tumors; (IV) While taking or have taken within the past two weeks uric acid-lowering drugs, azathioprine, 6-mercaptopurine, or drugs containing aspirin (>325 mg), or salicylates; (V) With serum creatinine >1.5 mg/dL and ALT exceeding two times of the upper limit of the normal value; (VI) With suspected or confirmed history of alcohol/drug abuse; or, upon the investigator's scrutiny, the enrollment of such a patient may lower the credibility or make the grouping more complex (e.g., highly possible to drop out due to the frequent change of working environment).

### Interventions

The fundamental treatment for all the enrolled patients (e.g., patients with type 2 diabetes, hypercholesterolemia, or hypertriglyceridemia) remained unchanged (no drug was added for those who had not used drugs). In the acupuncture group, the Yinbai, Dudu, Taibai, Shangqiu, and Yinlingquan were stuck, and the encountering of Qi (aching and tingling sensation at the sticking site) was regarded as a proper stick. Retain the needle for 30 min. The acupuncture was performed once daily for ten consecutive days. The included patients adhered to their usual diets and lifestyles. The observation was formally initiated at 8:00 am on day 1.

Acupuncture was not performed within the 48 hours, and only the 24-hour urine volume was recorded. The urine uric acid concentration and urinary creatinine concentration were detected from 25 to 48 hours. On the 46th hour, venous blood samples were collected to detect serum uric acid, creatinine, and triglycerides concentrations. After the 48th hour, the patients received acupuncture of the Five Shu Acupoints in spleen meridian each morning. Once Qi was encountered, retain the needle for 30 min. The acupuncture was performed once daily for ten consecutive days. Record the 24-hour urine daily, and, on the morning of the 11th day, the fasting levels of blood uric acid, blood creatinine, blood urine creatinine, urine uric acid, and urine triglyceride concentrations were recorded.

### Tests

Blood uric acid, blood creatinine, urine creatinine, urine uric acid, and urine triglycerides were determined using instrument. Rate of decline of serum uric acid = (Pre-treatment blood uric acid - Post-treatment blood uric acid)/pre-treatment blood uric acid  $\times 100$ ; 24-hour urine volume change rate = (Post-treatment 24-hour urine volume - pre-treatment 24-hour urine volume)/pre-treatment 24-hour urine volume  $\times 100$  [note: analysis of the change in urine volume is based on the 24-hour urine volume only since the habits (e.g., drinking water) differ remarkably many individual patients], the fraction excretion of uric acid (FEUA) = Urine uric acid  $\times$  blood creatinine/(blood uric acid  $\times$  urine creatinine)  $\times 100$ .

### Type-specific evaluation (9)

An FEUA of  $<7\%$  is defined as the underexcretion type,  $7\text{--}12\%$  as mixed type, and  $\geq 12\%$  as overproduction type.

### Statistical analysis

Data are processed and analyzed using SPSS 17.0 software package. The normally distributed measurement data before and after treatment are presented using (Mean  $\pm$  SD) and analyzed using paired t-test and ANOVA. Chi square test was applied for the analysis of the ranked data and non-normal measurement data. A P value  $<0.05$  was considered to be statistically significant.

## Results

### Enrolment

A total of 35 patients were enrolled in this study. Among

them one patient was excluded due to the self-medication of benzbromarone, one patient withdrew from the study because he could not tolerate the acupuncture pain, and one patient quit the study due to a private matter. The remaining 32 patients signed the informed consents and entered the final analysis.

### Changes in urine pH, urine uric acid, blood uric acid, triglycerides, creatinine, and urine creatinine (Table 2)

(I) In our cohort, the underexcretion type, mixed type, and overproduction type accounted for 40.63%, 25.00%, and 34.38%, respectively ( $\chi^2=1.781$ ,  $P=0.410$ ); (II) the blood uric acid level significantly decreased in all three group after the acupuncture ( $P<0.01$ ); (III) before the acupuncture, the urine uric acid level was significantly lower in the underexcretion type than in the mixed type and overproduction type ( $P<0.01$ ). After the treatment, the urine uric acid level became similar ( $P>0.05$ ). In the underexcretion type, the urine uric acid concentration significantly increased after the treatment ( $P<0.01$ ); (IV) before the treatment, the urine creatinine concentration was significantly lower in the overproduction type than in the mixed type ( $P<0.05$ ); however, it became comparable after treatment ( $P>0.05$ ). After the treatment, the blood creatinine concentration slightly decreased in the overproduction type ( $P<0.05$ ); (V) the urine pH value and triglycerides showed no significant change before and after treatment ( $P>0.05$ ).

### Fractional excretion of uric acid and the rate of decline of serum uric acid (Table 3)

(I) FEUA before treatment: underexcretion type  $<$  mixed type  $<$  overproduction type ( $P<0.01$ ); (II) the post-treatment FEUA significantly increased in both underexcretion type and mixed type ( $P<0.01$ ) but decreased in the overproduction type ( $P<0.01$ ); (III) the decrease of blood uric acid was comparable among these types ( $F=0.057$ ,  $P=0.944$ ). Also, the changes in the 24-hour urine volume were also comparable ( $F=0.191$ ,  $P=0.827$ ); (IV) the pooled FEUA significantly increased after treatment ( $P<0.01$ ); (V) after the acupuncture, the blood uric acid level decreased by 16.32–18.29%, while the urine volume increased by 24.22–29.32%.

### Adverse effects

The major adverse effect during the study was the

**Table 2** Changes in urine pH value, urine uric acid, blood uric acid, 24-hour urine volume, blood creatinine, urine creatinine, and blood lipid profile (mean  $\pm$  SD)

Item		Underexcretion type (n=13, 40.63%)	Mixed type (n=8, 25.00%)	Overproduction type (n=11, 34.38%)	Mean
Urine pH value	Prior to treatment	5.58 $\pm$ 0.61	5.63 $\pm$ 0.64	5.59 $\pm$ 0.77	5.59 $\pm$ 0.65
	After treatment	5.46 $\pm$ 0.48	5.50 $\pm$ 0.53	5.45 $\pm$ 0.27	5.47 $\pm$ 0.42
Urine uric acid level (mmol/L)	Before treatment	1.67 $\pm$ 0.96	3.98 $\pm$ 0.76 <sup>g</sup>	3.76 $\pm$ 1.23 <sup>g</sup>	2.96 $\pm$ 1.47
	After treatment	3.23 $\pm$ 1.65 <sup>b</sup>	4.12 $\pm$ 1.63	2.91 $\pm$ 1.90	3.34 $\pm$ 1.75
Blood uric acid level (mmol/L)	Before treatment	539.38 $\pm$ 70.40	541.25 $\pm$ 68.13	578.09 $\pm$ 85.19	553.16 $\pm$ 75.13
	After treatment	444.62 $\pm$ 92.58 <sup>c</sup>	451.25 $\pm$ 78.36 <sup>d</sup>	474.09 $\pm$ 82.44 <sup>e</sup>	456.41 $\pm$ 84.10 <sup>a</sup>
Triglycerides (mmol/L)	Before treatment	2.15 $\pm$ 1.11	2.32 $\pm$ 1.52	2.22 $\pm$ 1.06	2.21 $\pm$ 1.17
	After treatment	2.28 $\pm$ 0.86	2.35 $\pm$ 1.20	2.22 $\pm$ 1.11	2.28 $\pm$ 1.01
Blood creatinine (mmol/L)	Before treatment	94.00 $\pm$ 10.78	90.50 $\pm$ 10.42	91.91 $\pm$ 16.64	92.41 $\pm$ 12.68
	After treatment	93.92 $\pm$ 11.08	90.50 $\pm$ 8.11	87.82 $\pm$ 13.21 <sup>f</sup>	90.97 $\pm$ 11.22
Urine creatinine (mmol/L)	Before treatment	5.21 $\pm$ 3.03	6.96 $\pm$ 2.14	3.67 $\pm$ 1.51 <sup>h</sup>	5.12 $\pm$ 2.63
	After treatment	5.34 $\pm$ 3.20	5.65 $\pm$ 0.97	4.51 $\pm$ 1.94	5.13 $\pm$ 2.37

Note: The 24-hour urine volume before treatment was the mean 24-hour urine volume of the 3 days before treatment; the 24-hour urine volume after treatment was the mean 24-hour urine volume of the 10 days after treatment. Paired t-test, compared with the pre-treatment levels. <sup>a</sup>, t=-7.968, P=0.000; <sup>b</sup>, t=5.983, P=0.000; <sup>c</sup>, t=-3.624, P=0.003; <sup>d</sup>, t=-3.483, P=0.010; <sup>e</sup>, t=-32.026, P=0.000; <sup>f</sup>, t=-2.524, P=0.030. ANOVA, before treatment, compared with the underexcretion type; <sup>g</sup>, F=17.823, P=0.000; compared with the mixed type, <sup>h</sup>, F=4.431, P=0.021.

**Table 3** Fractional excretion of uric acid and the rate of decline of serum uric acid

Item		Underexcretion type	Mixed type	Overproduction type	Mean
FEUA	Before treatment	5.61 $\pm$ 1.23	9.92 $\pm$ 1.60	17.24 $\pm$ 5.22	10.69 $\pm$ 6.01
	After treatment	14.68 $\pm$ 7.01 <sup>b</sup>	15.46 $\pm$ 6.58 <sup>c</sup>	12.03 $\pm$ 5.61 <sup>d</sup>	13.96 $\pm$ 6.41 <sup>a</sup>
Change in the 24-hour urine volume	After treatment	27.39 $\pm$ 16.21	29.32 $\pm$ 20.85	24.22 $\pm$ 18.90	26.78 $\pm$ 17.87
Rate of the drop of blood uric acid	After treatment	17.05 $\pm$ 16.95	16.32 $\pm$ 13.74	18.29 $\pm$ 2.81	17.29 $\pm$ 12.53

Note: paired t-test: compared with the pre-treatment levels. <sup>a</sup>, t=2.161, P=0.038; <sup>b</sup>, t=4.861, P=0.000; <sup>c</sup>, t=2.423, P=0.046; <sup>d</sup>, t=-4.166, P=0.002. ANOVA, FEUA of three types before treatment. F=38.129, P=0.000.

acupuncture pain sensation. No obvious hematoma, ulceration, or other injury was found at the sticking site. No patient experienced fainting during acupuncture in the supine position. The acupuncture did not cause obvious damage to the local functions.

## Discussion

As shown in our current study, the acupuncture of the Five Shu Acupoints in spleen meridian can remarkably decrease the blood uric acid level in patients with primary hyperuricemia; during the acupuncture, both the 24-hour urine volume and the FEUA increases, whereas the blood

creatinine and triglycerides show no significant changes. For patients with the Underexcretion type and mixed type of hyperuricemia, acupuncture of the Five Shu Acupoints in spleen meridian can increase the FEUA; for patients with overproduction type, however, it increases the uric acid excretion mainly by increasing the urine volume. Thus, acupuncture of the Five Shu Acupoints in spleen meridian can decrease the blood uric acid level by promoting the excretion of uric acid and by increasing the urine volume.

Current research on uric acid metabolism indicates that two thirds of the blood uric acid in human body is excreted via kidney in the form of urate. The degree of excretion mainly depends on the status of glomerular filtration, renal

proximal tubule reabsorption, and excretion of the distal convoluted tubule. The urates are actively transported by urate transporters (10,11). Interventions (e.g., use of thiazide diuretics) on these links often lead to the decreased excretion of uric acid and increased reabsorption (12), while some drugs [e.g., benzbromarone (13)] may suppress the renal tubules' reabsorption of uric acid and thus promote the excretion of uric acid. The acupuncture of the Five Shu Acupoints in spleen meridian can remarkably reduce the blood uric acid level but has no obvious effect on blood creatinine and urine creatinine levels, which may be explained by the increased urine volume and uric acid excretion. Therefore, its activity in lowering uric acid is closely correlated with the regulation of glomerular filtration, renal proximal tubule reabsorption, and excretion of the distal convoluted tubule. By stimulating the acupuncture points on the body, the acupuncture can cause the responses of the neuroendocrine network; however, the corresponding changes in the specific molecular signaling pathways remain unknown.

From the perspective of TCM, the main function of the spleen is to regulate the transportation and distribution of nutrients and body fluids throughout the body. The dysfunction of spleen often results in the imbalance of nutrients and humoral metabolic disorders. Uric acid is an important nutrient that is dissolved in a body fluid. The accumulation of uric acid in the body often prompts dysfunction of spleen in transportation. Thus, regulating the spleen's functions in regulating transportation and transformation facilitates the maintenance of the normal levels of serum uric acid. The Five Shu Acupoints in meridians regulate the flow and movement of Qi from meridians towards the heart. The Five Shu Acupoints including Jing, Xing, Shu, Jing, and He reflect the occurrence and development of the Qi in meridians (Qm). The Jing acupoint reflects the occurrence of Qm, the Xing acupoint reflects the enhancement of Qm, the Shu acupoint reflects the transportation of the enhanced Qm, the Jing acupoint reflects that the Qm has merged and then further enhanced, and the He acupoint reflects that the Qm has merged into a "lake", which is also the source of Qm that steadily nourish the whole body (14,15). The Five Shu Acupoints reflect the progress and status via which the splenic function occurs and grows. Acupuncture of the Five Shu Acupoints in spleen meridian can regulate the occurrence, growth, transportation, enhancement, and aggregation of the Qi in spleen meridian, thus regulating the role of spleen in regulating the transportation and

transformation of Qi, which will favorably adjust the transportation and distribution of nutrients and body fluids in human body. This may explain the efficacy of acupuncture of the Five Shu Acupoints in spleen meridian in lowering blood uric acid from the TCM perspective.

Our study had some limitations: only the efficacy after ten days of treatment was observed, and the long-term effectiveness and its mechanism still require further investigation. Nevertheless, the effectiveness of the acupuncture of the Five Shu Acupoints in spleen meridian in lowering blood uric acid in patients with primary hyperuricemia is clinically meaningful. Unlike benzbromarone (which only promotes the excretion of uric acid) or diuretics (which may suppress the excretion of uric acid while promoting the production of urine), acupuncture of the Five Shu Acupoints in spleen meridian can not only promote uric acid excretion but also increase urine volume. This may also enlighten the future development of drugs with similar efficacies.

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