Editor-in-Chief

Dr. Jay Kalra
University of Saskatchewan, Canada

Editorial Board Members

Xue-Qiang Zha, China
Agezegn Asegid Mekonnen, Ethiopia
Abdurrahman Dundar, Turkey
Hongxing Liu, China
Ai-jiao Xiao, China
Soheila Molaie, Iran
Maria do Rosario Dias, Portugal
Hongxi Xu, China
Aiqing Li, China
Azeb Atenafu Gete, Ethiopia
Snezana Levic, United Kingdom
Gulam Mohammed Husain, India
Jing Liu, China
Alessandro S. Cavelzani, Italy
Alexander Nikolaevich Orekhov, Russian Federation
Bashir Ahmad Dar, India
Xinzhong Wu, China
Ruozhi Zhao, Canada
Tabinda Hasan, Saudi Arabia
Kezhong Zhang, United States
Marzieh Pirvaei, Iran
Sateesh Babu Arja, Curacao
Elaheh Ainy, Iran
Momir Mikov, Serbia
Harikesh Dubey, India
Carlos Rojas Malpica, Venezuela

Guojun Li, China
Yuchen Liu, China
Md. Azizur Rahman, India
Varadraj Prabhu Gurupur, United States
Zhiling Yu, China
Padmavati Manchikanti, India
Wibhu Kutanan, Thailand
Rajib Ahmed, United States
Ashok Kumar Srinivasan, India
Xingjiang Xiong, China
Liyanage Dona Ashanthi Menuka Arawwawala, Sri Lanka
Haibo Xu, China
Tsan Yang, Taiwan
Dmytro D. Ivanov, Ukraine
Jorge Cortes-Breton Brinkmann, Spain
U.S. Mahadeva Rao, Malaysia
Prasanta Kumar Sahoo, India
Kenichi Young-Chang Arai, Japan
Emre Demir, Turkey
Zafar Rasheed, Saudi Arabia
Thanuja Priyanganie Gunarathna, Sri Lanka
Wei Liu, China
Chao Ren, China
E.D. Thanuja Gunarathna, Sri Lanka
Bramanandam Manavathi, India
Contents

1 Identification of Active Component of Hachimi-jio-gan Ameliorating Diabetic Nephropathy
   Chan Hum Park   Takashi Tanaka   Takako Yokozawa

8 Changes and Significance of Cytokines in Serum of Rabbits with Acute Pulmonary Embolism
   Yulong Liang   Jianjing Liang   Wenjing Feng   Jinghui Mu

12 A Scientific Perspective of the Three Harmonies Principle of Taijiquan
   C.P. Ong

22 Advances in the Treatment of Acute ITP
   Yuheng Jiang   Jiahao Gu   Zai Gu   Yifeng Xu   Bin Jia   Jing Yang
Identification of Active Component of Hachimi-jio-gan Ameliorating Diabetic Nephropathy

Chan Hum Park\(^1\*\)  Takashi Tanaka\(^2\)  Takako Yokozawa\(^3\*)

1. Institute of New Frontier Research Team, Hallym Clinical and Translational Science Institute, Hallym University, Chuncheon, 24252, Republic of Korea
2. Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, 852-8521, Japan
3. Graduate School of Science and Engineering for Research, University of Toyama, Toyama, 930-8555, Japan

ARTICLE INFO

Article history
Received: 19 November 2021
Accepted: 13 December 2021
Published Online: 26 February 2022

Keywords:
Diabetic nephropathy
Hachimi-jio-gan
Corni Fructus
Morroniside
7-O-Galloyl-α-sedoheptulose

1. Introduction

Diabetic nephropathy is the main cause of microvascular complications in diabetic patients, and one of the leading causes of end-stage renal disease (ESRD) worldwide\(^[1]\). Multiple factors have been implicated in the pathogenesis of diabetic nephropathy, including hyperglycemia-elicited generation of advanced glycation end-products (AGE) and reactive oxygen species (ROS)\(^[2]\). A number of new therapies have been developed from experimental studies based on the pathogenic factors of diabetic nephropathy such as blood glucose control, blood pressure control, renin-angiotensin-aldosterone system blockade, sodium-glucose cotransporter 2 inhibitors,

Conventional medicine-based Chinese herbal prescriptions, have fascinated much attention due to their extensive and unique diversity of biological effects without toxicity and/or adverse effects. Treatment with Hachimi-jio-gan (Ba-Wei-Di-Huang-Wan in Chinese) improved the dysregulated levels of hyperglycemic condition-related oxidative stress generation, advanced glycation endproduct generation, and renal function parameters. These results indicate that Hachimi-jio-gan is a prospective therapeutic agent against the pathogenesis of diabetic nephropathy. Cornel iridoid glycosides and polyphenol are the active compounds of Corni Fructus, the active component of Hachimi-jio-gan, against kidney damage caused by diabetes. Additionally, major components of the Corni Fructus, morroniside and 7-O-Galloyl-α-sedoheptulose (GS) are considered to be important contributors to prevent and/or delay the onset of kidney damage caused by diabetes. Chief of all, GS is expected to be developed as a novel therapeutic drug for the diabetes-accelerated kidney damage.
lifestyle modification, including exercise and an energy-restricted diet, and numerous novel agents\textsuperscript{[3-7]}, but the rate of ESRD due to diabetic nephropathy has still lasted high in spite of the extensive usage of various therapies, focusing on the management of factors mentioned above. Thus, interventions to effectively delay the progression of diabetic nephropathy are urgently needed.

To date, there have been various researches focusing on the treatment to prevent diabetes and secondary complications with herbal medicines including Chinese prescriptions because of their absence of toxic and/or side effects. In Japan, the Chinese prescription Hachimi-jio-gan (Ba-Wei-Di-Huang-Wan in Chinese, description in Chinese medical book “Jin Gui Yao Lue”) is a Chinese prescription that contains eight medicinal herbs: root of \textit{Rehmannia glutinosa} Libosch. var. \textit{purpurea} Makino (Rehmanniae Radix) 27.27%, fruit of \textit{Cornus officinalis} Sieb. et Zucc. (Corni Fructus) 13.64%, rhizome of \textit{Dioscorea japonica} Thunb. (Dioscoreae Rhizoma) 13.64%, rizome of \textit{Alisma orientale} Juzep. (Alismatis Rhizoma) 13.64 %, sclerotium of \textit{Poria cocos} Wolf (Hoelen) 13.64%, bark of \textit{Paeonia suffruticosa} Andrews (Moutan Cortex) 11.36%, bark of \textit{Cinnamomum cassia} Blume (Cinnamomi Cortex) 4.54%, and tuber of \textit{Aconitum carmichaeli} Debx (Aconiti Tuber) 2.27%. Hachimi-jio-gan has long been used widely to treat several diseases, including chronic nephritis, sterility, and vegetative ataxia\textsuperscript{[8-11]}. Hachimi-jio-gan has also been used widely in the treatment of several disorders related with diabetes, and it has been used to the management of renal dysfunction in human subjects, although pharmacological evidence to prove the its therapeutic effects, and the corresponding mechanisms of Hachimi-jio-gan and its active components has not been reported yet. Therefore, we evaluated the effect of Hachimi-jio-gan on diabetic kidney damage using a type 1 diabetic nephropathy rat model that underwent subtotal nephrectomy (remnant kidney model) and streptozotocin (STZ) injection (type 1 diabetic model), and Otsuka Long-Evans Tokushima Fatty (OLETF) rats as a model of type 2 diabetic model, as shown in Figure 1. The data suggest that Hachimi-jio-gan may be a novel therapeutic approach to improving diabetic nephropathy\textsuperscript{[12,13]}. Furthermore, to carry out research on the phytochemical constituents of Hachimi-jio-gan, the antidiabetic effects of Corni Fructus (fruit flesh of \textit{Cornus officinalis} Sieb. et Zucc.), one of the Hachimi-jio-gan ingredients, and its phytochemical constituents (iridoid glycosides and polyphenol compound) were investigated using STZ-induced diabetic rats (Figure 1), and we sought to elucidate the major phytochemical constituents of Hachimi-jio-gan. In the present paper, we want to introduce a series of research contents reported so far.

2. Extract of Hachimi-jio-gan

Weighed eight medicinal herbs were boiled three times for 60 times in the 10 times volume of distilled water, filtered, and the filtrate was spray-dried. The yield of the solvent free extract was 10%, by weight compared to the original preparation. To investigate the components of Hachimi-jio-gan, an aqueous extract was analyzed by three-dimensional high-performance liquid chromatography (HPLC) analysis system equipped with an LC 10AD vp pump coupled with SPD-M10A VP UV-VIs detector. TSK-GEL ODS-80TS column (ϕ 4.6 x 250 mm, Tosoh, Japan) was used for separation. The mobile phase consisted of (A) 0.05 M AcOH-AcONH\textsubscript{4} and (B) CH\textsubscript{3}CN. The gradient elution used was as follows: 0 min, 10% B

Figure 1. Schema of this research on Hachimi-jio-gan and its reactive components.
and 60 min, 100% B. The flow rate was 1.0 mL/min. UV absorbance at 254 nm was monitored using an 3D-HPLC profiling data using an SPD-M10A vp UV-VIs detector. As shown in Figure 2, major components of Corni Fructus (morroniside and loganin) were the major compounds in Hachimi-jio-gan; paoniflorin, penta-O-galloylglucose, benzoylmesaconine, benzoylpaeoniflorin, 16-ketoalisol A, cinnamic acid, and cinnamaldehyde were also detected. Therefore, in order to clarify the source of a particular action of Hachimi-jio-gan, we chose to evaluate the usefulness of Corni Fructus, which contains morroniside and loganin as active ingredients.

![Figure 2. 3D-HPLC profile of Hachimi-jio-gan extract.](image)

3. Corni Fructus, One of the Major Ingredient of Hachimi-jio-gan

Corni Fructus, the dried ripe fruit of Cornus officinalis Sieb. et Zucc. (Cornaceae), is an important traditional herbal medicine used in Chinese medicine due to exhibiting various pharmacological effects, including blood glucose-lowering, tumor growth-inhibiting, and microbial growth-inhibiting effects, and to improve liver and kidney functions. To determine whether Corni Fructus exhibits the principal role in Hachimi-jio-gan, we investigated the effects of Corni Fructus using the same dose as for Hachimi-jio-gan, in order to compare the effect in STZ-induced diabetic rats. Administration of Corni Fructus inhibited hyperglycemic condition, proteinuria, renal AGE accumulation, and involved protein expressions, i.e., receptor for AGEs, N\(^\text{ε}\)-(carboxymethyl)lysine (CML), nuclear factor-kB, and transforming growth factor-\(\beta\)\(_1\) with these effects being alike to those of Hachimi-jio-gan. In addition, treatment with Corni Fructus attenuated renal dysfuntion, shown through serum creatinine (Cr) and Cr clearance, in diabetic rats.

4. Fractionation and Chemical Characterization of Bioactive Compounds from Corni Fructus

Under the supposition that Corni Fructus would be a main contributor to the anti-diabetic and reno-protective effects of Hachimi-jio-gan, we attempted to identify the active fraction and components of Corni Fructus. As shown in Figure 3, Corni Fructus extract (100 g) was applied to a column (32 x 5 cm) of Sephadex LH-20 column. Column was eluted with 10% stepwise increasing amounts of MeOH in water and ultimately 60% acetone to yield fractions: S1 (94.5 g), S2 (1.2 g), S3 (2.2 g), and S4 (1.6 g). Fraction S1 was further divided into two fractions (S1D1 and S1D2) by column (28 x 5 cm) of Diaion HP-20SS eluted with water-MeOH (0-100%, 10% stepwise mobile phase gradient elution) gave S1D1 (85.6 g) and S1D2 (7.9 g). TLC and HPLC analyses indicated that fraction S1D1 and S1D2 mainly composed sugars and iridoid glycosides, and fraction S2, S3 and S4 were contained phenolic substances. Fraction S2 was subjected to MCI-gel CHP20P column chromatography (28 x 2 cm) using water-MeOH (0-10%) to give the chromatographically pure 7-O-galloyl-\(\alpha\)-sedoheptulose. Further separation of S1D2 (1 g) by MCI-gel CHP20P (30 x 3.4 cm) using water-MeOH (0-100%, 10% stepwise mobile phase gradient elution) gave five subfractions: S1D2-1 (127.0 mg), S1D2-2 (68.8 mg), S1D2-3 (157.0 mg), S1D2-4 (405.2 mg), and S1D2-5 (136.6 mg). Subsequent chromatography of the fraction S1D2-1, S1D2-2, and S1D2-3 over Chromatorex ODS column chromatography (26 x 2.8 cm) using water-MeOH (0-20%, 0-30%, and 0-45%) yielded mevaloside (37.0 mg), loganic acid (34.8 mg), and 5-hydroxymethyl-2-furfural (9.6 mg), respectively. A similar separation of S1D2-4 afforded morroniside (167.0 mg) and loganin (138.3 mg). Their chemical structures were identified by spectral analysis (COSY, HSQC, and HMBC) and NMR comparison (\(^1\)H- and \(^{13}\)C-NMR). The chemical characterization isolated from S1D2 or S2 fraction is shown in Figure 3.
5. Antidiabetic Potential of Fractionated Corni Iridoid Glycosides and Polyphenol Fractions from Corni Fructus

As described above, we prepared Corni Fructus fractions and determined the fraction containing the potential constituents against diabetes, using one iridoid glycoside fraction (S1D2) and three polyphenol fractions (S2, S3, and S4), which were expected to possess potential activities than Corni Fructus, administered orally, respectively. Iridoid glycoside fraction (S1D2) and the low-molecular-weight polyphenol fraction (S2) could inhibit the pathogenesis of diabetic kidney damage, with each having different mechanisms: S1D1 (iridoid glycoside fraction) successfully reduced the hyperglycemic state and affected renal AGE accumulation, such as Nε-(carboxyethyl)lysine (CEL) and CML, while the S2 (low-molecular-weight polyphenol fraction) could decrease renal lipid peroxidation, the receptor for AGE, and inducible nitric oxide synthase. In addition, S3 and S4 fractions (the other polyphenol fractions) reduced body weight gain compared with the control group, although these fractions significantly inhibited the levels of increased thiobarbituric acid-reactive substances (TBARS) in the kidney, proposing that these two fractions may have radical scavenging activities but may include some toxic ingredients. Ultimately, these results suggest that antidiabetic potential of iridoid glycoside (S1D2) and low-molecular-weight polyphenol (S2) fractions obtained from Corni Fructus improve metabolic parameters related with the development of diabetic kidney damage[19].

6. Protective Effects of Morroniside and Loganin Isolated from Corni Fructus against Kidney Damage in Diabetic Rats

Iridoid glycosides such as morroniside and loganin are well-known as the major bioactive compounds of Corni Fructus[20-22]. This study investigated whether morroniside and loganin isolated from Corni Fructus exerts a beneficial effect on kidney damage in STZ-treated diabetic rats. Oral treatment of diabetic rats with morroniside resulted in significant reductions in elevating levels of serum glucose and urinary protein. The reduced levels of serum albumin and total protein in diabetic rats were significantly improved by morroniside administration. Moreover, morroniside modulated the enhanced level of serum urea nitrogen and showed a tendency to decrease Cr clearance. Morroniside also significantly reduced the increased serum glycosylated protein, and serum and renal TBARS levels. Renal protein expressions related to the AGE such as CEL as well as oxidative stress such as heme oxygenase-1 were significantly reduced following the treatment of morroniside[23,24]. These results suggest that morroniside is effective against diabetic kidney damage, which mediates action of the hyperglycemia and oxidative stress in serum and renal tissue. However, loganin has a weaker effect than morroniside against diabetic kidney damage, but has an indirect effect of the improving metabolic diseases in other organs such as hepatic tissue[24,25]. Therefore, these
results indicate that morroniside is one component with a partial role for the renoprotective effects of Hachimi-jio-gan and Corni Fructus against kidney damage caused by diabetes.

7. 7-O-Galloyl-d-sedoheptulose (GS) is a New Therapeutic Drug in the Diabetic Kidney

From the S2 fraction, we isolated GS of low-molecular-weight polyphenol\(^{[19]}\). To our knowledge, this compound is only detected from *Cornus officinalis*, and its biological activity has not yet been found. That being so, we decided to clarify the completed protective mechanisms against diabetic kidney disease, and examined whether the oral administration of GS reduces diabetes-induced oxidative stress and glycation products in the kidney.

Polyphenols, including flavonoids and phenolic acid are the most abundant antioxidants in human diet, being common constituents of fresh vegetables, fruits, and beverages include tea. They have been reported to have various beneficial effects, such as the prevention and/or delay of cancer\(^{[26]}\), neurodegenerative disorder\(^{[27]}\), atherosclerotic disorder\(^{[28]}\), and diabetes\(^{[29]}\), as well as indicate slow down the ageing process effects\(^{[30]}\), because an imbalance between production and accumulation of oxygen reactive species is believed to influence many disorders. Our previous study showed that (-)-epigallocatechin 3-O-gallate, a major green tea polyphenol, exerted a protective effect on kidney damage caused by hyperglycemic condition-related oxidative stress complicated in renal lesions index of diabetic nephropathy\(^{[31]}\). Based on the previous study, we tested GS, and exhibited its renoprotective effect on the diabetic condition; to date, our study is the only results on biological research. We revealed its beneficial effects on abnormal metabolism-related renal symptoms, including renal glucose uptake, AGE generation [methylglyoxal, glycoaldehyde (GA), receptor for AGE, CEL, CML, and GA-pyridine], and oxidative stress [TBARS and heme oxygenase-1], which is thought to play a key role in the pathogenesis of diabetic kidney disease. GS had strong effects on the suppression of AGE generation via the regulation of Maillard reaction and lipid peroxidation, as shown in Figure 4. In addition, GS effectively suppressed the rises in levels of serum Cr and urinary protein to nearly non-diabetic control values. The serum albumin level was significantly increased in the GS-administered mice\(^{[32]}\). These effects were consistent with those of Hachimi-jio-gan and/or Corni Fructus. The role of GS is expected to provide a novel therapeutic strategy against diabetic kidney disease.

8. Conclusions

The discovery of efficacious components is an important prerequisite for clarification of the precise mechanisms of herbal medicines. However, studies on the biological activities of the active components isolated from herbal medicines and Chinese prescriptions are limited. Therefore, we evaluated the effects of Hachimi-jio-gan ameliorating diabetic kidney damage using a diabetic nephropathy rat model. Hachimi-jio-gan treatment suppressed the higher levels of hyperglycemic condition-induced oxidative stress, AGE generation, renal protein dysexpression, and proteinuria. These results indicate that Hachimi-jio-gan is a prescribed herbal medication with potential against kidney damage caused by diabetes. In addition, we established that Corni Fructus, one ingredient of Hachimi-jio-gan, could ameliorate glucose-associated metabolic disorders and its mechanisms were closely related to Hachimi-jio-gan. Fraction S1D2 (containing iridoid glycosides) and S2 (containing low-molecular-weight polyphenols) were active fractions of Corni Fructus, the active ingredient of Hachimi-jio-gan, against kidney damage caused by diabetes. Furthermore, according to the identification of active ingredients of the traditional herbal medicine, Corni Fructus, morroniside and GS are expected to provide a novel therapeutic drug against kidney damage caused by diabetes. Chief of all, GS, which is a polyphenolic compound of Corni Fructus, is expected as a new therapeutic drug.

References

apeutic targets. Front Pharmacol. 11, 586892.


Changes and Significance of Cytokines in Serum of Rabbits with Acute Pulmonary Embolism

Yulong Liang¹* Jianjing Liang² Wenjing Feng³ Jinghui Mu¹

1. General Surgery, Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, 050000, China
2. Hebei University, Baoding, Hebei, 071000, China

ARTICLE INFO

Article history
Received: 25 November 2021
Accepted: 20 December 2021
Published Online: 30 June 2022

Keywords:
Acute pulmonary embolism
Thrombosis
Rabbit serum
Inflammatory cytokines
Hepatocyte factor

ABSTRACT

Objective: To observe the changes of cytokines in serum of rabbits with acute pulmonary embolism, and to provide a scientific basis for clinical treatment of the disease. Methods: The animal models of pulmonary embolism were established in 26 healthy rabbits by autologous thrombus reinfusion and normal saline injection, and the serum levels of cytokines (TNF-α, IL-1β, HGF) in the two groups were monitored by enzyme-linked immunosorbent assay. Results: The expression levels of serum inflammatory cytokines (TNF-α, IL-1β) increased in both groups of rabbits within 1-3 hours of the acute stage of embolism, but the expression levels of serum inflammatory cytokines in experimental group of rabbits with pulmonary embolism caused by thrombosis increased more obviously. There was no significant change in serum HGF of rabbits before and after embolization in group B. The serum HGF content of experimental rabbits at 1 h, 3 h, 12 h, 24 h and 48 h after embolization was significantly higher than that before embolization. And in the acute stage of embolism (1-12 hours), it showed a gradual upward trend. Conclusions: The expression level of serum growth factor is different in different acute stages of pulmonary embolism. Detecting serum cytokines in rabbits with acute pulmonary embolism is of great reference significance for improving clinical diagnosis.

1. Introduction

Pulmonary thromboembolism (PTE) refers to a disease in which pulmonary artery is blocked by detached thrombus or other substances, which belongs to a branch of peripheral vascular diseases. Typical symptoms include dyspnea, chest pain, hemoptyis, fever, etc. After embolization, the blood supply function of pulmonary artery in patients will decrease, which will cause lung tissue necrosis and induce pulmonary infarction in a short time, leading to pulmonary dysfunction in patients, with extremely high disability mortality rate, and seriously threatening human health and life safety. PTE has no special clinical symptoms, and there is no specific diagnosis method for this disease at present. Therefore, at first, the medical community in China has formed a consensus on this disease,

*Corresponding Author:
Yulong Liang,
General Surgery, Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, 050000, China;
Email: liangyuwuzhi@126.com

DOI: https://doi.org/10.30564/jim.v11i1.4466
Copyright © 2022 by the author(s). Published by Bilingual Publishing Co. This is an open access article under the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License. (https://creativecommons.org/licenses/by-nc/4.0/)
that is, it is a rare disease in China, which also leads to a high misdiagnosis rate and missed diagnosis rate of this disease clinically in China. However, with the continuous development and progress of medical technology, through the unremitting exploration of countless clinical medical scholars, the research on this disease in China’s medical field has made substantial progress. In recent years, the efficiency of finding and diagnosing this disease in bed has become higher and higher, which provides a favorable direction for the next clinical treatment. Studies have shown that the expression level of serum cell growth factor has obvious changes in the early stage of pulmonary dysfunction, suggesting that the expression level of serum cell growth factor has guiding value for the early diagnosis of acute thrombotic pulmonary embolism.

In view of this, in this study, rabbits were selected as the research object to establish an animal model of pulmonary embolism by autologous thrombus reinfusion, and the changes of growth factors in serum of rabbits with acute thrombotic pulmonary embolism were observed, so as to provide scientific basis for further clinical study of the pathological process of acute pulmonary embolism and more effective clinical treatment \[1\].

2. Data and Methods

Twenty-six healthy pure New Zealand white rabbits were selected as the research object, and they were divided into control group and experimental group according to the random principle, with 13 rabbits in each group. In the second group, there were 5 female rabbits and 8 male rabbits, the maximum body weight was 3.8 kg, the minimum body weight was 2.9 kg, the average age was (3.24±0.32) kg, and the average age was (5.2±0.8) months. In the experiment group, there were 6 female rabbits and 7 male rabbits, with the largest body weight of 3.6 kg, the smallest of 3 kg, and the average age of (3.31±0.26) kg, 4-7 months, and the average age of (5.3±0.8) months. The data of the two groups of rabbits showed that the initial state was similar, and the difference of general conditions between the two groups was not significant.

2.1 Research Materials

Iodophor disinfectant, intravenous syringe, sterile catheter, medical water bath box, normal saline, phenobarbital sodium anesthetic, 5F sheath dilator, suture device, centrifuge, enzyme-linked immune costume experimental kit (produced by Jinan Kesheng Medical Technology) \[2\].

2.2 Method

Before the start of the experiment, a tandem immunoabsorption method was used. The experimental rabbits in group B adopted autologous thrombus reinfusion method to establish pulmonary embolism model. The first step is to prepare embolus. Select the rabbit ear vein to extract appropriate amount of blood and inject it into sterile catheter. In order to ensure the accuracy of blood test results, the rabbit ear vein should be disinfected locally before blood extraction. Set the catheter at rest until the blood is coagulated, then put it in the water bath box, adjust the temperature of the water bath box to 70 °C for 10 minutes, then use disposable syringe to push the thrombus in the catheter into the sterile bending plate, and make it into a 3-4 mm embolus, and rinse it repeatedly with normal saline for later use. The second step is autologous thrombus reinfusion. The rabbits were anesthetized by intraperitoneal injection of phenobarbital sodium at a dose of 150 mg/kg. Then, the rabbits were fixed, and femoral venous autologous thrombus was selected for reinfusion. Firstly, after removing the leaked skin from the thigh rabbit hair, routine disinfection was performed with iodophor, and then Seldinger puncture was performed along the femoral artery. The 5F sheath expansion tube with an inner diameter of 0.056 inch produced by Cordis Company was selected and inserted into the right atrium. The emboli prepared in advance by the sheath expansion tube were injected in several times. In order to ensure the successful reinfusion of the emboli and avoid their staying in the sheath expansion tube, after each injection of embolus, inject 2 mL of normal saline into the expanded tube of the sheath for flushing. Repeat the injection of embolus to ensure that the amount of embolus reinfusion is more than 1 mL/kg, or stop the injection when the rabbits have obvious symptoms of hypoxia such as shortness of breath and cyanosis of the lips. In the same way, the rabbits in the control group were injected with normal saline. Combined with the results of pulmonary angiography and pathological section, pulmonary embolism in this group of rabbits was confirmed \[3\].

2.3 Observation Indicators

After successful modeling, 1 mL of rabbit ear vein blood was taken and centrifuged at 300 r/min. The supernatant was extracted and the expression levels of tumor necrosis factor-α (TNF-α), inflammatory cytokine interleukin-1β (IL-1β) and hepatocyte growth factor (HGF) in serum of two groups of rabbits were measured by enzyme-linked immunosorbent assay at 1 h, 3 h, 12 h, 24 h and 48 h after embolization. After the experiment, rabbits were killed by injecting excessive anesthetic, dissected, and lung tissue was taken to observe the distribution and mor-
phology of emboli in pulmonary vessels. A small amount of pulmonary embolism tissues were embedded in graphite, then treated with HE staining, and pathological observation was made with the aid of medical microscope [4].

2.4 Data Processing

Using SPSS20.0 statistical software, the data of counting data (n,%) and measuring data (s) were processed by chi-square test and t test, with P<0.05 being statistically significant.

3. Results

3.1 Expression Level of Inflammatory Cytokines in Serum

According to the data in Table 1, before pulmonary embolism, the expression levels of inflammatory cytokines (TNF-α, IL-1β) in serum of two groups of rabbits were similar, and after pulmonary embolism, the expression levels of inflammatory cytokines in serum of two groups of rabbits were different at different times. The expression level of inflammatory cytokines in serum of rabbits in both groups increased within 1-3 hours of acute embolism, but the expression level of inflammatory cytokines in serum of rabbits in experimental group with pulmonary embolism caused by thrombosis increased more obviously, as shown in Table 1.

3.2 Results of Pathological Examination of Lung Tissue

Compared with the control group, the pathological examination of rabbit lung tissue in the experimental group showed that there were many dark red bleeding spots on the lung surface, many thrombi in the pulmonary artery and severe alveolar atrophy.

Table 1. Comparison of serum inflammatory cytokines expression levels between two groups (±s)

<table>
<thead>
<tr>
<th>Serum index</th>
<th>group</th>
<th>Before embolization</th>
<th>Post embolism</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1h</td>
</tr>
<tr>
<td></td>
<td>control group</td>
<td>2.06±0.61</td>
<td>2.07±0.63</td>
</tr>
<tr>
<td>TNF-α (ng/mL)</td>
<td>Experimental group</td>
<td>2.11±0.72</td>
<td>3.43±0.76</td>
</tr>
<tr>
<td>IL-1β (pg/mL)</td>
<td>control group</td>
<td>85.03±7.12</td>
<td>85.26±7.06</td>
</tr>
<tr>
<td></td>
<td>Experimental group</td>
<td>86.15±8.71</td>
<td>119.27±11.34</td>
</tr>
</tbody>
</table>

4. Discussion

Acute pulmonary embolism is an extremely dangerous disease, which can be divided into thrombotic pulmonary embolism, fat embolism, amniotic fluid embolism and air embolism according to the pathogenic factors, among which thrombotic pulmonary embolism is the most common one. The cause of the disease is complicated, and there is no conclusion in the medical field. However, according to relevant literature, many inflammatory mediators of cytokine network may play a certain role in the formation of the disease. In addition, some studies have found that after acute lung injury, the expression of hepatocyte growth factor in serum will be abnormal. Then, as a type of lung injury, will the serum hepatocyte content change? In order to test this conjecture, combined with the theory that inflammatory mediators participate in pathology, this study selected 26 rabbits for grouping study, of which 13 rabbits established acute pulmonary embolism model by thrombus reinfusion, and the other 13 rabbits were injected with normal saline in the same way, and then the expression levels of inflammatory cytokines and hepatocyte factors in serum of two groups of rabbits were measured by enzyme-linked immunosorbent assay. The results showed that before pulmonary embolism, the expression levels of inflammatory cytokines (TNF-α, IL-1β) and hepatocyte factor (HGF) in serum of two groups of rabbits were similar. After the occurrence of pulmonary embolism, the serum inflammatory cytokines of the two groups of rabbits have different expression levels at different times. The expression level of inflammatory cytokines in serum of rabbits in both groups increased within 1-3 hours of acute stage of embolism, but the expression level of inflammatory cytokines in serum of rabbits in experimental group with pulmonary embolism caused by thrombosis increased more obviously. The content of hepatocyte (HGF) in serum of experimental rabbits in group A was significantly higher than that before embolization from 1 hour to 48 hours after embolization, and showed a continuous rising pattern.
within 1 to 1-12h hours. It shows that the expression of inflammatory cytokines and hepatocyte factors in serum of rabbits with thrombotic pulmonary embolism will be abnormally increased in acute.

To sum up, the changes of serum growth factors (TNF-α, IL-1β, HGF) in the rabbit model of acute pulmonary embolism can prove that the expression levels of serum growth factors in patients with different types of pulmonary embolism are different at different times, and the clinical reference value is accurate, which has far-reaching significance for accurate clinical diagnosis and symptomatic treatment.

References


A Scientific Perspective of the Three Harmonies Principle of Taijiquan

C.P. Ong*
Independent Reseacher, Potomac, Maryland, USA

ABSTRACT

The Three Harmonies helps to regulate whole-body motion in harmony by balancing and aligning the movements of the body segments. Taijiquan uses the fangsong-relaxation modality to resolve the switching back and forth of the active muscle forces and the passive tensional forces of tendons, ligaments and fascial tissues. Fangsong induces the modulation of the muscles to resettle in a better state of balance, thus is necessarily a manipulation of the fascial tissues enveloping the muscles, organs and structures. In so doing, fangsong-relaxation cultivates the cognition and sensation of the fascial tensional network, which traditional Taiji theory refers to as Qi. Taijiquan harnesses Qi in the discipline of body motion to balance and align the momenta of the body segments in force transmission. This gives rise to maximal force potential in balance—the force of neijin (internal strength)—in response of application. Crucially, the settling into balance by fangsong functions as a neutral countermovement in the stretch-shorten cycle that primes the muscle-tendon unit in an ever-ready state of action, which endows neijin with the liveliness of response. Secondly, the fangsong manipulation of the fascial tissues serves as a fascial massage and release that provides relief to chronic pain syndrome caused by tenseness of muscles and fascia, a therapy that accrues with the many health benefits of Taijiquan. Lastly, but not least, the attentiveness required in the fangsong process develops into the meditation component of the practice which brings tranquility and the insight of mindfulness. Taijiquan thus bestows the triple gems of neijin, health well-being, and equanimity.

Keywords: Tai Chi, Yin-Yang, Harmony, Qi, Neijin, Fangsong, Chinese Medicine, Wellness

1. Background

Performance in sports and martial arts is an art of body motion, which is an articulation of the movements of body segments linked at the joints. How well one performs depends on how well the segments work in functional harmony in the mechanics of motion transmission. To excel, the body must be able to maneuver the movements in an interacting situation with sufficient strength and power in timeliness.

Physiologically, this requires an integration of the sensory and motor systems and the cognitive awareness of kinesthetics at the myriad joints. We may have control of the voluntary muscles to effect an action, but the control

*Corresponding Author:
C.P. Ong,
Independent Reseacher, Potomac, Maryland, USA;
Email: cpTaiji@gmail.com

DOI: https://doi.org/10.30564/jim.v11i1.4654
Copyright © 2022 by the author(s). Published by Bilingual Publishing Co. This is an open access article under the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License. (https://creativecommons.org/licenses/by-nc/4.0/).
of the individual muscles is not direct. We have control of the arm flexing and of the finger touching our nose with precision, but we do not have the awareness of the biceps and triceps working in an agonist-antagonist pair.

While the proprioceptors and motor sensors adjust for balance, there does not appear to be a neural control center to determine whether a posture as a whole is good or not. For instance, quite instinctively, we bend forward to reach for and pick up a box. The body is not aware that the trunk’s extensor muscles would have to exert an enormous force of 264 kg wt (for a 70 kg person) to support the lifting of a 10-kg box in the stooping posture. This is because the trunk’s extensor muscles, being close to the spine, have only a short lever arm of about 5 cm to the fulcrum at the lumbar-sacral joint \(^1\). We know that it is a dumb posture only after the fact when the back is hurt. By adopting a squat posture, the leg extensor muscles can contribute greatly to the lifting effort, and reduce the stress on the spine and back. Using the squat posture is not a neural strategy, but a learned one.

One may train with dedication, yet the body often still may not fire the right muscles to produce satisfactory results, as is evident in weekend golfers who find it hard to improve their drive significantly. It is clear from the physiques of players that developing muscle bulk is not a decisive determinant. Muscles can only do one thing, to contract to generate body motion. It is not muscle size but the quality of body motion that delivers the goods in performance.

A knock-out (KO) punch occurs when the head is in the way of the motion of the fist. The KO force is created in the collision between the fist and the head. The larger the momentum that can be transmitted to the fist the greater the potential of devastation. It is the quality of motion defined by the alignment of the momenta of body segments that delivers the KO, fastball, or long drive.

Indeed, often in the anxiety to punch hard and fast, the fist would fly out first, depriving the action of the momentum of the trunk. The torso is the largest component of the body segments, constituting about half of the body mass. Thus, the failure to apply the angular momentum of the torso would impair the force output in performance. Much of the frustration of being unable to improve performance in training can be attributed to the failure to harness the thoracolumbar fascia to regulate the torso’s rotational motion.

Our torso is not predisposed to turn as a whole. Rather, the chest and abdominal regions tend to rotate in opposite directions at the thoracic-lumbar region. This is due to the effect of lordosis, the spinal curvature, by Gracovetsky’s Spinal Engine Theory, which is discussed in the author’s paper \(^2\). Another factor that can affect training is the body’s leg length discrepancy.

Given the hundreds of joints, the discipline of balancing and aligning the body segments is a monumental problem. To compound it, adjustments made at one joint can affect that at the others, requiring a recalibration each time, due to the tensile integrity of the musculoskeletal frame, which renders the task nigh impossible.

Amazingly, we find a remarkably practical solution to this intractable problem in Taijiquan’s slow-motion methodology. The Taiji theory of regulating body motion is based on Yin-Yang Principles, a philosophy that predates science. Moreover, the concepts and pedagogy in the traditional literature are written in classical verses, more for form than for clarity, so are subject to interpretations. Nevertheless, the training relies on the age-old concept of Qi energy to discipline body motion by the process of fangsong-relaxation. As it turns out, Qi helps to develop the sensation of body kinetics.

Although Taiji theory does not translate well in physics and physiology, the body relates readily to the functions of Qi and fangsong modality. This paper asserts that these functions rely on the medium of fascial tension which lends connectivity to the body segments and the viscoelastic behavior of the muscle-tendon units.

Doing so clarifies how Taiji training cultivates the cognitive sensation of fascial tension as Qi to regulate balance and to align the momenta of the segments in whole-body motion. This generates the ideal Taiji motion, one in accordance with the Yin-Yang Principles. The significance is that in response of application, the force that ensues from the ideal motion will be timely, and of the right force vector.

We draw on the Ten Essential Principles of Taijiquan by Chen Changxin (1771-1853), which are quite relatable when the concepts are framed on the musculoskeletal structure \(^3\). By focusing on one of them, Three Harmonies Principle, as a representative, we are able to bring out the biomechanics of the ideal motion while not being overextended in scope. This paper complements the author’s recent publication, Healthcare and Sports from the Perspective of Qi, Fascia, and Taijiquan \(^4\).

Chart 1 gives an overview of the discussion of the first
2. Muscle-tendon Unit and Viscoelasticity

A skeletal muscle typically attaches to bones via tendons at both ends, which is described as a muscle-tendon unit (MTU). When the muscle component contracts, it stretches and generates a tension in the tendons, resulting in a tensile force that moves the attached bones at the joint.

A MTU is subject to the external forces of gravity, physical interaction, or other connected MTUs; it will lengthen, shorten, or remain the same, depending on whether the sum of the applied forces is stronger, lesser, or equal to its tensile force.

There is a constant interplay between the muscle’s contractile force and the tensional force. Muscle contraction occurs with the expenditure of ATP energy, so the loading by the muscle force is active. Meanwhile, the tensional force in the tendons is passive and is generated by their elastic property.

At the end of muscle contraction, with the overall strain maintained, internally, the tendons adjust in strain by the recoil of the tensional force. This lessens the tensile force, causing a relaxation of the stress in the MTU. This exhibits the characteristic behavior of viscoelastic material undergoing stress-relaxation when held under a constant strain.

If the muscle contraction in the MTU maintains a constant tensile force, the tendon will stretch, causing a “creep” in length. This manifests the characteristic viscoelastic behavior of undergoing creep in strain when held under a constant stress.

The stress-strain behavior of a MTU is viscoelastic. Our body does not behave like a rubber band. In flexing our arm, it cannot snap back in recoil to slap us in the face when the extensor muscles are relaxed. Unlike the property of elasticity, the response to loading and unloading is not immediate. The deformation and recovery of MTUs are gradual and time-dependent.

The stress-strain relationship of viscoelastic material is not governed by a constant Hooke’s Law. The stress is proportional to the rate of strain. At higher strain rates, tendons become stiffer and thus more effective in force transmission. So fast-twitch muscles in MTUs transmit stronger forces.

Contributing to the viscoelastic property of MTUs are the connective tissues covering the muscles and their adjacent structures. The muscle unit is enveloped by epimysium fascia; its fascicle subunit-bundle of muscle fibers, by perimysium; and the individual fibers, by endomysium. These fascial connective tissues and the collagenous ligaments that secure the bones at the joints are viscoelastic. In the muscle contraction, tension is also created in the fascial connective tissues and the ligaments. The MTU’s tensile force that moves the connected bones is the sum of the exchange of forces between the muscle contractile force and the tensional force of the tendons in series, and the tension of the components of the connective tissues and ligaments in parallel. More discussion of viscoelasticity of MTU can be found in Taylor [5], and of tendon elasticity in Alexander [6].

The fangsong modality, the key operational process of Taijiquan to be discussed soon, utilizes the viscoelastic property of the MTUs and the fascial connective tissues.

3. Fascial Tensional Network

The skeletal frame is held together by muscles, tendons, ligaments and fascial connective tissues. These fascial coverings extend across the entire frame and envelop internal organs and other structures, thus forming a continuous body-wide web of physical connectivity with viscoelastic properties, referred to as the fascial tensional network.

The connective tissues are made up of protein fibers (collagen and elastin), ground substance (the fluid content), and fibroblasts (cells), but they vary in composition and form, depending on function. The deep fascia that surrounds individual muscles is a denser connective tissue with a higher proportion of collagen fibers. The fascia of loose connective tissues which envelop and support organs is more fluid with a larger content of ground substance and spreads throughout the body, filling the spaces between structures and surrounding the blood and lymph vessels. For a more comprehensive review of fascia, see Schleip [7].

The tension in the fascial network is generated by the interacting MTUs and fascia that sum up to the
tensile forces that move and support the body segments connected at the joints. More than a physical connectivity, fascia provides a tensional link in force transmission. The task of regulating force transmission then is to cognize the tensional link and manipulate it. However, one is confronted with the same problem of the myriad joints as the fascial tensional network is formed of a complex of tensional links which pass through many intersections at the joints.

Taiji training does not focus on the individual tensional links but on perception of the fascial tension at a joint and between joints of an action at the functional level of balance and alignment. The modality of fangsong to be discussed next, cultivates the cognitive sensation of the fascial tension as to its functional effect in the resolution. We shall see that fangsong nurtures Qi as the cognition of kinesthesia via the fascial tensional network and harnesses it in the discipline of body motion.

4 Qi and Fangsong (放松)

*Fangsong*, which means to relax by letting go, is a modality to resolve muscle forces, tensional forces of tendons, ligaments, and fascia, against gravity and forces of other bodies, towards balance. It is the most significant operative word in Taijiquan. The very practice of the art is about fangsong. To see how fangsong works, stretch out an arm to the side level with the shoulder and hold it stationary. A combination of muscles is activated in the task, often with the shoulder muscles dominating. What are the preferred combinations? The fangsong mechanism helps to resolve it.

Before long, the arm feels tense and fatigue sets in, causing discomfort. Instinctively, the body responds by relaxing or letting go that acts to reduce the tenseness, thereby bringing some relief. This represents the rudimentary mechanism of fangsong: to relax or let go upon sensing tenseness. It tempers the tensile forces of the MTUs to rebalance, thus also of the myofascia.

On the other hand, one may sense a laxity, a lack of tensional connectivity to the hand, which is an indication of an imbalance of the muscle-and-tendon exchange within the MTUs. To correct this, the body can respond by stretching the arm to transmit tension to the hand. As active stretching may inadvertently introduce tenseness, the stretch-command is modified to “stretching internally” to minimize the prime-moving muscles.

This internal stretching is induced by the training admonition to “use mind-intention (yi 意 ) but not force (li 力 ).” Although the biomechanics is unclear, the instruction has the effect of restraining excessive muscle forces. Another practice exhortation is to let “the shoulder sink and elbow drop” (chen jian zhui zhou). The fangsong of the arm is best simulated by having someone hold the tip of middle finger and letting the arm hang like a rope. This induces the support of the arm against gravity more by eccentric muscle contraction and passive tensile forces.

The fangsong mechanism is guided by the dual rule: fangsong-relax upon sensing tenseness of excessive muscle activity and stretch internally upon sensing laxity or deficiency of muscle activity. However, the rule is not about allocating so much muscle activity here and so much there as balancing in a scale, which the body cannot do.

First we develop the cognition of what is tense and what is slack. Then the fangsong operation is simply to be less tense or less slack. Pragmatically, it is to settle in the middle ground between tenseness and laxity. Then by refining the fangsong practice, the margin of errors gets smaller and smaller, converging to higher states of balance. Effectively, fangsong settles the body segments into a better balance each time, drawing more on the passive tensile forces of the MTUs.

The continual application of fangsong cultivates the cognitive perception of the MTU activities as to their errors of being excessive or deficient and to their resolution. Taijiquan’s slow-motion modus operandi is very conducive to the attentiveness necessary to perceive the fangsong mechanisms. The sensation of tenseness or laxity is transduced from the feedback of the mechanoreceptors in the muscle spindles and the golgi tendon organs, as well as of proprioception.

Crucially, the cognitive perception, though subjective, is grounded on the fangsong tempering of the tensional and muscle forces of the MTUs coupled with the operational resolution of balance, based on the medium of fascial tension. Also, the tempering and settling have the effects of massaging and manipulating the fascial connective tissues. This gives us the proposition that the cognitive perception based on fascial tension, developed thus, is what Taijiquan perceives as Qi. For a more comprehensive discussion of Qi, see the author’s paper, *Science of Qi*.[6]

This provides a scientific basis of the traditional theory of Taiji practice as one primarily of developing Qi and the harnessing of Qi via the fangsong modality to discipline body motion to be in accord with the principles of Yin-Yang balance.

However, the task of applying fangsong to the hundred joints of the body remains, which clearly is daunting. This is where the Three Harmonies Principle comes in with a simplification scheme of the major joints into three corresponding pairs. More importantly, the review of
the Three Harmonies Principle from the perspective of biomechanics offers more insight to fangsong, Qi, and neijin. (See Chart 2 for an overview.)

Chart 2. Three Harmonies Principle Overview 2

5. The Principle of Three Harmonies (Sanhe 三合)

The Principle of Three Harmonies, externally, refers to the three pairs of corresponding joints: the shoulder and hip (kua 胯), the elbows and knees, and the hands and feet. By classifying the body’s myriad joints into a matrix of the three correspondences of joints, fangsong can be systematically applied to resolve their harmonies.

This sets up a training pathway for fangsong to temper the MTUs to resolve the tensile forces towards balance and alignment a pair at a time. Since the major joints represent the basis of the body frame, the classification strategy will develop the Qi-perception of the fascial tension body-wide.

The fangsong resolution of the three correspondences can then be extended to cross-pairings, between the left hand and the right foot, the left elbow and the right knee, and the left shoulder and the right hip. Then the left and right can be switched in the alternative cross-pairings. It can also be further extended to other pairings between the head and hand, the hand and body, and the body and footstep. In the process, the Sanhe Principle inspires the harnessing of the fascial tensional network as it is developed, namely, the utilizing of Qi to discipline body motion grounded on balance and harmony.

Here, we will review in more detail the shoulder-kua correspondence, which defines the torso. This will be done under three subsections: the thoracolumbar fascia, the kua junction, and dantian centrality.

6. The Shoulder-Kua Correspondence

Since the torso forms about half the mass of the body, its momentum is a determinant in force transmission. The force output potential of waist-power actions in sport and work rides on the torso moving as a whole in unified momentum. This requires a discipline of the muscles of the torso and the load transfer between the ribcage (chest) and the kua.

   i) The thoracolumbar fascia (TLF)

   Unlike the tendons of arm muscles, which are rope-like at the ends on attaching to the bones, many tendons of the torso are sheet-like where the muscles attach along the edges on a wide area. The most prominent tendon is the thoracolumbar fascia (TLF).

   The TLF is often depicted as the white diamond-shape region of connective tissues at the lumbar region of the back (Figure 1). The body’s two largest muscles, the lats, attach on the upper two sides, and the glutes on the lower two sides. Also, the trapezius muscles above attach at the vertex region of the TLF. The fascia extends from the iliac crest to the nuchal fascia at the nape of the neck. The psoas major, the quadratus lumborum, and the erector spinae muscles are ensheathed between the TLF’s three layers. The abdominal muscles wrap around to attach on both sides [9].
in the load transmission of the torso, thus in the discipline of its angular momentum.

The harmony of these forces is induced by the fangsong resolution of the shoulder-kua correspondence, which chips away at the errors of the muscle activities of the trunk. This cultivates the Qi-perception of the TLF with fascial connectivity to the linea alba on the front, which helps harmonize the abdominal muscles and the erectus abdominis.

Inspired by the Three Harmonies Principle, the Qi-cognition of the TLF tension is further extended body-wide to the fascial tensional network via the fangsong of the matrix of joints. At each step of the way, the fascial connective tissues are manipulated and released from tightness by fangsong.

ii) The paramount status of the kua junction

The kua complex consists of the pelvis and the triangle of joints, the sacroiliac joint and the two hip-joints. It is identified by the inguinal fold on the front, the lower region of the thoracolumbar fascia at the back, and the gluteus maximus rounding the butt. It forms the platform where the torso sits, poised in balance, to lend support to the maneuverings of the upper body.

Interspersed in the slow-motion Taiji calisthenics are some movements of fist and elbow strikes, which are expressed with explosive power called fajin (发劲), as in a demonstration by Chen Zhenglei [16]. These power movements share the same musculoskeletal demands of the waist-power actions in sports. However, to generate the explosive fajin, Taiji training is still primarily focused on the fangsong of the kua complex to produce the right motion in harmony but not on resistance or weight-regime exercises to exert muscle forces.

Any force action generated in the upper body must be supported by an equal and opposite reaction force at the base of the lower body (by Newton’s Third Law). For maximal force, the action-reaction control must be at the kua junction as it divides the upper body and lower body most proportionately. If it was set at the knees or ankles, often inadvertently in sports, to pack more mass in the upper momentum, injuries would result due to the disproportionately increased pressure at the lower joints.

Taijiqian places paramount emphasis on the fangsong of the triangle of joints in the kua complex to ensure that the torso turns as a whole in the power actions. The main obstacle to the discipline of the torso’s angular momentum is the effect of lordosis by the spinal engine (Gracovetsky). As mentioned briefly in the background, the spinal engine facilitates walking by causing the thorax to rotate in the opposite orientation to that of the lumbar to zero out the rotational momentum in generating propulsion [11].

The Qi-perceptivity helps to neutralize the spinal engine effect by applying fangsong to keep the lordosis in the sagittal plane and the kua platform level, thus ensuring the unified rotation of the torso. This consolidates the kua junction as the hub of force transmission between the upper body and the lower body to the ground. It places the control of the action-reaction force at the kua junction, thus defining its paramount status.

In this way, via the fascial tensional network, the action at the kua drives the force up the upper body to a punch, say, while the reaction force drives down to anchor the feet solidly on the ground. The biomechanics of the pelvic girdle and the sacral iliac joints in the load transfer between the spine and legs is studied by Vleeming, A et al. [12].

iii) Dantian Centrality

Because of the paramount status of the kua, it stays under focus in the fangsong resolution of the major joints of the Sanhe Principle, implanting the role for the kua junction as a basis of reference. This entails a constant fangsong tempering at the triangle of joints, forging a point of centrality of the kua complex. This center of reference coincides with the dantian, a point located at three-finger width below the navel, and a third of the way inside.

The center may seem localized to the kua but it serves as the center of reference of the three pairs of joints via the kua, thus of the whole-body frame. In other words, the dantian is nurtured as the center of the body-wide fascial tensional network. Thus, Qi is cultivated as the cognitive sensation of the fascial tensional network centered at the dantian [13].

In the viewpoint of Qi, the unwieldy task of resolving the errors of muscle activities of the myriad joints operationally becomes one of fangsong resolution to cultivate Qi centered at the dantian. This is cognized as Qi accumulating in the lower abdominal region, concentrating at the dantian, and functionally, as Qi sinking in the dantian (Qi chen dantian 气沉丹田). Therefore, the fangsong process is also viewed as cultivating dantian Qi. This describes the concept of dantian centrality (yi dantian wei hexin 以丹田为核心) as expounded by Chen Xiaowang [14].

At the core of the mastery of Taijiquan is the cultivation of the fullness of dantian Qi. The Qi cultivation incorporates a utilitarian aspect, namely, that it is harnessed as it is developed to discipline the mind and body, thus enhancing its growth further. It leads to the actualization of the dantian functioning as the center of the fascial tensional network, perceived as Qi. This operative feature that provides for manipulation and control of body motion by the conscious sensation of Qi adds a dimension of art...
to the physiology and physics of fascial tension, and to fascial manipulation and release.

7. The Internal Three Harmonies

The Principle of Three Harmonies discussed above are of physical or external character. It is complemented by the Three Internal Harmonies of (1) the “heart (xin 心) and mind-intention (yi 意),” (2) “Qi (气) and force (li 力),” and (3) “muscle-tendon (jin 筋) and bone (gu 骨).”

i) The Harmony of “heart (xin) and mind-intention (yi)”

Health and sport performance can be adversely affected by one’s state of emotion. Emotion affects one’s response. Taijiquan addresses the mind and body connection by developing a meditation component in the course of the slow-motion practice.

For the fangsong mechanism to work we must have perception of what we are doing. This means that we must be attentive to the practice. But the mind is restless like a monkey, with thoughts darting in and out. And we are vulnerable to emotions, which can undermine the practice.

Inherent in attentiveness is the awareness of the mind wandering off, although it may be a while before one becomes conscious of it. At the moment of the awareness of the mind wandering, one mindfully trains it to trigger a return to attentiveness. This tempers and restrains the unruly mind that reinforces attentiveness. And one develops mindfulness of the practice.

This constitutes the meditation component that forestalls distracting thoughts, thus nurturing the harmony of the heart and mind. The mindfulness developed progressively sharpens the perceptiveness of the fangsong practice to resolve the tensional errors at the joints and consolidate the dantian centrality. It forms the operational factor that ensures that the margin of errors in the fangsong-resolution process becomes progressively smaller, converging to increasingly higher states of Taiji balance.

A greater prize of mindfulness is that one becomes aware of the perturbing factors of anger, hatred, avarice, and a slew of other unsettling emotions. Mindfulness triggers a restraint that subdues the unwholesome thoughts, which leads to a more tranquil mind.

The very nature of the practice of harmonizing “mind and heart” is one of self-cultivation.

The journey leads to the higher realms of meditation that bestow more experiential insights of being with the present and mindfulness, with the rewards of tranquility and equanimity. In the meanwhile, the harmonizing process promotes the balanced regulation of the limbic system, enhancing health wellbeing.

ii) The Harmony of “muscle-tendon (jin) and bone (gu)”

The character jin 筋 refers to tendon, muscle, or veins, which in the context of the principle, turns out to aptly describe the muscle-tendon unit, the fundamental unit in the force transmission system of the body. There is a constant exchange between the active muscle forces and the passive tension of the tendons. The harmony principle expresses the balance of the interplay of forces in the MTU, namely, the harmony of jin and gu.

The internal balancing by the fangsong mechanism induces a restful state of the MTU. This maintains the MTU in balanced tension for the muscle contraction forces to transmit efficiently to the bone with minimal time lag.

Also, the balanced state at rest corresponds to the restful length of the myofibril. By the sliding filament theory, the sarcomere (the basic unit of myofibril) has a narrow length range from 2 microns to about 2.35 microns where the actin and myosin filaments overlap optimally, thus set to generate maximal force on activation. Thus, regulated by the harmony principle, the MTU is primed for action with the capacity of maximal strength.

In the thoracolumbar fascia, the fangsong mechanism of letting the structures settle in balance, uncannily sorts out the forces in harmony, switching back and forth between the passive fascial tension and the active muscle forces.

iii) The Harmony of “Qi and force li”

Force transmission is a function of the momenta of body segments. The fangsong discipline works to align the momenta to ensure that the segments do not move out of kinetic sequence in whole-body motion. The harmony principle here refers to the alignment of momenta in the body motion and the Qi associated with it. The tensile forces of the interacting MTUs in the fangsong alignment of momenta are perceived via the fascial tensional network by Qi.

The issue of force here is not that of the tensile forces of the MTUs, which can only generate body motion, but the force that ensues when the motion is resisted, as when the fist and head collide. This force results from the rate of change of momentum (Newton’s Second Law of Motion). Thus, the larger the momentum generated by alignment, the greater the force potential in application. This force potential is a consequence of the aligned momenta in motion associated with Qi, namely, of the harmony and Qi and motion. In other words, the harmony of Qi and li-force encompasses the alignment of momenta and thus its force potential.

To sum-up, we find here the scientific rationale of the ideal Taiji motion as one inspired by balance and harmony in momenta of the body segments. In practice, this is the nurturing of Qi by fangsong tempering of motion.
guided by the Three Harmonies Principle to be in Yin-Yang balance, which embodies the functional state of better alignment and harmony. In physics, we see the ideal motion as giving rise to force that is engendered of aligned momenta, thus is of maximal force potential. As the resulting strength of this force does not appear to come from the visible muscle groups, but from internal discipline, it is dubbed Internal Strength or Neijin.

8. Neijin (内功) or Internal Strength

Neijin is inspired by Yin-Yang balance but underlying it is the Three Harmonies Principle. It is the core strength developed in Taijiquan training by the fangsong settling of the body in balance and alignment, concomitant with the cultivation of Qi, summed up as the harmony of Qi and li. In short, neijin is li-force forged with Qi, aptly represented by the equation:

$$Neijin = Qi + Li-force.$$  

From the standpoint of biomechanics, the force of neijin is not just about strength, but of maneuveribility to change in timeliness. Neijin ensues from body motion that is tempered by fangsong to be in accord with Yin-Yang principles, inspiring the body’s consummate balance and momentum alignment. Neijin is the source of the body’s versatility and maneuverability of martial potency. In an encounter, the body uncannily responds with the right force vector with timeliness.

To illustrate, when pushed, the common response is concentric in powering to prevent from being shoved. The response of neijin is not to push back, but to fangsong and guide the attacker’s incoming force away from the body into “emptiness” in the skill of yin jin luo kong. And upon sensing the attacker faltering, neijin responds to take timely advantage to send him flying by “borrowing his faltering momentum” (jie li lai da ren).

The much touted skill of applying “four ounces to repel a thousand pounds” (si liang bo qian jin) is one of leverage. However, to effect such a huge lever-advantage, even if the fulcrum could be set at six inches from the load, the moment arm would have to be over 2,000 feet long, which would be impossible to replicate with the anatomy. Worse still, because structurally the muscles are close to the bones, the levers in the body perform at a disadvantage. The leverage adduced to in the skill comes from the body functioning as a screwdriver with the control at the kua as the handle while the opponent is holding the tip. The torque is generated by the body’s rotational motion, tapping on the coiling energy (chansi jin 委丝劲) of neijin.  

Neijin is developed with a requisite store of strength, without which one would have been shoved off before any skills could come into play. While the store of neijin is necessary to shore up balance and support, pivotal is its role in effecting the right force vector in response.

In the earlier example of being pushed, trapped in the response of pushing back, one is unable to adapt to make changes for other better courses of action. To change, the pushing-back muscles must conclude the current action for a new action to be initiated, with the attendant cost of tensional reloading and some time lag.

This costly response is resolved by the mechanism of the stretch-shorten cycle which facilitates a pre-stretch in initiating an action. For example, we drop our body to a squat before jumping. The dropping action stretches the tendons, priming the extensor MTUs to jump. Crucially, the extensor muscles are activated microseconds in eccentric contraction to help arrest the downward movement. When the downward movement ends, the same muscle contraction becomes concentric in powering the upward movement of the jump. Also, the recoil of the stretched MTUs provides an initial boost of the jump phase.

This countermovement strategy is deployed in generating the sport actions of golf, tennis, baseball, javelin, etc. In the golf-drive, the club is swung up in a countermovement before down swinging in the drive. As the golfer turns his gaze towards the flag pole in the hole, while still in the upswing, it activates the driving muscles, contracting eccentrically to help arrest the motion, and then the same contraction becomes concentric in powering the upward movement of the jump. Also, the elastic recoil of the MTUs.

The countermovement initiation is expounded in the Principle of Six Advances (Liu jin) of Chen Changxin’s Ten Essential Principles, which is articulated as: To move left, must initiate at right (shang zuo bi jin you); to move right, must initiate at left (shang you bi jin zuo).

Indeed, the fangsong settling (song chen 松沉) of the body in balance turns out to serve as an ingenious neutral countermovement that gives rise to the liveliness of neijin’s response. The act of fangsong settling into balance constitutes a pre-stretch, priming the body in an ever-ready state of preparedness (li ru ping zhun bei 立如枰准备). Enconced in the state of balance, the response of “sinking and following” (pian chen ze sui 偏沉随) to the opponent’s force pressure, generates the countermovement of the action of the right force vector. (The last two phrases are common practice dictum from the Taijiquan Discourse by Wang Zongyue).

The response of the force vector is packed with the right punch as it is supported by the alignment of momentum of the whole body motion, and transmitted from
the kua. This defines the distinction of the response of neijin, lively and timely of the right force vector in martial application.

9. Conclusions

Although we have explicated the role of Qi in generating the ideal Taijiquan motion in terms of physiology and biomechanics, the concept of Qi itself remains elusive to scientific definition and measurement. The Qi concept embodies a functional dimension—the operational effects of Yin-Yang balancing. The appreciation of Qi is based on our senses, but grounded on functionality of balance, which makes Qi very relatable to the body. Indeed, the very practice of the art of Qi nurturing forges a solution-path that leads to the harmony of the body’s functional entities.

To reiterate, the nurturing of Qi in Taijiquan, inspired by Yin-Yang balance, translates to the balancing and aligning of the body segments—the harmony of the system of interacting muscles, tendons, ligaments, and fascia via the fascial tensional network. The internal strength or neijin developed by Qi training is borne of body motion disciplined by the Yin-Yang principles. The gem of neijin is mined by the fangsong modality in the arduous kungfu process of mastering the art. Taijiquan’s martial potency is based on neijin, which gives rise to the lively and timely response of the right force vector in application.

However, while neijin may be fascinating in martial prowess, driving the popularity of Taijiquan is not neijin but the therapeutic health benefits that flow soon after from the practice. The immediate tangible beneficial effect is the confidence of one’s gait. The constant admonition of fangsong instills a body response of settling in balance at every turn and move. Crucially for an elderly, this response of settling is triggered in an accidental slip, helping to mitigate fall injuries. That Taijiquan is more effective in preventing falls compared to other exercise regimens, is well documented.

As fangsong is functionally modulating the muscles and fascia, very soon after taking up Taijiquan, practitioners begin to enjoy the therapeutic relief of chronic pains caused by poor body structures adopted habitually at work. Indeed, the fangsong settling of the body in balance is also manipulating fascial release to alleviate the causes of chronic pain syndrome.

The Principle of Wuzang (“Five Internal Organs”), another of the Ten Essential Principles, addresses the functional harmony of the system of internal organs, which are enveloped in fascial connective tissues. The permeating effects of Qi nurturing regulate the bioenergy dynamics of the organs in homeostasis, the passport to health. This benefit of health well-being accrues and is enjoyed daily throughout one’s Taiji journey.

The attentiveness in the slow-motion practice engages the mind beyond a physical activity; it puts one on a meditation path to the realm of spirituality (shen). The meditation component is enhanced further by the practice of standing in stationary postures (zhanzhuang 站桩) or by sitting meditation.
Of the mind, the insight of mindfulness operationally works to subdue the emotions of anger, hate, envy, greed, desire, and unwholesome thoughts that perturb and cloud the mind. This brings clarity and tranquility with the attendant health benefits of meditation. Thus we have the triple gems bestowed by Taijiquan: neijin, health, and equanimity.

Disclosure

An excerpt of this paper was presented at The First International Taiji Science Online Forum, December 4-5, 2021, organized by the Taiji Science Foundation.

References


[18] Li, F., Harmer, P., Eckstrom, E., et al., 2019. Effectiveness of Tai Ji Quan vs Multimodal and Stretching Exercise Interventions for Reducing Injurious Falls in Older Adults at High Risk of Falling: Follow-up Analysis of a Randomized Clinical Trial. JAMA Netw Open. 2(2), e188280. DOI: https://doi.org/10.1001/jamanetworkopen.2018.8280

Advances in the Treatment of Acute ITP

Yuheng Jiang1  Jiahao Gu1  Zai Gu1  Yifeng Xu1  Bin Jia1  Jing Yang2*

1. School of Emergency Trauma, Hainan Medical University, Haikou, Hainan, 570100, China
2. School of Nursing, Hainan Medical University, Haikou, Hainan, 570100, China

ARTICLE INFO

Article history
Received: 5 May 2022
Accepted: 30 May 2022
Published Online: 30 June 2022

Keywords:
ITP
Hormone therapy
IVIg treatment
Splenectomy
Thrombopoietin receptor agonist

ABSTRACT

Immune thrombocytopenia (ITP), also known as idiopathic thrombocytopenic purpura, is a hematologic disease in which platelet destruction increases and production decreases, mainly mediated by immunity. However, up to now, the pathogenesis of ITP is not clear, which has caused great trouble in treatment. Therefore, this paper intends to review the recent literature on ITP treatment to provide some reference for clinical treatment. This paper combines the evidence of ASH immune thrombocytopenia and the Chinese Guidelines for the Diagnosis and Treatment of Adult primary immune thrombocytopenia (2020 edition). In this paper, the treatment process of ITP was divided into first-line treatment and second-line treatment, and it was concluded that first-line treatment was often used when newly diagnosed with ITP: combination of high-dose dexamethasone and low-dose gamma globulin. However, it should be noted that only 60%-80% of patients responded to first-line treatment, and most of them relapsed during dosing reduction or drug withdrawal. Second-line treatment is recommended in this case. The standard treatment is splenectomy, but due to its uncontrollable nature and side effects, it should be used cautiously. A new treatment approach, thrombogenin receptor agonist, has great development potential, and multidrug combination therapy for ITP has positive clinical significance.

1. Introduction

Immune thrombocytopenia (ITP), also known as idiopathic thrombocytopenia purpura, is a hematologic disease with increased platelet destruction and reduced production, mainly mediated by immunity. ITP is mainly manifested as isolated thrombocytopenia (platelet count <100×10⁹/L) accompanied by clinical symptoms of skin and mucosal bleeding. ITP can affect people of all ages, but mainly occurs in children, women of childbearing age and the elderly. Its pathogenesis is complex, involving multiple processes of humoral immunity and cellular immunity, and its clinical treatment is difficult. In this review, we will review the current progress in the treatment of ITP based on the evidence-based guidelines for ASH immune thrombocytopenia, the Chinese Guidelines for the Diagnosis and Treatment of Adult Primary immune thrombocytopenia (2020 edition) and

*Corresponding Author:
Jing Yang,
School of Nursing, Hainan Medical University, Haikou, Hainan, 570100, China;
Email: onlymyang@163.com

DOI: https://doi.org/10.30564/jim.v11i1.4691
Copyright © 2022 by the author(s). Published by Bilingual Publishing Co. This is an open access article under the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License. (https://creativecommons.org/licenses/by-nc/4.0/).
recent major studies.

2. First-line Treatment

2.1 Hormone Therapy

For newly diagnosed ITP, patients with platelet count < 30×10^9 /L are generally recommended to be treated with glucocorticoids [1]. Meanwhile, Chinese Guidelines for the Diagnosis and Treatment of Adult Primary Immune thrombocytopenia (2020 Edition) indicated that high-dose dexamethasone (HD-DXM) 40mg/d×4d, oral or intravenous administration, and patients with ineffective or recurrent disease could repeat one cycle. During treatment, blood pressure and blood glucose levels should be monitored to prevent infection and gastrointestinal ulcer [2].

Large-dose DXM is the first choice in clinical practice, and its effect is mainly reflected in the negative regulation of the combination of antibody and autoantibody formation, inhibition of C3b and Fc receptor function, and reduction of platelet phagocytosis due to monocyte macrophage system. Reduce destruction and increase generation [3].

In addition, XM single drug treatment of ITP can rapidly improve PLT level, with significant efficacy within 30 days [4]. Wang Xiaojun et al. treated 26 ITP patients who had not received other treatment before hospital only with high-dose dexamethasone therapy, acid inhibition, gastric mucosa protection and other adjuvant treatments, and the results showed that 18 cases (69.23%) of the 26 cases were significantly effective, 3 cases (11.54%) were effective, and 2 cases (7.69%) were improved within two weeks. The total effective rate was 88.46% [4,5]. However, long-term clinical data analysis showed that the treatment with large dose OF DXM alone could not achieve satisfactory efficacy, and patients were prone to relapse or even refractory ITP [5]. Research shows that DXM combination therapy effect is DXM monotherapy effect significantly increased, in recent years, DXM combination treatment of ITP has become many scholars study the direction of the common combination of IVIg, ai QuBo palmer ethanolamine, etc., to the later several drug treatment mechanism and treatment effects were discussed.

2.2 IVIg Treatment

Gamma globulin (HD-IVIG) is a preparation rich in immunoglobulin, which has antiviral, antibacterial and antitoxin effects and can also enhance human immunity. It is often used in the treatment of ITP combined with glucocorticoid at the present stage. Numerous studies have pointed out that: Gamma globulin can effectively prevent thrombocytopenic purpura with antiplatelet antibodies, blocking antibody and platelet, and mononuclear cells and macrophage phagocytosis of platelets, clinically often associated with glucocorticoid (such as dexamethasone, methyl prednisolone steroids) combination, to achieve the purpose of the treatment of ITP, 50 ITP patients were randomly divided into control group (25 cases) and treatment group (25 cases) through controlled experiment. The control group was only given standard treatment of glucocorticoid regimen, and the experimental group was given intravenous infusion of IVIg400mg/kg: D-1 on the basis of this treatment, and the total effective rate was 76% in the control group and 92% in the treatment group for 5 days. It can be seen that the combined treatment effect is obvious [10,11].

It is worth noting that the cost of gamma globulin is high, and the massive use will undoubtedly increase the economic burden of patients. Recent studies mainly focus on the effect of the dosage of gamma globulin on the therapeutic effect when DXM is combined with gamma globulin. Data show that when IVIG is used in the treatment of ITP with low dose and normal dose. Differences in platelet parameters and efficacy were not statistically significant [11,12], so low-dose IVIG can be considered for clinical treatment.

3. Second-line Treatment

3.1 Splenectomy

Second-line treatment is recommended for patients with ITP ≥3 months and corticosteroid dependence or no response [1]. Splenectomy is one of the standard treatments of second-line therapy. The spleen is the largest lymphatic organ in the human body and an important site for antibody production, antigen presentation and the persistence of autoimmune responses [26]. Splenectomy plays a clinical role in the treatment of ITP mainly by removing platelet destruction and some important parts of anti-platelet antibody production [27]. Splenectomy at this stage can be divided into Open splenectomy (splenectomy, splenectomy,OS) and laparoscopic splenectomy (aparoscopic splenectomy, LS). At the same time, COMPARED with the former, LS has the characteristics of smaller postoperative wounds and faster recovery of patients. The main limitation of LS is splenomegaly (spleen weight over 500 g), but it is worth noting that laparoscopic splenectomy can also be considered as a treatment plan even in the case of extreme
spleenomegaly (spleen weight over 2000g) [29]. Therefore, spleenomegaly that causes technical difficulties is not characteristic of ITP. Several clinical trials have observed that LS has excellent efficacy for ITP patients. Liao Rui [28] used LS to treat clinically refractory ITP patients, and the results showed that 65 of the 78 patients (83.3%) had stable remission after LS, without further treatment of ITP. Ducassou Stephane [13] conducted an experimental study on 137 ITP patients using four second-line treatment approaches (splenectomy, hydroxychloroquine, azathioprine and rituximab), and the results showed that the cure rate of all patients was 62% after 24 months, among which the cure rate of 56 patients who underwent splenectomy was 85%. The cure rate was 60% for 23 patients on hydroxychloroquine, 46% for 24 patients on azathioprine, and 37% for 34 patients on rituximab. Therefore, splenectomy is still an effective way to treat ITP.

However, it is worth mentioning that splenectomy has the risks of intraoperative splenic artery hemorrhage, thrombosis, damage to pancreas and tail of pancreas, resulting in local pancreatic fistula, local abscess formation, infection and other complications [14,15]. Therefore, considering the trauma, irreversibility, and unpredictability of splenectomy, traditional open splenectomy should be used with caution if drug therapy fails [16]. According to previous international consensus reports, splenectomy should be performed 12 to 24 months after the diagnosis of ITP, when patients still have a high probability of recovery [17]. At the same time there are constantly new clinical data showed that compared with traditional open surgery, laparoscopic splenectomy, as a kind of minimally invasive surgery with small trauma, rapid recovery, low infection rate of significant advantages to become the gold standard for surgical treatment of ITP [18], given the recent research has shown that preoperative platelet amount is not the absolute contraindication of laparoscopic splenectomy [30]. As well as the development of endoscopic technology, the improvement of surgical techniques and the increase of clinical experience, more and more clinicians advocate advancing the schedule of LS surgery for ITP patients, so as to reduce the complications caused by hormone therapy (such as obesity), so as to improve surgical safety and postoperative efficacy [31].

### 3.2 Thrombopoietin Receptor Agonist (TPO-RA)

Thrombopoietin receptor agonists (TPO-RA) are a newly emerging drug for the treatment of ITP in recent years. ASH guidelines suggest that TPO receptor agonists are preferred when patients want to avoid surgery and achieve lasting remission [1]. Currently, new TPO-RA products that have passed clinical trials and been approved for marketing include Altrepopol, romistine, lusantrepol and Avantrepol [19]. Among them, altrepopa and romistine are the most widely used in clinical application. Romistine is an Fc fusion protein attached with four 14-amino acid TPO peptides (peptidomes), which stimulate TPO receptors by binding to the extracytoplasmic domain (extracytoplasmic domain similar to endogenous TPO) [20]. Aitrippa is an orally taken non-peptide TPO-R agonist, which is structurally independent of eTPO and selectively interacts with TPO-R rather than competing with TPO.

This results in increased proliferation and differentiation of bone marrow progenitor cells into megakaryocytes and increased platelet production [34]. TPO-RA can restore the balance of FcγR by up-regulating the expression of inhibitory FcγRIIb, thereby reducing the activity of FcγR mediated monocytes/macrophages, and thus achieving the effects of continuous treatment on ITP, such as stimulating and regulating B cells and T lymphocytes, reconstructing immune tolerance and reducing inflammatory response [21,32]. TPO-RA can also reduce hematopoietic stem/progenitor cell apoptosis, improve DNA damage repair, and protect and maintain its hematopoietic function [22]. The commonly used doses of romistin and atribopina are 1-10μg/ (kg·w) and 25-75 mg/d, respectively, which should be adjusted at any time according to the number of peripheral blood plates of patients, so that the number of peripheral blood plates of patients can be stabilized at (50-200)×10^9/L [17]. The platelet response rate of patients after treatment can reach 50%-90%, and it is well tolerated after long-term use, and the myeloid reticular fibrosis in a few patients can be reversed even after the termination of treatment [25]. A large number of recent studies have shown the possibility of sustained remission in ITP patients after tPO-RA discontinuation. Although it is not clear which type of patients can achieve sustained remission and how to stop TPO-RA, evidence of sustained remission in ITP patients after TPO-RA discontinuation is still increasing. This may change the traditional treatment model that some patients need long-term maintenance therapy [23].

### 4. Prospect of Combined TCM and Western Medicine Therapy

A large number of current studies and experimental results show that the feedback effect of TCM combined with Western medicine in the treatment of ITP is significantly better than that of the single western medicine group. At the same time, the current treatment of ITP is usually carried out by means of hormone remission and shock therapy, which inevitably leads to some toxic and side
effects and adverse reactions. Through the combination of traditional Chinese and Western medicine treatment, on the one hand, a more ideal therapeutic effect can be obtained; on the other hand, the mild effect of Traditional Chinese medicine can also alleviate some possible side effects and adverse reactions. Bao chapter meter, etc. [36] through blood spirit soup recipe, to Yin deficiency blood hot jump walkers with three groups of patients with clinical syndrome differentiation to agent such as use of compatibility of traditional Chinese medicine treatment, joint for small single dose of glucocorticoid drugs at the same time give the liquid form, syndrome differentiation of traditional Chinese medicine treats joint group syndrome symptoms curative effect for the group total effectiveness 86.67%, not compatibility with Chinese traditional medicine group cure rate to reach 50.00%, The total effective rate of TCM syndrome treatment in the treatment group was also significantly increased, and the adverse reactions were lower than cyclosporine (P<0.01). Similar results, the clinical study conducted by Wu Qing et al., with the help of stir-black Gui-pi Decoction, also achieved almost the same good long-term effect, and the PLT level of patients in the combined application of Chinese medicine treatment group was significantly higher than that of the clinical control group (P<0.05) [37]. Xu Xiaodu, peng han [38,39] proposed, for the all of the patients with chronic or recurrence in patients with ITP, and refractory with various drugs cause recursede ITP, hormone drug dependence caused by all kinds of type secondary ITP patients, with traditional Chinese medicine (TCM) scheme combined the clinical treatment of western medicine, has good effect to improve effect and decrease toxicity [40]. In Han Peng’s study, the TCM syndrome score of the observation group was (6.85±1.4) points lower than that of the control group (11.78±3.01) points after the combined treatment of Traditional Chinese and Western medicine, and the syndrome score of the TCM perspective also improved significantly. At the same time, the current Chinese clinic for children on the basis of the drug treatment of ITP virus is currently a hot research topic, such as Yang Xiaqian, Shao Jingbo, Huang Zhihui people in [43] 41 - through the comparison of different types and cool blood detoxification application analysis found that the effect of [44], compared with the method of the obvious advantages, the hormone group stopped after a week .The recurrence rate was 57.1%, higher than that of hormone + Chinese medicine group (18.8%,P=0.008). The combination of traditional Chinese and western medicine showed certain advantages in both effect and safety in children.

According to the theory of Traditional Chinese medi-
cine, nourishing Yin and Yang, namely, using hypotenuse, rhubarb [45] and other drugs to supplement Yin and qi, also has guiding significance for ITP patients’ rehabilitation [46]. Starting from the theory of cell and molecular, wang tao, Qiu Yingyu thinks, recuperation of traditional Chinese medicines by yiqi huoxue fang, associated with T cell subgroup of recovery, the secretion of cytokines and repair metabolism [47] play a promote and promote role, the basic theory of traditional Chinese medicine combined with clinical treatment of western medicine is a clinical research hotspots at present [48].

ITP is an autoimmune disease, which is manifested by decreased platelet content and associated potential complications. In this paper, the treatment mechanism, clinical treatment means and treatment effect of ITP are sorted out and then appropriate clinical treatment means and treatment suggestions are given to ITP patients at different stages. High-dose corticosteroids are often the first choice for first-line treatment of ITP, which mainly targets patients with early thrombocytopenia. Combined with the latest research progress, it can be found that the combination of drugs in first-line treatment can improve the treatment efficiency, reduce drug resistance of patients, and save the treatment cost. Now common first-line treatment combination with IVlg, drugs to boost platelet production, Ai QuBo palmer ethanolamine, etc., but only 60%-80% of the patients respond to first-line therapy, and mostly in the process of reduction or withdrawal recurrence, thus have to second-line therapy, the common secondary treatment splenectomy, drugs to boost platelet production, rituxan, etc., Second-line therapy is often used for the treatment of chronic thrombocytopenia in clinical practice, with obvious effects and advantages of low recurrence. With the improvement of endoscopic technology and clinical surgical skills, laparoscopic splenectomy (LS) has been gradually praised by experts and scholars for its wide range of application, small tissue damage, good recovery and other advantages. The advance of the surgical process in the course of patients also has great research and practical significance, among which tpo-RA, as a platelet promoting agent, is also the golden key to the second-line treatment of ITP. Recent theoretical studies tend to study the mechanism of Tpo-RA to achieve sustained remission and the classification of action targets. This makes it possible for late clinical use to enable patients to achieve sustained remission while discontinuing medication and avoiding surgery.

References


