ACUPUNCTURE IN NEPHROLOGY: STATE OF THE ART

ABSTRACT

Traditional Chinese Medicine (TCM) has different concepts of physiology, semiology, etiopathogenesis, and treatment, and it has been increasingly recognized as an effective therapeutic approach in several medical fields. Acupuncture is a sensorial and peripheral stimulation technique that uses the integrated properties of the nervous system to exert its therapeutic actions. The increased number of studies on neuroanatomy and neurophysiology has allowed us to begin understanding its effects. In this study, we propose a brief discussion on the concepts and principles that guide TCM, and review the scientific evidence of its use in Nephrology. We also report our experience with acupuncture and moxibustion on the progression of experimental renal disease. This is a new and promising ancillary therapeutic strategy in nephrology and it may be associated with conventional methods in the management of end-stage renal disease.

Keywords: nephrology, end-stage renal disease, acupuncture, traditional Chinese medicine.

INTRODUCTION

The concepts of semiology, etiopathogenesis, and treatment in Traditional Chinese Medicine (TCM) are different than in Western Medicine; however, its simple and philosophical language is being understood and proven by modern science, which demonstrates the validity and authenticity of its concepts. Although it is very old, and the first reports of its use date from 2,300 B.C., systematic studies using the Scientific Method only started in the mid 1970s. Currently, it is increasingly accepted in Western Medicine as treatment for several diseases.

The traditional Chinese medical system has a broad approach of the health-disease concept, in which several aspects are taken into consideration. Nutritional and hygienical aspects are very important, as well as the approach of disturbing emotions that affect the mind of an individual. This body-mind integration can be achieved through meditation techniques, such as Qi Kun and Tai Chi Chuan. Similarly, Chinese massage (Tui-Na), phytotherapy, and acupuncture are effective techniques to prevent and cure diseases.1,2

Acupuncture stimulates specific points, which mobilizes specific substances in the body, harmonizing and strengthening the organism in the prevention and discontinuation of pathologic processes.3 The word acupuncture, which joins the Latin roots acus (needle) and punctum (puncture), was created to describe this Chinese procedure, but the Chinese word Zhen Jiu means needle and moxibustion (MO); nowadays, electroacupuncture (EA), laser, and electromagnetic devices are used for the same end.

Although acupuncture and MO are ancient techniques, they are state of the art therapeutic procedures. The social and historical validation of acupuncture and TCM has been confirmed in the last decades, in which a large number of studies not only confirmed the tradition but also added new clinical applications.4 In the last 30 years, scientific advances, especially in Neuroscience, has been shedding light on its neurobiological basis, mainly by using experimental models and EA in the acupuncture point (AP) E-36.1,4,6,8,9,10 In the present study, we discuss the principles of TCM and the recent studies that integrate its concepts in Nephrology.

TRADITIONAL CHINESE MEDICINE (TCM) AND NEPHROLOGY

The main theoretical basis of TCM for the diagnostic and therapeutic reasoning is the basic tripod: the Yin/Yang theory, Zang/Fu Theory
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(organisms and viscera), and the Five Movements Theory. In TCM, the kidneys (Shen) have fundamental importance, being closely related to the origin of human energies. Among its functions, we should mention the storage of Ancestral Energy (Jing), generation of the Primordial Yin and Yang, and production of Yaun Qi (Energy Source), which promotes the vitality of other organs essential to life. Thus, Shen controls the process of birth, growth, development, and reproduction.11

An imbalance in natural and internal forces is present in kidney diseases, but, in the general context, the whole organism is involved. This is demonstrated by physiological imbalances that affect all organs: alkalosis/acidosis secondary to a disruption in pulmonary ventilation, insulin resistance in pancreatic disorders, hypertension and its effects in the heart, and so on. In TCM, deficiency in the Qi of the kidneys is related with several pathologies, such as hypertension, tachycardia, hyperthyroidism, diabetes mellitus, chronic nephritis, urogenital infections, low back pain, menstrual disorders, and pulmonary tuberculosis among others.12 In the five elements theory, the kidneys are responsible for the initial energy of the cycle and control of the element Fire (Heart). Thus, kidney disorders are associated with a smaller energy flow to all other elements and significant cardiovascular changes. In acupuncture/MO, specific points of the renal system are stimulated, minimizing the effects of dysfunctions generated by those changes and, therefore, leading the organism to better functional conditions.

ACUPUNCTURE IN NEPHROLOGY

Recently, studies applying the concepts of TCM and acupuncture in Nephrology have been instituted. Holub (1999) demonstrated that patients with different types of glomerulonephritis treated with acupuncture showed a statistically significant improvement in renal function, when compared to the control group, reflected by maintenance of the capacity to concentrate the urine, reduction in proteinuria and hematuria, and marked reduction in blood pressure (BP).13 Similarly, in a study by Ma (2004), 42 patients with changes in renal function secondary to multiple bouts of gout were treated with acupuncture and the results indicated an improvement in renal function, such as normalization of the serum levels of creatinine, BUN, and uric acid associated with a reduction in the 24-hour urine protein loss and urine output.10 Besides, Huang (2007) demonstrated an improvement in kidney function in animals with lipopolysaccharide (LPS)-induced acute renal failure treated with acupuncture on AP E-36 (Zusanli), reflected in the parameters evaluated, such as urine output, serum creatinine and BUN, and histopathological analysis.9 Sakakinara et al. (2007) reported a case of neurodegenerative disease characterized by dysfunction in the circadian cycle and nocturnal polyuria treated for 6 months with moxibustion (MO) on AP VG-3 (Zhongji), E-30 (Qichong), BP-6 (Sanyinjiao), and R-5 (Suiquan), whose subjective and objective parameters, such as control of diuresis and a significant reduction in nocturnal polyuria, improved considerably.11

Progression of the renal disease (PRD) is a crucial subject in Nephrology, since a deeper understanding of the pathophysiological mechanisms of this process could help block it, or, at least, delay its progression. Although the understanding of renal physiology and pathophysiology with the development of new investigative techniques using genetics and molecular biology concepts has increased, we are still unable to change its progressive nature, which culminates with ESRD, even when adequate treatment is instituted. Several pathophysiological mechanisms are deemed responsible for the progressive renal deterioration after kidney damage, including hemodynamic factors, biochemical and cellular inflammatory mediators, proteinuria, and hypertension.

The anti-inflammatory and anti-hypertensive effects are among the beneficial effects attributed to acupuncture in renal diseases.14 The anti-inflammatory effects probably result from the modulation of mediators of the natural immune response of structures of the Central Nervous System, such as the efferent pathway of the vagus nerve. Since macrophages, dendritic cells, and mast cells, which normally respond to neuronal stimulation with the production and secretion of a wide range of inflammatory mediators, including cytokines, products of arachidonic acid metabolism, and vasoactive amines, are in close contact with the branches of the vagus nerve, they function as a bridge between local signals (paracrine) and the vagus nerve.15 Thus, several studies have demonstrated that acupuncture can modulate the inflammatory action of macrophages, leading to a reduction in the production of TNF, IL-1β, IL-6 and IL-18, and an increase in the production of anti-inflammatory cytokines (IL-10), controlling the extension of the inflammatory response.1,16

High blood pressure (HBP) is one of the main factors that contribute for PRD. Sodium retention and the expansion of the intravascular volume, increased vascular contractility due to the effects of vasoconstrictors, such as angiotensin II (AII), and, mainly, neurogenic factors, secondary to the increased activity of the sympathetic nervous system promoting the inflammatory process, are involved in the pathophysiology of HBP.17 This association has been known since immemorial times, which can be seen in the well-known text Huang Di Nei Jing (2,796 b.C.) that was
translated as “The Medicinal Classic of the Yellow Emperor”, where it is described that the arterial pulse is abundant, tense, and full like a cord, swelling is present and it is associated with “a deficiency in the Qi of the Kidneys, which affects the Heart”. As mentioned before, the kidneys (Shen) are the basis of the Yin and Yang and they are the storage site of the essential energy (Jing). Besides, they store the Fire in the Door of Life (Ming Men), being the source of Water and Fire called Original Yin and Yang. In this context, HBP is a syndrome that results from the imbalance between Yin and Yang, with an essential pattern of Yin deficiency in the Kidneys (Shen) promoting patterns of inner excesses, such as hyperactivity of the Yang and stagnation of the Qi of the Heart (Xin) and Liver (Gan).19

The beneficial effects of EA and MO on HBP are described in the literature in clinical and experimental models. The efficacy of acupuncture in the treatment of hypertension and myocardial hypertrophy in hypertensive animals, probably due to inhibition of the sympathetic system, has been reported.21 In 1982, Yao et al. used stimulation similar to that of acupuncture in spontaneously hypertensive rats (SHR) and compared it to the effects on normotensive rats. Initially, an increase in BP was observed in both groups, which was followed by a prolonged reduction, which was significantly higher in the SHR, along with a reduction in sympathetic tonus, reflected in the firing rate of the splanchnic nerve that was reverted by the administration of naloxone. Similarly, Lee et al. (1997) applied MO to AP B-15 (Xinxhu) and B-27 (Xiaochangshu) in SHR rats and observed a reduction in BP. In 2000, Li et al. studied rats with induced-hypertension and demonstrated that EA on AP E-36 point (Zusanli) for 20 minutes reduced the BP, probably mediated by the release of NO in the periaqueductal gray matter (PGM) through the activation of inhibitors of the sympathetic system. Wu et al. (2004) demonstrated that acupuncture on AP VB-34 (Yanglingquan) resulted in a reduction in BP and prevented myocardial cell hypertrophy in SHR. More recently, Huang et al. (2005) demonstrated that EA on AP E-36 (Zusanli) and EX-37 (Lanwei) decreased systolic BP and changed the expression of nNOS and iNOS mRNA in the rostroventrolateral region of the medulla (RVLM) in rats. This region is the common final integration pathway of the sympathetic and cardiovascular systems. Similarly, Ma et al. (2005) applied EA to AP E-36 (Zusanli) and suggested that the hypotensive effect involves modulation of nNOS synthesis in the medial region of the NTS (somatic tract nucleus) in rats. A clinical study with 67 patients, ages 45 to 75 years, with mild or moderate hypertension treated with acupuncture demonstrated a reduction of 5.4 and 3.0 mmHg in systolic and diastolic blood pressure, respectively, without side effects.26

Based on those studies, it seems that the probable mechanisms of EA and MO would be their effects on humoral adjustment and neurogenic factors, especially in the SNS, that contribute for the regulation of the BP. Thus, those procedures could exert their actions by reducing the sympathetic activity and, consequently, the cardiac output and systemic peripheral resistance. It is known that sympathetic hyperactivity is an early event after renal injury of different etiologies and it can contribute for PRD.27

Experimental renal injury can lead to sympathetic hyperactivity associated with the activation of the afferent renal nerve and hypertension. The efferent activity of the ARSN increases renin secretion through the stimulation of β1 adrenergic receptors juxtaglomerular cells, increases the reabsorption of sodium and water in the proximal tube by activating α1 adrenergic receptors in tubular epithelial cells, and decreases the glomerular filtration rate and renal plasmatic flow (RPF) by activating α1 adrenergic receptors in renal arterioles, which increases vascular contractility.28 The reduction in FPR increases the discharge of the afferent renal nerve. Experimental studies in animals after 5/6 nephrectomy showed an increase in renal sympathetic activity through the increase in the production of plasma norepinephrine and local release of noradrenalin (spillover). Therefore, the information of damaged kidneys is delivered to the central nervous system (CNS) by afferent renal nerves, leading to an increase in sympathetic tonus, promoting the secretion of renin, with an increase in sodium reabsorption and expansion of the intravascular volume, which collaborates for the increase in glomerular pressure and proteinuria that can culminate in glomerulosclerosis and tubular-interstitial damage.29

The hyperactivity of the sympathetic nervous system (SNS) was demonstrated in studies with hypertension and non-dialytic acute renal failure by recording peripheral sympathetic activity with microneurography and elevated plasma norepinephrine levels. A reduction of the sympathetic activity can help the treatment of hypertension and PRD. Campese et al. (1995) demonstrated that rhizotomy in the remaining kidney delays PRD, which has been proved by serum creatinine levels, mean arterial pressure, and histopathological analysis.33

Since the 1990s, investigators are interested in explaining the possible mechanisms of SNS modulation by EA and MO. In 1999, Chao et al. suggested that the inhibitory effects of EA on reflex sympathetic cardiovascular responses was secondary to the activation of opioid receptors in RLVM and that this effect could be reverted by intravenous microinjections of naloxone in RLVM. Longhurst et al. (2000) demonstrated, in an animal model of coronary artery disease, that EA improves the
response of the BP and reduces myocardial ischemia by activating opioid receptors in RLVM and reducing sympathetic stimulation." Li et al. (2001) studied the effects of EA on AP PC-5 and PC-6 points in cats and demonstrated that modulation of the cardiovascular response involves the activation of µ and δ receptors by β-endorphin and enkephalins in RLVM. Later, the same group demonstrated that the inhibitory effects of EA in RLVM are related with the activation of neurons in the central lateral region of PAQ in cats, resulting in a reduction in cardiovascular sympathetic responses.

As mentioned before, the anti-inflammatory effects of acupuncture are among its main indications. In models of inflammation of the gastric mucosa induced by indomethacin, both EA and MO were beneficial in preventing and treating the lesions. In another model that evaluated the effects of MO on AP B-23 (Shenshu) in rats with arthritis, the results indicated the presence of direct inflammatory effects and reduction of the edema by intensifying the immunologic response.

**ACUPUNCTURE AND THE PROGRESSION OF RENAL DISEASE**

Stimulated by the abundant scientific information on EA and MO, whose therapeutic effects can interfere with some of the physiopathological mechanisms that contribute for the deterioration of the renal function and the lack of studies on their use in renal disease, we decided to undertake this study on the association of EA and MO on PRD in the rat model of progressive renal disease, and evaluate, through biochemical, functional, and structural parameters, the effects of the association of EA on AP E-36 (Zunanzli) and R-3 (Taixi) and MO on AP B-23 (Shenshu) on renal function.

We observed that animals treated with EA and MO had lower mean arterial pressure, significantly lower proteinuria, and a reduction in the activity of the renal sympathetic nerve. Besides, their capacity to concentrate urine was higher, with a significant reduction in urine output. The improvement in all those parameters was reflected on the normalization of serum creatinine levels. The animals treated also showed significant histopathological improvement, with lower glomerular index and better tubulointerstitial preservation. Consequently, we can state that EA and MO had an unquestionable beneficial effect on the progression of renal disease in the experimental 5/6 nephrectomy model by interfering with several factors capable of influencing the natural course of progressive renal disease. Therefore, as stated above, we can assume that those effects were due to the modulating actions of EA on the different pathophysiological mechanisms responsible for the progression of renal disease, such as inflammation, sympathetic hyperactivity, and hypertension.

We conclude that the concepts of TCM and, more precisely, the use of acupuncture and moxibustion, have a high potential in the management of renal disorders. Evidently, more studies are required to increase our understanding of the mechanisms responsible for this positive effect of acupuncture and moxibustion, and to integrate those techniques with the classical treatment of patients with ESRD. We will, then, have another tool in our therapeutic armamentarium to fight this destructive process, by interrupting and/or reversing its unstoppable progression to complete loss of renal function.

**REFERENCES**