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Research Progress on the Clinical Efficacy and Mechanism of Acupuncture in the Treatment of Essential Hypertension

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Abstract: ***Essential hypertension is a prevalent cardiovascular disorder that poses a significant threat to human health. In recent years, along with the advancements in medical technologies, acupuncture has emerged as a highly regarded therapeutic approach. Its merits lie in the ability to precisely identify the disease condition while circumventing any potential side effects. This paper comprehensively reviews the recent research progress on the clinical efficacy and underlying mechanisms of acupuncture in treating essential hypertension. Particular emphasis is placed on exploring the impacts and mechanisms of different acupoint selection principles, as well as diverse acupuncture angles and depths on hypertension. The intention is to offer a reference for the clinical application of acupuncture in the treatment of essential hypertension.***

Keywords: Acupuncture, Primary Hypertension, Clinical Efficacy, Mechanism, Selection of Acupoints Principles, Needle Insertion Angle, Needle Insertion Depth**.**

1. Introduction

Primary hypertension is a cardiovascular syndrome characterized by elevated arterial pressure in the systemic circulation. It is a significant risk factor for cardiovascular and cerebrovascular diseases. The prevalence of hypertension in China has been increasing year by year, with a total number of 245 million cases and an incidence rate of 23.2% [1]. Compared with the five national-scale hypertension sampling surveys conducted in 1958-1959, 1979-1980, 1991, 2002, and 2012-2015, although the total number of participants, age distribution, and diagnostic criteria in each survey were not completely consistent, the overall prevalence rate has shown an increasing trend. As a traditional Chinese medicine therapy, acupuncture has the effects of dredging meridians, regulating blood and Qi, and balancing yin and Yang, and has unique advantages in the treatment of essential hypertension.

2. Clinical Efficacy

Hypertension belongs to the category of "vertigo" and "headache" in traditional Chinese medicine, which mainly involves the heart, liver, kidney and other organs. Therefore, the acupoints of liver, bladder, heart meridian and Governor Vessel with the effects of calming liver, suppressing yang, stabilizing palpitation and stopping dizziness are mainly selected for acupuncture treatment of hypertension in clinic. A large number of clinical studies have shown that acupuncture in the treatment of essential hypertension has significant antihypertensive effect, and can improve the clinical symptoms and quality of life of patients. For instance, the liver meridian is closely linked to regulating emotional well-being and blood flow, while the bladder meridian is involved in balancing the body's vital energy (qi) and eliminating excess heat. The heart meridian addresses issues related to the cardiovascular system, and the Governor Vessel serves as a central channel that connects and harmonizes the functions of various organs. By stimulating these acupoints, acupuncture aims to restore the body's natural equilibrium and address the underlying causes of hypertension.

2.1 Acupoint Selection

2.1.1 Selection of single acupoint and combined acupoint

From the perspective of traditional Chinese medicine, acupuncture treatment of hypertension is through the regulation of the balance of yin and Yang of the human body, in order to achieve the effect of eliminating evil and strengthening the body. Studies have shown that a single acupuncture at Renying (ST9), Taichong (LR3), Quchi (LI11) and Fengchi (GB20) acupoints can have a good antihypertensive effect [2-4]. Literature data mining found that most acupoints selected for acupuncture treatment of hypertension were specific acupoints, and Taichong (LR3), Quchi (LI11), Fengchi (GB20) and Zusanli (ST36) were the most frequently used acupoints [5,6]. The team of Ji Lai-xi selected Renying (ST9), Quchi (LI11) and Zusanli (ST36) to form the acupoint "hypotensive formula". Spontaneous hypertensive rats were selected as the experimental objects, and acupuncture intervention was given to explore the mechanism of acupuncture hypotensive and the protective effect on target organs. The results showed that acupuncture acupoint "hypotensive formula" had a positive hypotensive effect, and could partially reverse renal damage, improve the process of myocardial hypertrophy, improve the ability of myocardial anti oxidative stress, and delay vascular remodeling [7-10]. Academician Shi Xue-min proposed the treatment principle of "activating blood circulation and dispersing wind, harmonizing liver and spleen". Renying (ST9) acupoint is the main acupoint, and Hegu (LI4), Taichong (LR3), Zusanli (ST36), Quchi (LI11) and other acupoints are combined with acupuncture to treat patients with primary hypertension. The curative effect is remarkable [11].

2.1.2 Acupoint selection based on syndrome differentiation

According to the principle of syndrome differentiation and treatment of traditional Chinese medicine, the corresponding acupoints were selected for the treatment of hypertensive patients with different syndrome types. For example, Taichong (LR3), Xingjian (LR2), Quchi (LI11) and other acupoints can be selected for patients with liver yang hyperactivity type hypertension. For hypertension with hyperactivity of liver Yang (accounting for 42.6% of primary hypertension), the combination of Fengchi (GB20) (purging wind and clearing heat) and Taichong (LR3) (calming liver and suppressing yang) was selected [12]. Patients with deficiency of both qi and blood use the combination of tonifying acupoints, Zusanli (ST36) (invigorating the spleen and Qi) and Guanyuan (RN4) (strengthening the foundation). Meta-analysis showed that the scheme could improve cardiac output and reduce peripheral resistance, achieving hemodynamic optimization [13]. Fenglong (ST40), yinlingquan (SP9), Zusanli (ST36) and other acupoints can be selected for patients with phlegm dampness type hypertension. Fenglong (ST40) could significantly reduce the insulin resistance index (HOMA-IR from 3.2 ± 1.1 to 2.1 ± 0.8), and the average systolic blood pressure decreased by 14.3 mmHg. The mechanism may be related to the regulation of adiponectin / leptin ratio [14].

2.1.3 Acupoint selection by time rhythm

Selecting acupoints according to the time, such as taking the bladder meridian Shugu (BL65) acupoint at Shenshi, can improve the antihypertensive effect by 19.4%. A randomized controlled trial of 120 patients showed that the 24-hour blood pressure compliance rate in the time acupuncture group (72.5%) was significantly higher than that in the conventional acupuncture group (53.3%) [15]. The mechanism may be related to the regulation of cortisol circadian rhythm. Cortisol decreased from 19.8 ± 3.2 μ g/dl to 15.1 ± 2.7 μ g/dl at 8am in the time group ($p<0.05$) [16]. Selecting specific acupoints when the moon changes, such as Sanyinjiao (SP6) in the new moon period, can enhance the curative effect of female menopausal hypertensive patients. The study showed that the program reduced the frequency of hot flushes by 58%, and the reduction of systolic blood pressure at night increased by 6.2 mmHg compared with the control group [17].

2.2 Different Acupuncture Angles and Depths

2.2.1 Angle

The study of sphenopalatine ganglion puncture showed that the target nerve plexus could be precisely stimulated when the needle was punctured from Xiaguan (ST7) at an angle of 45 ° back and up to a depth of 47.2 ± 3.1 mm, while the vertical needle needed to reach 52.4 ± 4.2mm to achieve equivalent stimulation [18]. This suggests that angle optimization can reduce invasiveness and improve treatment safety. The study comparing vertical needling (90°) and flat needling (15°) Sanyinjiao (SP6) found that the probability of Qi sensation (acid swelling conduction) caused by vertical needling was 78%, while that of flat needling was only 32% [19].

2.2.2 Depth

The choice of acupuncture depth should be based on anatomical research and individual differences. MRI study on Weizhong (BL40) showed that the safe depth increased by 0.53 mm for every 1 kg/m^2 increase in BMI, and the average depth of men was 2.13 mm deeper than that of women [20]. For example, the vertical needle depth of individuals with BMI 24 kg/m ² in BL40 should be controlled at 34.3 ± 6.1 mm, and the angle should be 64.8 ± 6.2° 20. Similarly, the safe depth of Jianjing (GB21) was positively correlated with shoulder width ($r=0.57$), suggesting that the depth should be adjusted according to the body shape in clinic [21].

Deep needling, such as reaching the myofascial layer, can activate a δ and C nerve fibers and inhibit sympathetic nerve activity through the spinal cord medulla pathway. Animal experiments showed that electro acupuncture at the deep part of Zusanli (ST36) could reduce the systolic blood pressure of spontaneously hypertensive rats (SHR) by 18 ± 3 mmHg, while superficial stimulation only reduced the systolic blood pressure by 7 ± 2 mmHg [22]. This may be related to the more effective activation of γ - aminobutyric acid neurons in the rostral ventrolateral medulla (RVLM) by deep needling [23].

Ultrasound study showed that when the depth of acupuncture at the knee joint acupoints reached 15-30 mm, the synovial blood flow velocity increased by 40%, and the local inflammatory factors (IL-6, tnf- α) levels decreased more significantly [24]. Similar mechanisms may act on hypertension related acupoints (such as Taichong (LR3) to reduce peripheral vascular resistance by improving microcirculation.

3. Mechanism of Action

The mechanism of acupuncture in the treatment of essential hypertension has not been fully clarified, but the current study shows that acupuncture may exert antihypertensive effect through the following mechanisms.

3.1 Neuroendocrine Regulations

Over activation of sympathetic nerve is one of the important pathological mechanisms of hypertension. Acupuncture can reduce blood pressure by regulating the activity of sympathetic nervous system [25,26]. Studies have shown that electro acupuncture stimulation of specific acupoints such as Renying (ST9) can significantly reduce blood pressure, and its mechanism includes: directly reducing the level of sympathetic neurotransmitters (reducing the concentration of plasma epinephrine and norepinephrine) [27], regulating renal sympathetic nerve activity, and downregulating the expression of vascular β - adrenoceptor to improve vascular tone [14,28]. In addition, acupuncture at p5-6 (Jianshi Neiguan) and s36-37 (Zusanli Shangjuxu) can activate afferent nerve fibers and inhibit sympathetic hyperexcitability. Low frequency electro acupuncture (2Hz) can promote the release of endogenous opioid peptides (encephalin, β - endorphin) and mediate the central sympathetic inhibitory effect via μ opioid receptors [29,30]. It is worth noting that the regulatory effect of acupuncture on the hypothalamus pituitary adrenal axis (HPA axis) can reduce the plasma cortisol concentration, further alleviate the sympathetic activation state by reducing the release of stress hormones,

and form a neuroendocrine synergistic antihypertensive network [31].

3.2 Improve Vascular Endothelial Function

Acupuncture can improve vascular endothelial function by regulating the expression and release of endothelial active factors. Studies have found that acupuncture can significantly increase the bioavailability of nitric oxide (no) and reduce the production of endothelin-1 (ET-1). No is an important vasodilator produced by endothelial cells. No is produced under the induction of eNOS, which has the functions of relaxing blood vessels and anti-atherosclerosis, reducing peripheral vascular resistance, and preventing the further development of hypertension [32], While ET-1 has strong vasoconstrictive effect. Therefore, the imbalance of et/no system is an important factor leading to the occurrence of hypertension. Acupuncture can restore the balance of vascular endothelial function by regulating this system, so as to reduce blood pressure [33]. Some studies have shown that acupuncture in the treatment of patients with subarachnoid hemorrhage can effectively reduce the level of ET-1 and increase the level of no, so as to restore endothelial function [34]. Some studies have shown that electro acupuncture stimulation of Wistar rats can effectively regulate the levels of ET-1 and eNOS, thereby alleviating the occurrence of pulmonary hypertension [35].

A study showed that Baihui (DU20) Point penetration acupuncture combined with western medicine treatment can significantly increase the level of no, reduce the levels of ET-1, von Willebrand factor, P-selectin, so as to control blood pressure, reduce blood pressure variability, and improve vascular endothelial function [36]. Another study showed that Baihui (DU20) Point penetration acupuncture can improve the levels of heat shock protein and oxytocin in patients with hypertensive intracerebral hemorrhage after minimally invasive surgery, thereby reducing endothelial cell damage and alleviating the clinical symptoms of patients [37]. Some studies have found that electro acupuncture at Zusanli (ST36) in hypertensive rats can increase the content of peripheral serum NO and exert the antihypertensive effect [38].

3.3 Inhibit Inflammatory Response

3.3.1 Regulation of acupuncture on inflammatory signaling pathways

Acupuncture plays an anti-inflammatory role by regulating a variety of inflammatory signaling pathways, thereby improving hypertension symptoms. Studies have shown that acupuncture can inhibit the activation of nuclear factor kappa B (nf- κ b) signaling pathway and reduce the release of pro-inflammatory cytokines (such as tnf- α, IL-1 β and IL-6) [26,39,40]. These pro-inflammatory cytokines play an important role in the pathogenesis of hypertension. For example, tnf- α can activate the nuclear factor - κ B (nf- κ b) signaling pathway, leading to vascular endothelial cell dysfunction and vasoconstriction, thereby increasing hypertension [27,28,41,42]. In addition, acupuncture can further alleviate the inflammatory response by activating JAK-STAT signaling pathway, promoting the expression of anti-inflammatory factors [39].

3.3.2 Regulation of acupuncture on oxidative stress

Patients with hypertension are often accompanied by elevated levels of oxidative stress. Acupuncture can increase the expression of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPX) by activating the nuclear factor E2 related factor 2 (Nrf2) signaling pathway, thereby reducing the generation of reactive oxygen species (ROS) [29,43]. This mechanism not only helps to reduce blood pressure, but also reduces hypertension related cardiovascular complications [44].

3.4 Regulation of Renin Angiotensin Aldosterone System (RAAS)

As an important part of the renin angiotensin aldosterone system, Ang II participates in the endothelial injury of hypertension caused by arteriosclerosis. It binds to Ang II receptor 1 on endothelial cells and produces vasoconstrictors such as ROS and ET-1 under the induction of nadh/nadph oxidase. A study showed that electro acupuncture stimulation of Wister rats can partially inhibit the expression of Ang II receptor 1, relieve cerebral vasoconstriction and improve blood flow supply [45]. Relevant studies have shown that acupuncture in spontaneously hypertensive rats can reduce the levels of Ang II and ROS in rats, inhibit the activity of NADH oxidase, promote the expression of eNOS, and alleviate endothelial injury [46].

4. Conclusion

Numerous clinical studies have demonstrated that acupuncture is an effective complementary therapy for essential hypertension. It not only exhibits a significant antihypertensive effect but also improves the clinical symptoms experienced by patients, such as headaches, dizziness, and palpitations. Furthermore, acupuncture has been shown to enhance the overall quality of life for individuals suffering from hypertension. This holistic approach to treatment aligns with the principles of TCM, which emphasize treating the root cause of the disease rather than merely alleviating its symptoms. As a result, acupuncture offers a promising alternative or adjunctive therapy for managing hypertension, particularly when combined with conventional Western medical treatments.

Acupuncture has significant clinical efficacy in the treatment of essential hypertension, and its mechanism of action involves many aspects. In the future, we need to further carry out high-quality clinical research to explore the mechanism of acupuncture in the treatment of essential hypertension, and provide more reliable evidence for the clinical application of acupuncture in the treatment of essential hypertension.

Acupuncture exerts its antihypertensive effect through multiple ways. The mechanisms include neuroendocrine regulation, improvement of vascular endothelial function, inhibition of inflammatory response, and regulation of renin angiotensin aldosterone system. These effects work together, which can not only effectively reduce blood pressure, but also reduce hypertension related cardiovascular complications. Future research can further explore the specific molecular mechanism of acupuncture in the treatment of hypertension,

as well as its optimization strategy in clinical application. Investigate the intricate interactions among these mechanisms, shedding light on how they synergistically contribute to acupuncture's therapeutic outcomes. By understanding these interactions, researchers may be able to identify key targets for enhancing the efficacy of acupuncture treatments.

Moreover, studies could explore the potential of combining acupuncture with other therapeutic modalities, such as medication or lifestyle changes, to achieve even better blood pressure control and reduce the risk of cardiovascular events. The integration of acupuncture into multidisciplinary treatment plans may offer a holistic approach to managing hypertension, addressing both the physiological and psychological aspects of the condition.

Additionally, future research should focus on identifying patient subpopulations that are most likely to benefit from acupuncture therapy. This could involve studying genetic markers, comorbidities, or specific hypertension phenotypes that respond favorably to acupuncture. By tailoring acupuncture treatments to these subpopulations, healthcare providers can ensure that patients receive the most effective and personalized care possible.

In conclusion, while acupuncture has already demonstrated its value in treating essential hypertension, there is still much to learn about its underlying mechanisms and optimal clinical application. Ongoing research efforts are crucial for advancing our understanding of this ancient therapy and harnessing its full potential to improve patient outcomes.

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