



Research Progress in the Treatment of Lumbar Intervertebral Disc Herniation Based on the Theory of "the Liver Is in Charge of Tendons and the Kidney Is in Charge of Bones"

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Abstract: "Liver is the master of tendon and kidney is the master of bone" is an important theoretical source for the treatment of lumbar disc herniation (LDH) in traditional Chinese medicine (TCM). Most of the patients with LDH are in liver and kidney deficiency, and the treatment of LDH is often based on traditional Chinese medicines that tonify the liver and kidneys. With the development of modern medicine, some progress has been made in recent years on the pathogenesis, diagnostic imaging and therapeutic mechanism of LDH based on the theory of "the liver is in charge of the tendons and the kidney is in charge of the bones", and this article will briefly review these aspects to provide a reference for the better utilization of this theory in the treatment of LDH.

Keywords: lumbar disc herniation; liver masters tendons; kidney masters bones; tonifying liver and kidney

1. Introduction

Lumbar Disc Herniation (LDH), also known as lumbar disc fibrous annulus rupture nucleus pulposus herniation, which is characterized by lumbar pain and lower extremity sciatic nerve radicular pain due to the degeneration of lumbar intervertebral discs, which ruptures the fibrous annulus and protrudes the nucleus pulposus under the action of external force and irritates or compresses the nerve root[1]. The pathological basis of LDH is degenerative changes in intervertebral discs, and cumulative injury is the main cause of degeneration and also the main reason for herniation. The pathology of LDH is based on degenerative changes of the intervertebral disc, and cumulative injury is the main cause of disc degeneration, as well as the main cause of disc herniation. The incidence rate of LDH is in the range of 2-3%, and with the rapid development of the society and changes in lifestyle, its incidence rate is on the rise year by year [2-3]. Traditional Chinese medicine (TCM) classifies LDH as "lumbago", and "paralysis", and believes that the occurrence of this disease is closely related to the liver and kidneys. At the same time, Chinese medicine stresses that "prolonged illness is often associated with deficiency", and LDH, as a chronic disease with a long course, puts the body in a state of deficiency of the liver and kidney, so the treatment of LDH is mostly based on tonifying the liver and kidney as the root. The development of modern medical technology has deepened the understanding of the etiology of LDH, and also provided scientific evidence of Chinese medicine theory for the effective treatment of LDH through the principle of the theory.

2. The theoretical origin of the theory

The theory of Zang Xiang in Chinese medicine is an important part of the basic theory of Chinese medicine, "Suwen" says: the five viscera: "the heart is the main vein, the lung is the main skin, the liver is the main tendon, the spleen is the main flesh, the kidney is the main bone." This explains the correspondence between the five viscera and the body's organs. The intervertebral disc belongs to the category of "tendon" in traditional Chinese medicine, liver is the master of the tendon, kidney is the master of the bone, so the treatment of LDH should focus on the lesions of the liver and kidney organs.

2.1 The liver is the master of tendons and LDH

There are two theoretical connotations of the Chinese medicine theory of "the liver is the master of the tendons". First, the tendons of the body depend on the moistening of the blood of the liver, "Su Wen" says: "The liver, the base of the strike pole, the soul's residence, its Hua in the claw, its full in the tendons to produce blood and gas...", explaining the growth of the tendons depends on the liver and blood moistening, only the liver and blood sufficient tendons can be fully moistened.

Secondly, the liver's qi and blood sufficiency or not affects the human body's Joint movement, tendon function is the basis of all joint flexion and extension movement, and the liver and tendon function is closely related. "Su Wen" said: "Human's movement, are all the tendon force is also, the liver is the main tendon...", here elaborating on the "liver - tendon - exercise. This explains the synergistic relationship of "liver - tendon - movement" [4]. Liver's blood storage and excretion failure, often cause systemic fascial lesions, so the lesions of tendons are closely related to liver injury.

2.2 Kidney masters bone and LDH

Kidney is the foundation of the innate nature, the root of life, the main division of human growth and development. In Chinese medicine, the kidney plays a decisive role in the overall growth and development of human beings, especially in influencing the development of bones. "Su Wen" Images: "Kidney, the main sting, the sealing of the base, the essence of the place; its Hua in the hair, its full in the bone," that is, the kidneys are the base of the sealing of the essence, the tissues in the bone of its full of nutrients."Su Wen" said "thus strong, kidney gas is injured, high bone is bad", "high bone" is the lumbar vertebrae, clearly pointed out that kidney deficiency leads to lumbar spondylosis reason[5].

2.3 Liver and kidney homology and LDH

In addition to the main tendons and bones of the liver and kidney, they are also interdependent and co-ordinate the movement of the whole body. According to the association of the five organs, five elements and the heavenly stems and earthly branches, the liver belongs to "ethyl wood" and the kidney belongs to "deca water", so "liver and kidney homology" is also known as "ethyl and deca homology"[6]. "Sheng Ji Zong Lu" recorded: "the kidney main waist, the liver main tendon, tendon gathered in the knee. If the kidneys are deficient and the liver is injured and tired, the tendons and bones will be affected by the disease, so the waist and knees are unfavourable", which specifically explains the association between the liver and kidney organs and LDH. Under the guidance of the theory of "the liver and the kidney have the same origin", "the liver and the kidney have the same treatment" is the treatment of LDH and other degenerative lesions of sinews and bones.

3. Modern research on the theory and LDH

Broadly speaking, tendon includes skin, subcutaneous tissue, fascia, muscle, tendon, ligament, joint capsule, synovial fluid sac, articular cartilage discs, intervertebral discs, tendon sheaths and other soft tissues[1]. LDH belongs to the category of Chinese medicine tendon injuries and diseases, and the masters of the tendons and bones are the liver and kidney, the blood storage of the liver is the physiological basis of the liver's mastery of the tendons, and the liver mastery of the tendons is the functional basis of the human body's growth and activity [7]. "Za Bing Yuan Liu Xi Zhuo" records, "lumbago, essence and gas deficiency and evil guest disease also... kidney deficiency of its own...", that the essence of lumbago lies in the kidney deficiency, lumbago of the standard lies in the wind, cold, dampness, heat and phlegm, The main cause of LDH is the kidney deficiency. Therefore, the etiology of LDH mainly includes internal and external aspects, the internal cause lies in the "deficiency of the liver and kidney", and the external cause mainly refers to a variety of acute and chronic injuries and wind, cold and dampness invasion.

3.1 The pathogenesis of LDH is closely related to the principle of the theory

The spine is the central axis of the body, supporting the weight of the head, trunk and upper limbs, slowing down oscillations, maintaining the balance of the trunk, and protecting the spinal cord and nerves [8]. As stated in "Zhu Bing Yuan Hou Lun", "the kidney is the master of the waist and feet, the kidney essence is deficient, the wind and cold multiply, so the lumbar pain", it is believed that LDH is caused by deficiency of the liver and kidney of the patient, and the wind, cold, and dampness take advantage of the deficiency to enter the patient, which leads to damage of the tendons and veins and the stagnation of the qi and blood and thus results in the occurrence of the pain symptom.

Modern medical research has shown that the pain of LDH patients is also related to the state of autoimmunity and inflammation [8]. There is no direct correlation between the symptomatic severity and the degree of compression, but the local inflammation of intervertebral discs and neurological disorders due to autoimmunity caused by the nucleus pulposus. Inflammation causes pathological damage to the structure and function of the intervertebral disc and neural tissue[9]. It has been found that herniated intervertebral disc tissues exhibit a large number of inflammatory cellular responses, producing a variety of inflammatory analgesic substances including phospholipase A2, prostaglandins (PG), interleukin (IL) 1, IL-6, matrix metalloproteinases (MMPs), nitric oxide (NO), and tumour necrosis factor alpha (TNF- α), etc., which act on nerve fibres in the vicinity of the disc, leading to receptors that provoke pain [10-12]. In addition, IL-1 itself has a direct effect on increasing sensitivity to pain [13]; and IL-6 promotes intervertebral disc autoimmune responses by regulating the function of immune cells [14].

3.2 Imaging link between the theory and LDH

Imaging examinations such as CT and MRI have high diagnostic value in the diagnosis of LDH, and these two imaging methods are commonly used in the clinic to determine lumbar disc herniation and lumbar disc free [15]. A number of studies have shown that LDH Chinese medicine typing is closely related to imaging manifestations. LDH patients with deficiency of the liver and kidney have more herniated lumbar vertebrae in the posterior segment, and the number of patients with this type of LDH with severe small joint degeneration, lateral recess stenosis, spinal stenosis, and Schmidt's nodule on MRI is higher than that of patients with other types [16-17]. Wang Enjia et al [18] found that intervertebral disc herniation was predominantly of the central type in patients with liver and kidney deficiency type LDH. By comparing and analysing the imaging data of intervertebral discs in group 211, Fang Junhua et al [19] found that intervertebral discs in patients with liver and kidney deficiency type were mostly bulging. These findings strongly suggest that there is a correlation between the imaging manifestations of LDH patients and "deficiency of the liver and kidney".

4. Progress of research on the treatment of LDH with Chinese medicines that tonify the liver and kidneys

The general idea of Chinese medicine in treating LDH is to tonify the liver and kidney. According to the "Zheng Zhi Zhun Sheng", "the treatment is only to tonify the kidney as the first step, and then follow the evil seen in order to administer the treatment; if the standard is urgent, then treat the standard, if the principal is urgent, then treat the principal; for the first pain, it is appropriate to remove the evil stagnation and regulate the meridian tunnel; for the prolonged pain, it is appropriate to replenish the true essence and nourish the qi and blood." For LDH chronic stage or long duration of the disease, the body is mostly weak, the treatment is appropriate to tonify the liver and kidney, promote paralysis and activate collaterals [1]. Modern pharmacological studies have shown that the mechanism of action of classical formulae on LDH mainly includes regulating immunity to reduce inflammatory response and effective analgesia.

4.1 Du Huo Ji Sheng Tang

Studies have shown that Duiyu parasitic soup has the effect of improving microcirculation at the site of lumbar disc herniation and eliminating congestion, oedema, and adhesion of nerve root tissues [20]. Cheng Wei et al [21] found that the efficacy of the formula in treating LDH with deficiency of liver and kidney was remarkable, and its mechanism of action might be related to improving the body's immunity to inhibit the production of inflammatory cytokines. The key role of the transcription factor NF- κ B in the regulation of inflammation has been well established [22-24]. The NF- κ B pathway mainly promotes the release of inflammatory factors, which are often activated in the inflammatory response and aggravate the chronic inflammatory damage of tissues [25]. Chlorogenic acid extracted from Cortex Eucommiae is able to achieve inhibition of inflammatory responses by suppressing the NF- κ B signalling pathway [22]. The A20 protein encoded by the TNF- α inducible protein 3 gene affects the development and function of dendritic cells, B cells, T cells and macrophages by regulating the NF- κ B pathway and thus the development and function of dendritic cells, B cells, T cells and macrophages [24]. Xie et al [26] demonstrated that the p65 protein in the NF- κ B pathway could promote adjuvant-induced inflammation and upregulation of A20 protein expression in nociceptive rats. The neuronal pain and inflammation in DH rats could be alleviated by up-regulating the expression of A20 protein, which may be one of the mechanisms of LDH treatment by Dokuto Parasite Soup.

4.2 Bu Gan Jian Yao Fang

After Tan Xuyi et al [27] intervened LDH model rats with this formula, the IL-1 expression level and neurological function score of the model rats decreased compared with the pre-intervention level, which proved that the formula had the effect of reducing the level of inflammatory factors in the degenerated intervertebral discs and improving the neurological function score. Tan Xuyi et al [28] further confirmed that this formula can effectively regulate the NF- κ B signalling pathway, which in turn exerts anti-inflammatory, analgesic and immune-regulating effects. Qiu Xiangzhong et al [29-31] found that the formula was able to reduce the expression of TNF- α , IL-1 β , and IL-6, the downstream products of NF- κ B signalling pathway in the intervertebral discs of rats in the lumbar disc degeneration model. In addition, Zheng Yang [32] also found that the formula has a key regulatory effect on proteoglycan, another important component of the extracellular matrix of the nucleus pulposus. When the loss of proteoglycan occurs in the intervertebral disc, the internal osmotic pressure homeostasis is affected, which triggers the dehydration and degeneration of the intervertebral disc, whereas the formula can promote the transcription of the mRNA of proteoglycan proteins, and then up-regulate the expression of proteoglycan proteins and alleviate symptoms such as pain and other symptoms induced by the degeneration of intervertebral disc. Pain and other symptoms caused by intervertebral disc degeneration.

4.3 Du Zhong Yao Tong Wan

Fang Pengfei et al [33] effectively reduced the local inflammatory reaction of lumbar intervertebral discs in patients with Du Zhong Yao Tong Wan, and further studies showed that the formula could inhibit the abnormal activation of the NF- κ B signalling pathway, up-regulate the level of IL-10, and down-regulate the expression of factors such as IL-1, TNF- α , P50, P65, I κ Ba, etc. to reduce abnormal inflammatory immune response, thus alleviating the pain of the low back, and improving the patients' quality of life [34]. Chen Qiqing et al [35] found that this formula effectively alleviated the pain symptoms in a rat model of LDH chronic lower limb pain by observing and recording the thresholds of mechanical foot-contraction reflex and latency threshold of thermal foot-contraction reflex in a rat model of LDH chronic lower limb pain, and found that the main active ingredients contained in the formula were quercetin, lignocerosol, and glycyrrhizic acid chalcone A through the predictive pharmacological analyses of the network of this formula in the treatment of LDH. The main active ingredients and their possible mechanisms for the treatment of LDH in this formula are as follows: (1) Quercetin inhibits nociception in mice in a dose-dependent manner, and its analgesic mechanism is related to the inhibition of oxidative stress and the reduction of the production of inflammatory factors such as TNF- α , IL-1 β , IL-6, IL-10, and the inflammatory mediator COX-2 [36]. production [36-37]; quercetin can also effectively inhibit fibrillary acidic protein in model rat glial cells to reduce their neuropathic pain [38]. (2) Lignans can hinder the activation of glial cells and NLRP3 inflammatory vesicles by regulating p38 MAPK activity in the dorsal horn of the spinal cord, thus inhibiting neuroinflammation and achieving analgesia [39]. (3) Licorice chalcone A can inhibit a variety of pro-inflammatory mediators, and can also significantly inhibit the release and proliferation of IL-2 in T-lymphocytes, which has a better anti-inflammatory and analgesic effect clinically [40]. (4) Panax ginseng saponin is an opioid peptide-like receptor stimulant, which exerts a neuroleptic effect on thermal irritability and chemical-induced pain by agonizing opioid peptide receptors [41]; Panax ginseng saponin can down-regulate the expression of relevant proteins, such as IL-1 β and IL-6, and inhibit the NF- κ B signalling pathway, thus reducing the state of inflammation and inhibiting inflammatory oedema [42]. (5) Ginsenosides act on COX-2, prostaglandin E synthase and other proteins to inhibit PG synthesis and exert anti-inflammatory and analgesic effects [42]. (6) Cortex Eucommiae polysaccharides can delay the activation of astrocytes in the dorsal horn of the spinal cord, thereby inhibiting the inflammatory signaling pathway and thus exerting analgesic effects [43].

4.4 Bu Shen Zhuang Jin Tang

Bu Shen Zhuang Jin Tang (Radix Rehmanniae Praeparata, Cornus Officinalis, Radix Pseudostellariae, Radix Paeoniae Alba, Radix et Rhizoma Chuanchuanensis, Cortex Eucommiae, Radix Angelicae Sinensis, Poria cocos, Fructus Wogastrodiae, and Radix Achyranthes bidentatae) from Shang Ke Bu Yao is a treatment of the late stage of injury, and is effective in treating the liver- and kidney-deficiency type LDH. Li Hui et al [44] demonstrated that the formula had significant efficacy in promoting the absorption of inflammatory mediators, dilating capillaries and reducing vascular permeability, and through these effects achieved the therapeutic goals of eliminating oedema, promoting nerve repair, relieving spasm, and preventing adhesions or degeneration. Qin Hongzhao et al [45] confirmed the significant therapeutic effect of the formula combined with acupuncture in treating patients with liver and kidney deficiency type of LDH through research. Quercetin can reduce the expression of COX-2, inducible nitric oxide synthase [46]. Kaempferol can activate the p38 MAPK signalling pathway and exert anti-inflammatory and neuroprotective effects. Cowslip polysaccharides have anti-inflammatory effects, can effectively inhibit the production of PGE2 and alleviate LDH-induced pain; they also produce immunomodulatory effects, which can strengthen the anti-inflammatory effect and play a synergistic role of anti-inflammatory and immune effects [47].

5. Conclusion

In the process of development of traditional Chinese medicine, the theory of the five viscera as the centre of the Zang Xiang through the meridians will be the whole body viscera, body organs and organs into a whole and constitute in the physiological function of the coordination of each other, material changes in the interconnection of each other, the pathological changes of each other's influence of the five major functional systems. It is not difficult to find out that the reasonable application of liver and kidney tonic Chinese medicines can relieve the symptoms of LDH such as low back pain and radiating pain of the lower limbs, etc. However, the author believes that we can continue to study the treatment of LDH with the theory in the following three aspects. Firstly, we should establish an animal model of liver and kidney deficiency in accordance with Chinese medicine theory, and investigate the mechanism of action of the classic formulae for the treatment of LDH. Secondly, the relevant cells can be cultured in vitro to study the effects of liver and kidney tonic Chinese medicines on cell proliferation, apoptosis, autophagy, senescence, and release of inflammation and other related factors, and reveal the Thirdly, the clinic should focus on the analysis of big data to summarise the pattern of different liver and kidney tonic drugs

in the treatment of LDH, to improve the clinical efficacy.

In conclusion, therapeutic efficacy of this kind of formula in the treatment of LDH is remarkable, and the modern pharmacological research has provided a scientific basis for the treatment of LDH by the therapy, the relevant research should be further strengthened and the Chinese medicine should give full play to its advantages. so as to achieve the advantage of "treating the disease must be based on the root cause".

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