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Original Article

Exploring the effect of the waist-rubbing method on immune balance in rats with lumbar disc herniation

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Abstract: Objective: To evaluate the therapeutic effect of the waist-rubbing method on lumbar disc herniation (LDH) and explore its immunoregulatory mechanisms. Methods: Forty Sprague-Dawley rats were randomly divided into three groups: control, model, and treatment groups. The control group did not undergo modeling, while LDH models were established in the other two groups. Behavioral tests were conducted on all rats at designated time points, and neurological function scores were compared among groups. After 15 days of corresponding interventions, peripheral blood samples were collected for flow cytometric analysis of T-cell subsets. Serum levels of corticosterone (CORT), glucocorticoid receptor α (GR_{α}), interferon-γ (IFN-γ), interleukin-4 (IL-4), IL-17, and transforming growth factor-β (TGF-β) were detected using enzyme-linked immunosorbent assay. Results: Compared with the control group, the model group showed significantly increased Th1/Th2 and Th17/Treg ratios, elevated serum levels of IFN-γ and IL-17, and decreased CORT, GR_{α}, IL-4 and TGF-β levels (all $P<0.05$). Compared with the model group, the treatment group exhibited significantly reduced ratios of IFN-γ+CD8+ T cells, IL-17+CD8+ T cells, FOXP3+CD4+ T cells and IL-4+CD4+ T cells, accompanied by increased serum CORT, GR_{α}, IL-4, and TGF-β levels and decreased IFN-γ and IL-17 levels ($P<0.05$). Conclusion: The waist-rubbing method may alleviate autoimmune disorders in LDH by enhancing hypothalamic-pituitary-adrenal (HPA) axis activity and restoring Th1/Th2 and Th17/Treg balance, providing mechanistic support for the traditional concept of "tonifying the kidney to relieve pain".

Keywords: Waist-rubbing method, lumbar disc herniation, immune balance, HPA axis, tonifying the kidney for relieving pain

Introduction

Lumbar disc herniation (LDH) is a common disease caused by degeneration of lumbar intervertebral disc and rupture of annulus fibrosus, resulting in protrusion of the nucleus pulposus which irritates and compresses the nerve root [1]. Clinically, it presents as low back and leg pain with restricted mobility. LDH affects individuals aged 20-50 years, with a higher prevalence in men, and its onset has shown a trend toward younger populations in recent years [2]. It ranks first among spinal canal diseases in incidence and carries significant morbidity [3]. Conservative therapy remains the mainstay of treatment of LDH, such as Tuina [4]. However, studies on the immune mechanisms underlying LDH remain limited and incomplete.

Therefore, this study employs a rat bipedal upright LDH model to investigate the therapeutic effects of the waist-rubbing method. By examining related cytokines, we aim to elucidate the immunological mechanisms of Tuina in LDH, as well as provide a scientific basis and novel insights for its clinical application.

Materials and methods

Experimental materials

Experimental animals: Forty adult Sprague-Dawley rats (both sexes, 250-310 g; license No. SCXK (Su) 2020-0009) were used in this study. The animals were maintained under specific pathogen-free (SPF) conditions with free access to standard chow and water. All experimental procedures were reviewed and approved by the Animal Ethics Committee of Nanjing University of Chinese Medicine.

Main experimental reagents: Flow cytometry detection kits and corresponding antibodies;

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enzyme-linked immunosorbent assay (ELISA) kits for cortisol (CORT), glucocorticoid receptor-α (GR_{α}), interferon-γ (IFN-γ), interleukin-4 (IL-4), IL-17, transforming growth factor-β (TGF-β); pentobarbital sodium; and disinfectant solution.

Main instruments and equipment: Flow cytometry, micro-CT scanner, constant-temperature incubator, fully automated microplate reader, and low-temperature high-speed centrifuge.

Groups and modeling

The rats (n=40) were randomly divided into three groups using a random number table: blank (n=10), model (n=15), and waist-rubbing groups (n=15). Except for the blank group, the remaining rats were subjected to a forelimb-free model according to previously described methods [5].

The modeling procedure was performed under aseptic conditions. The rats were anesthetized with an intraperitoneal injection of 2% pentobarbital sodium (0.5 ml/100 g). The forelimb hair was shaved, and the skin was disinfected with iodine solution. A longitudinal incision was made in the upper one-third region of both forelimbs. The skin, fascia, and muscle layers were sequentially separated to expose the vessels and nerves within the deltoid region. The brachial plexus nerve was transected using a scalpel, and the vessels were thoroughly ligated with silk thread. Next, the proximal humerus was resected using forceps, and the entire upper limb was detached with a scalpel. The surgical field was irrigated with physiological saline, and the incision was sutured in layers. Chloramphenicol eye ointment was applied to the wound to prevent postoperative infection. Postoperatively, the rats were housed individually and allowed to recover. One week later, food and water were placed on an elevated platform above the cages, forcing the rats to feed while standing upright on their hind limbs. This long-term postural stress induced continuous gravitational loading of the lumbar spine, leading to intervertebral disc herniation. The entire molding process lasted approximately 14 weeks.

Model identification and exclusion criteria: ① Rats exhibited lethargy and limping gait during movement. ② Micro-CT scanning of the lumbar spine revealed marginal osteophyte formation, thickening of the ligamentum flavum, and intervertebral disc herniation into the spinal canal.

Rats that met both criteria were considered successfully modeled. Those that did not meet the criteria were excluded. Among the 30 rats used for modeling, 26 successfully developed LDH, yielding a modeling success rate of 86.7%. Subsequently, 20 successfully modeled rats were randomly selected and divided into the model and treatment groups, with each group consisting of 10 rats.

Treatment plans

Treatment was initiated one week after successful modeling and continued for 15 consecutive days. The control group and model group received no specific treatment interventions. Rats in the waist-rubbing group received Tuina therapy performed on the lumbosacral region. After the rat was securely immobilized, the operator lightly pressed the index and middle fingers on the lumbosacral region while keeping the shoulder and wrist relaxed. Elbow joint flexion and extension movements were used to drive the index and middle fingers to perform uniform, linear, back-and-forth friction at a frequency of approximately 80 strokes per minute. Each waist-rubbing session was applied continuously for 1 minute per treatment.

Sample collection and index detection

Sample collection: Rats were anesthetized with 2% pentobarbital sodium, and blood samples were collected from the abdominal aorta for subsequent analyses. After blood collection, the rats were euthanized under deep anesthesia. The collected blood volume was sufficient to meet the requirements of all planned assays.

Behavioral assessment: Paw withdrawal latency (PWL; for pain sensitivity evaluation) and mechanical withdrawal thresholds (PWT; for sensory function recovery evaluation) were measured one day before surgery and on days 7, 14, 21 and 28 postoperatively.

Neurological function scoring: Neurological function of the right hind limb was evaluated according to the scoring system proposed by Siegal, with six graded levels: (1) grade 0 (2 points) - normal function; (2) grade 1 (4 points)

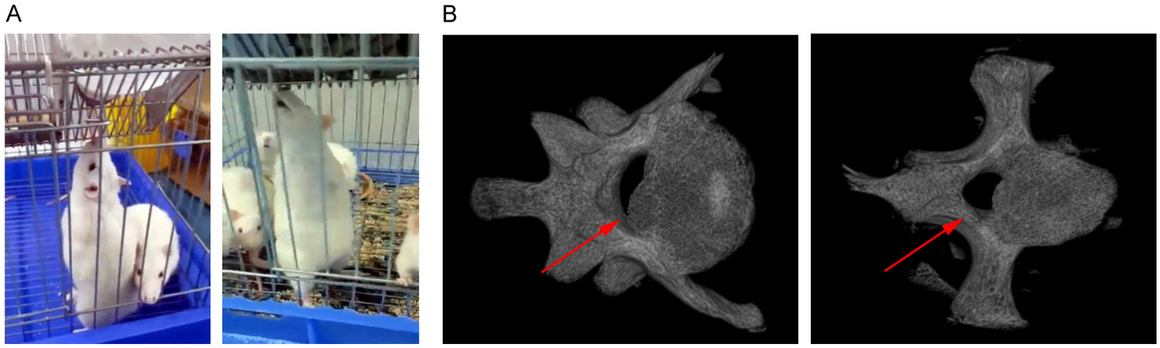

Figure 1. The upright feeding situation and CT image of model rats. A: Upright feeding; B: CT image of the lunar spine of the model rats (Red arrows indicate diseased region).

- hind-limb weakness with reduced tail-flick response; (3) grade 2 (6 points) - hind-limb paralysis with mild walking difficulty; (4) grade 3 (8 points) - hind-limb paralysis with evident gait instability; (5) grade 4 (10 points) - inability to stand stably but partial hind-limb movement retained; grade 5 (12 points) - complete paralysis with no voluntary hind-limb movement.

Index detection: Peripheral blood T-cell subsets were detected by flow cytometry. The total antibody volume was calculated according to the manufacturer's instructions, and antibodies were diluted 10-fold to prepare a staining mixture. A 100 μL aliquot of single-cell suspension was transferred into a 1.5 mL EP tube, blocked with 0.5 μL Fc Block for 5 minutes at 4°C in the dark, and then stained with CD4 antibody mixture for 30 min at room temperature.

Cells were fixed and permeabilized using BD Fix/Perm Buffer, washed twice with BD Perm/Wash Buffer, and stained intracellularly with IFN-γ, IL-17, Foxp3, and IL-4 antibodies for 30 min at room temperature. After a final wash, samples were resuspended in Stain Buffer for analysis. Flow cytometry gating was performed for single cells, followed by $CD4^+$ and $CD8^+$ subsets, and cytokine-positive populations. Data were analyzed using FlowJo software (version 7.6.1).

Serum levels of CORT, GR_α, IFN-γ, IL-4, IL-17 and TGF-β were detected using commercial ELISA kits, following the manufacturer's protocols. All assays were carried out strictly in accordance with the kit's instructions.

Statistical analysis

All statistical analyses were performed using SPSS version 24.0. Data were expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was conducted, followed by the least significant difference (LSD) post hoc test for pairwise comparisons. A two-tailed P value <0.05 was considered statistically significant. Imaging and morphological results were presented in graphical form for comparison.

Results

Establishment of the Forelimb-free rat model

Following forelimb resection, rats were housed in elevated cages, which forced rats to stand upright on their hind limbs to obtain food and water, with the purpose to induce lumbar disc herniation (**Figure 1A**). Micro-CT imaging revealed marginal osteophyte formation on the edges of lumbar vertebrae and posterior protrusion of intervertebral discs - some showing early ossification - into the intervertebral foramen (red arrow, **Figure 1B**), confirming successful establishment of the LDH model. All modeled rats showed varying degrees of lumbar disc herniation accompanied by claudication-like gait symptoms. No animals were lost during the experiment, and all samples were included in the final analysis.

Waist rubbing improved paw withdrawal latency and thresholds in LDH rats

Compared with the control group, the scores for PWT and PWL in both the model and treatment groups were significantly reduced on days 7, 14, 21, and 28 after modeling (P<0.05). In contrast, rats in the waist-rubbing group showed significantly higher PWT and PWL values than those in the model group on days 14,

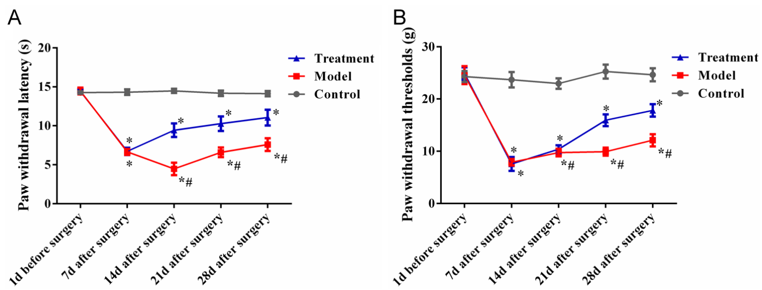

Figure 2. Comparison of the behavioral detection results among groups. A: Comparison of paw withdrawal latency among groups; B: Comparison of paw withdrawal thresholds among groups (g); *P<0.05 vs control; #P<0.05 vs model.

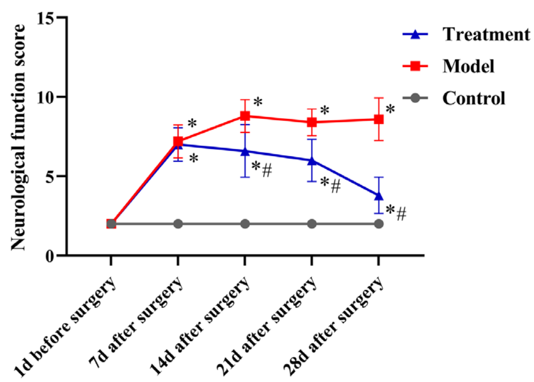

Figure 3. Comparison of neurological function score among groups. *P<0.05 vs Control group; #P<0.05 vs treatment group.

21 and 28 after modeling (P<0.05), indicating that the waist-rubbing method effectively alleviated pain hypersensitivity in LDH rats (**Figure 2**).

Waist rubbing improved neurological function scores in LDH rats

Compared with the control group, the neurological function scores of rats in both the model and the treatment groups were significantly elevated on days 7, 14, 21, and 28 after modeling (P<0.05). Furthermore, the treatment group showed significantly higher neurological function scores than the model group on days 14, 21, and 28 post-modeling (P<0.05), suggesting that the waist-rubbing intervention effectively promoted functional recovery in LDH rats (**Figure 3**).

Waist rubbing regulated immune T cell levels in LDH rats

The ratios of IFN-γ+CD8+ T cells, IL-17+CD8+ T cells, FOXP3+CD4+ T cells, and IL-4+CD4+ T cells in the peripheral blood in the model group were significantly higher than those in the control group (all *P*<0.05). Compared with the model group, rats in the waist-rubbing treatment group exhibited significantly lower ratios of T cell subsets (*P*<0.05) (**Figure 4**).

Waist rubbing decreased inflammatory cytokine levels in LDH rats

Compared with the control group, serum levels of CORT, GR_{α}, IFN-γ, IL-17, IL-4 and TGF-β were significantly increased in the model group, while these levels were significantly decreased after waist rubbing (**Figures 5**, **6**).

Discussion

There are three major perspectives regarding the pathogenesis of LDH: mechanical compression, chemical radiculitis, and intervertebral disc autoimmunity. Since Naylor *et al.* first proposed the autoimmune theory of LDH pathogenesis, accumulating evidence has supported the validity of this concept [6, 7]. Many studies have investigated the immune status of patients with LDH and suggest that autoimmune disorders may be the primary cause of low back and leg pain, while disc herniation acts as an inducing factor [8, 9]. However, systematic research on the autoimmune response in LDH remains limited. Most available studies only focus on describing changes in a few immunological indicators, such as IgG or IgM, lacking comprehensiveness and objectivity [10]. In addition, research on the use of Tuina therapy to treat LDH from the perspective of modulating autoimmune inflammation is scarce. This gap hampers the theoretical advancement of the discipline and restricts clinical application. Therefore, this study was designed to integrate classic theories of traditional Chinese medicine with experimental verification, employing an ancient waist-rubbing technique to treat LDH and elucidate its underlying immunoregulatory mechanisms.

Conventional LDH animal modeling mainly involves surgical removal of autologous intervertebral disc tissue fragments near the sciatic nerve root to induce artificial nerve compression [11, 12]. However, this approach does not accurately reproduce the pathoge-

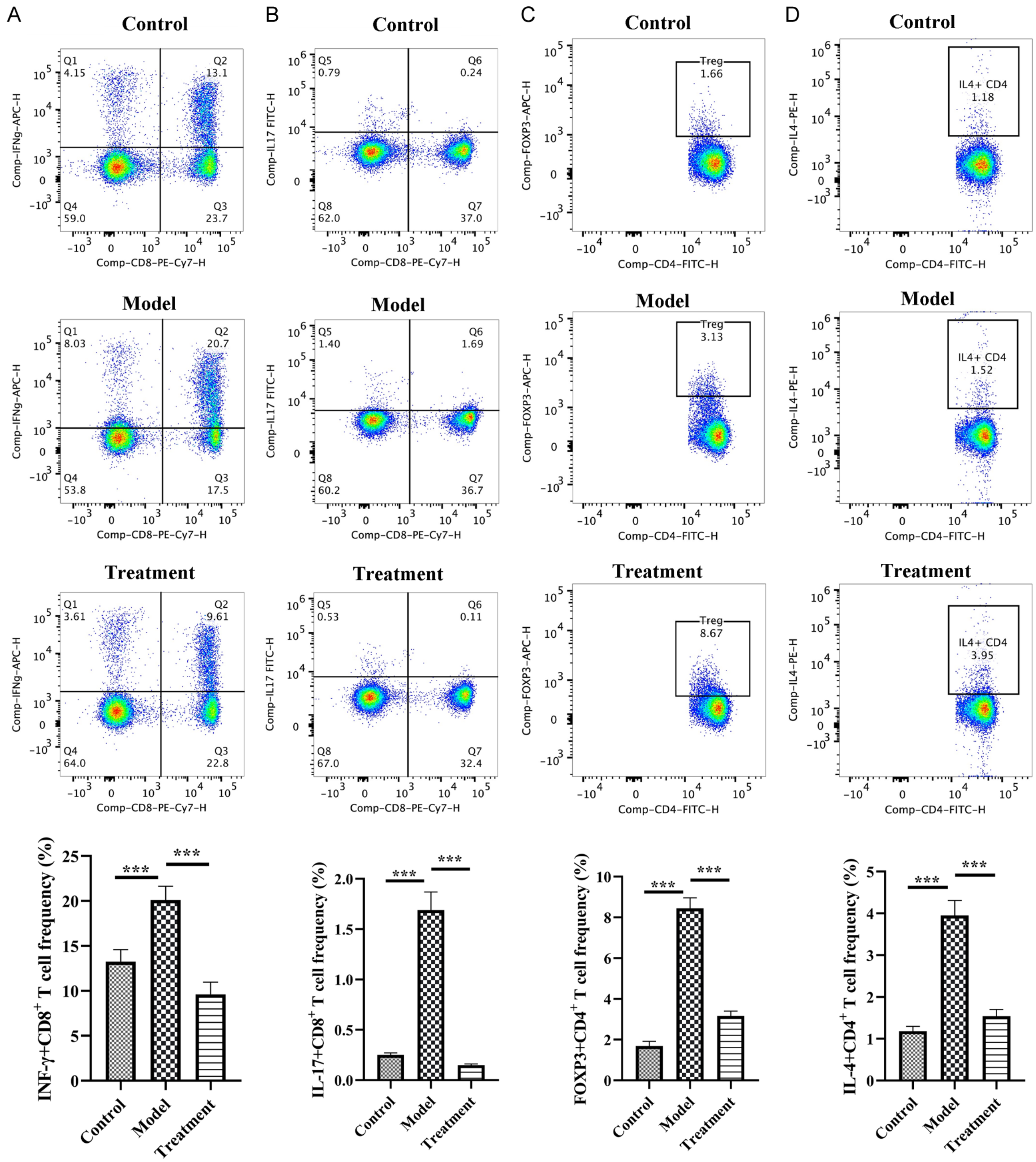

Figure 4. Comparison of T cells ratio among groups (%). A: IFN-γ+CD8+ T cell ratio; B: IL-17+CD8+ T cell ratio; C: FOXP3+CD4+ T cell ratio; D: IL-4+CD4+ T cell ratio; ***P<0.0001.

nesis of LDH. It is widely recognized that LDH arises from long-term mechanical stress and strain on the lumbar region, leading to intervertebral disc degeneration and protrusion. Moreover, it remains unclear whether the observed autoimmune responses in such surgical models are attributable to disc herniation itself or to surgical trauma. To overcome these limitations, the present study employed a bipedal upright LDH rat model established through forelimbs amputation. This model better replicates the biomechanical conditions and progressive degenerative process observed in human LDH while minimizing external interference, thereby providing a more reliable experimental platform for exploring the autoimmune mechanisms underlying LDH.

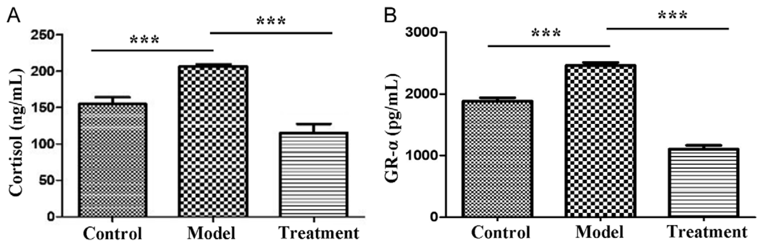

Figure 5. Comparison of cortisol and GR_{α} level among groups. A: Cortisol level in each group; B: GR_{α} level in each group; ***P<0.0001.

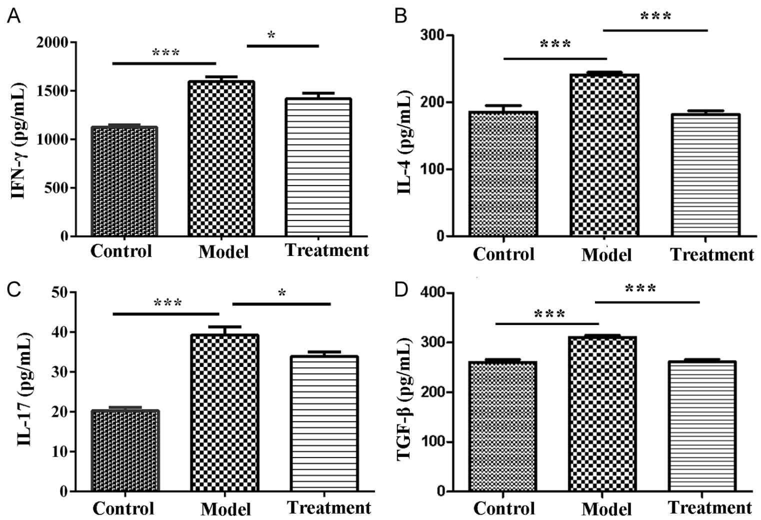

Figure 6. Comparison of inflammatory factors among groups. A: IFN-γ level; B: IL-4 level; C: IL-17 level; D: TGF-β level; *P<0.05, ***P<0.0001.

In the inherent immune response, CD4+T lymphocytes differentiate into two categories: T helper (Th) cells and regulatory T (Treg) cells [13]. Th1 cells mainly secrete IFN-γ, while Th2 cells mainly secrete anti-inflammatory cytokines such as IL-4 [14]. Th1 cells exert pro-inflammatory effects, while Th2 cells play an anti-inflammatory role [15]. Similarly, Th17 cells mainly secrete IL-17 and promote inflammation, while Treg cells mainly secrete TGF-β and suppress excessive immune responses [16, 17]. Th1/Th2 balance and Th17/Treg balance represents a key indicator of immune homeostasis, ensuring normal immune responses and preventing the occurrence of autoimmune diseases [18].

In the present study, the Th1/Th2 and Th17/Treg ratios were markedly increased in LDH rats compared with controls, indicating a disrupted immune equilibrium and a shift toward excessive autoimmune inflammation. This hyperactive immune state likely contributes to the persistent low back and leg pain characteristic of LDH. After treatment with the waist-rubbing method, the balances of both Th1/Th2 and Th17/Treg were restored to varying degrees, and their ratios decreased, indicating that autoimmune inflammation was suppressed and pain was relieved. However, why does LDH exhibit autoimmune disorders? If immune imbalance was solely caused by exposure of nucleus pulposus antigens following disc herniation [19], then similar immune disturbances should occur in conditions such as vertebral fractures, lumbar spondylolisthesis, and artificial disc replacement, yet they do not. From another perspective, the waist-rubbing method does not directly alter the spatial configuration of intervertebral discs, repair dislocations, or decompress nerve roots; rather, it achieves significant pain relief through indirect modulation of systemic immune balance. These findings imply that the pathogenesis of LDH-related immune disturbance extends beyond simple mechanical injury, involving deeper neuroimmune and endocrine regulatory mechanisms.

The hypothalamic-pituitary-adrenal axis (HPA) serves as the central component of the neuroendocrine system [20]. It interacts and influences with the immune system through hormones and their receptors, neurotransmitters, and inflammatory factors, jointly maintaining the dynamic balance of the internal environment [21]. Disruption of this equilibrium can trigger autoimmune diseases [22]. In this study, serum levels of CORT and GR_{α} - the terminal products and functional indicators of the HPA axis - were significantly increased in the model group compared to the control group [23]. These findings indicate that LDH rats exhibit impaired HPA axis function, leading to excessive CORT secretion and weakened anti-inflammatory regulation in the spinal canal, resulting in autoimmune disorders. Clinically, in addition to pain and numbness in the lower back and legs, most LDH patients present with symptoms consistent with “kidney deficiency” in TCM, including fear of cold, cold limbs, fatigue, decreased vitality, impotence, premature ejaculation, white tongue coating, and deep pulse [24], consistent with the pathological state of HPA axis dysfunction observed in LDH rats. The convergence of clinical observations and experimental results suggest that they both imply impaired secretion of adrenal cortical hormones representing a core mechanism of LDH pathogenesis.

After comprehensive analysis, the pathogenesis of LDH can be summarized as follows: prolonged and chronic lumbar strain induces fatigue and dysfunction of the HPA axis, accompanied by increased expression of GR in local tissues. This dysfunction results in insufficient secretion of hormones such as CORT, thereby disrupting the Th1/Th2 and Th17/Treg balance under the stimulation of herniated nucleus pulposus in the spinal canal. The ensuing immune imbalance triggers a persistent autoimmune inflammatory response, ultimately leading to chronic low back and leg pain. Recent evidence suggests that the brain is involved in the regulation of chronic pain caused by LDH, with both the functional and structural regions of the brain undergoing adaptive changes in response to pain intensity [25]. This provides strong evidence that the HPA axis is intricately involved in LDH pathophysiology. From this perspective, HPA axis hypofunction, corresponding to “kidney deficiency” in TCM, can be the fundamental or underlying cause of LDH development.

The technique employed in this study originates from the TCM Tuina book *The Secret of Dynamic Qigong and Tuina* (Qing Dynasty). The text records: “For those suffering from lower back pain who cannot bend forward, pinch the Yaoshu point fifty to seventy times, rub it fifty to seventy times, and perform static Qigong accordingly”. This book highlights the close relationship between kidney deficiency and lower back pain and advocates rubbing as an effective therapeutic approach. The rubbing method involves reciprocating linear friction movements applied with moderate pressure through the close contact of the palm with the body surface. The immediate mechanical effect generates sustained warmth that penetrates subcutaneous and muscle layers, thereby dilating local capillaries, improving microcirculation, and promoting repair of soft tissues such as fascia, ligaments, bursa, and muscle fibers. In the present study, rubbing was applied to the lumbosacral region to stimulate adrenal activity. The generated warmth enhances CORT secretion, thereby suppressing overactive immune response. Unlike infrared heating or moxibustion, the warmth produced by manual rubbing is dynamic, rhythmic, and intimately connected to the practitioner’s touch, imparting both physical and emotional comfort to the patient. This soothing warmth not only relaxes tense soft tissues but also exerts psychophysiological benefits by enhancing limbic system function and promoting the release of endogenous pain-relieving substances such as endorphins. These effects collectively support recovery of the HPA axis, which regulates both emotional and physiological stress responses.

From the perspective of TCM, “the waist is the residence of the kidneys”, representing the convergence of kidney Qi The lumbosacral region contains several acupoints with kidney-tonifying and analgesic effects, including Shenshu (BL23), Mingmen (GV4), Yaoyangguan (GV3), and Guanyuanshu (BL26). Therefore, applying the rubbing technique to this area provides gentle, continuous, and safe stimulation that enhances adrenal cortical function.

Conclusion

In summary, the mechanism of the waist-rubbing method in treating LDH appears to involve enhancement of HPA axis function and restoration of Th1/Th2 and Th17/Treg immune balance. These effects collectively suppress autoimmune inflammatory responses and alleviate lower back and leg pain. Future research should further elucidate the immunological mechanisms underlying LDH and explore innovative clinical approaches that target autoimmune regulation to improve therapeutic outcomes.

Acknowledgements

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Disclosure of conflict of interest

None.

Abbreviations

LDH, Lumbar disc herniation; Th1, Helper T cells 1; Th2, Helper T cells 2; Th17, Helper T cells 17; Treg, Regulatory T cells; HPA, Hypothalamic-pituitary-adrenal axis; CORT, Cortisol; GR_{α}, Glucocorticoid receptor α; IL-17, Interleukin-17; IL-4, Interleukin-4; TGF-β, Transforming growth factor-β; IFN-γ, Interferon-γ; ELISA, Enzyme-linked immunosorbent assay.

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