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Exploration on the feasibility of moxibustion in prevention and treatment of COVID-19 from the perspective of modern medical mechanism[☆]

从现代医学机制探讨艾灸防治新型冠状病毒肺炎的可行性[☆]

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ABSTRACT

Novel coronavirus pneumonia (COVID-19) is rampant in many countries and regions and there is no time to delay the exploration of the scheme for its prevention and control. The pathogenic characteristics of novel coronavirus and the effect of moxibustion for warming up *yang* and strengthening the antipathogenic *qi* were analyzed in this paper. From the perspective of modern medical mechanism, during the prevention and treatment of novel coronavirus infection, moxibustion may be able to prevent and treat COVID-19 by improving the body's immunity so as to conquer virus, by anti-inflammation to alleviate the inflammatory response of COVID-19 and by improving lung function to inhibit pulmonary fibrosis.

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Novel coronavirus pneumonia (COVID-19) is a new respiratory infectious disease. With the spread of this epidemic, cases have emerged in many countries and regions. As of 8 a.m. on 25 May 2020, the number of confirmed cases of infection worldwide has exceeded 5.456 million and the number of deaths has exceeded 345,000. It is of urgent need to explore the scheme for prevention and treatment of COVID-19. Facing to such a new type of virus, there is no specific medication for treatment and the development of its vaccine is not a day's work. The experts from National Health Commission of the People's Republic of China, at press conferences held early in the spread of the virus, had speculated that the virus might mutate, which increases the difficulty in developing targeted medications and vaccines. In this general background, it is necessary and important that traditional Chinese medicine (TCM) is proactively participating in the prevention and treatment of COVID-19.

Manifestation and nature of COVID-19

The disease is clinically manifested as fever, dry cough and fatigue, accompanied with nasal obstruction, runny nose, headache, sore throat, myalgia and diarrhea in a few cases. Its incubation period is 1 day to 14 days in generally. The patients with viral infection and asymptomatic carries may be the source of infection and the population is generally susceptible. According to the analysis of Jibai XIONG, the master of Chinese medicine, the infectious characteristics of this disease are in line with the description in Chapter 72 of *Sùwèn* (《素问》 *Basic Questions*). "Where the epidemic disease arrives, it is easy to infect each other, no matter young or old, with similar symptoms". Hence, in TCM, this disease is in the category of pestilence [1]. It is said by Youke WU in Ming Dynasty, in *Wēnyìlùn* (《温疫论》 *Treatise on Warm-Heat Pestilence*) that pestilence results from epidemic pathogen and the people will suffer from it whenever being contagious, no matter young or old, strong or weak.

Regarding the nature of pathogen, the Academician, Xiaolin TONG, from Guang'anmen Hospital of China Academy of Chinese Medical Sciences, believes that this pathogen pertains to cold because the disease started at the winter solstice, just around "the 1st nine-day period in winter" according to Chinese lunar calen-

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dar. The climate in Wuhan is extremely humid and the continuous rainy days aggravate the damp pathogen during the epidemic. It is shown that the nature of this disease refers to *yin* disorder, caused by pathogenic cold and damp, dominated by *yang* damage [2].

Moxibustion is the first choice in the treatment of *yin*-cold disorder

Yin pathogen easily damages *yang qi*. Consumption of *yang qi* or loss of *yang qi* threatens the life. Novel coronavirus impairs human body and depletes *yang qi*. “When the people are of the old age, *yang qi* is declining, hence, the hands and feet are not warm anymore and the primary *yang* is exhausted”. This may be the reason why elderly patients are more seriously ill and once they are at the serious stage, the fatality rate will be greatly raised. In view of this situation, the principle of treatment should be warming and tonifying the primary *yang*. It is said in *Biānquè Xīnshū* (《扁鹊心书》 *The Teachings of Bian Que*) that “when the genuine *yang* and the primary *qi* are deficiency, the people will be ill, when the genuine *yang* and the primary *qi* are collapse, the people will be dead, moxibustion is the first option to save the life.”

Moxibustion acts on warming meridians, expelling cold, rescuing *yang* from collapse, removing stasis and resolving masses, preventing diseases and keeping healthy. Academician, Xiaolin Tong also advocates that with moxibustion combined for warming *yang* and eliminating cold and damp while the Chinese herbal medication is used based on syndrome/pattern differentiation, the body immunity may be improved. Moxibustion works not only for strengthening the antipathogenic *qi*, but also for eliminating pathogens. It motivates the antipathogenic *qi* in the human body and enhances body resistance. Moxibustion may also prevent from diseases and benefit health care. For the pathogenic cold and damp in the body, moxibustion may expel cold pathogen and promote circulation in meridian and collateral by its warming and heat effect. Regarding the heat transformed by the long-term accumulation of cold and damp, moxibustion may open the sweat pore of skin, keep the pores open so as to ensure the elimination of the heat [3].

Potential modern medical mechanism of moxibustion in prevention and treatment of COVID-19

Moxibustion may improve the body immunity and the ability to anti disease

Lymphocytes can be divided into T lymphocytes, B lymphocytes and natural killer (NK) cells, which are the main executor for immune system function regulation. During the immune response, when the number and the function of each lymphocyte subset are abnormal, a series of pathological changes may occur. Therefore, the imbalance of lymphocyte subsets is an important indicator of abnormal immune response [4]. In the patients with COVID-19, the levels of white blood cell (WBC), L (%), red blood cell (RBC), hemoglobin (HGB), CD3⁺, CD4⁺, CD8⁺, blood urea nitrogen (BUN) and uric acid (UA) are lower than those in healthy people respectively [5]. The reason for the decrease of lymphocytes in the patients may be related to the fact that COVID-19 directly or indirectly kills lymphocytes or inhibits lymphocyte generation, which will lead to the low immune function of patients [6].

Modern research shows that moxibustion improves the body immunity by regulating various immune cells and immune factors. Ginger-isolated mild moxibustion significantly regulates the immune function of children with cough variant asthma and the level of CD4⁺ and the ratio CD4⁺/CD8⁺ are higher than those in the western medication group and the level of CD8⁺ is lower obviously than the western medication group [7]. Another study have

shown that moxibustion with grain-size cone at Zúsānlǐ (足三里 ST36) has a positive regulatory effect on the cellular immune function of elderly patients in bed. Compared with the group without moxibustion of grain-size cone, the levels of CD3⁺ and CD4⁺ and the ratio of CD4⁺/CD8⁺ are increased after treatment in the group of moxibustion with grain-size cone and the level of CD8⁺ decreased obviously [8]. Complement system is an important part of non-specific immunity, which is an important part of fighting against pathogen infection and participates in the specific immune response of the body. The active substances synthesized after complement activation have the functions of regulating and mediating inflammation, eliminating immune complex, reducing immune pathological injury, etc. Moxibustion on governor vessel effectively improves the biased state of constitution of people with *yang* deficiency constitution and significantly increases the levels of C3 and C4 in serum complement. Hence, C3 and C4 may be the targets of moxibustion on governor vessel in regulating human immune level [9]. For the patients with digestive malignant tumor and receiving chemotherapy, herbal moxibustion at Shénquè (神阙 CV8) significantly increases the levels of NK cells, CD8⁺ cells, CD4⁺ cells and CD3⁺ cells and improves the immune function and the quality of life [10]. Moxibustion also improves the survival status in the tumor bearing mice of gastric cancer [11]. Moxibustion based on the solar term effectively improves the sub-health state of *yang* deficiency constitution and increases the levels of immunoglobulins, such as immunoglobulin M (IgM), immunoglobulin A (IgA) and immunoglobulin G (IgG) [12].

Moxibustion presents anti-inflammatory effect and may alleviate inflammatory response of COVID-19

From the perspective of pathophysiological mechanism of modern medicine, the specific mechanism is unknown on inflammatory storm caused by novel coronavirus infection. However, a previous study has shown that viral infection may trigger a large amount of cytokine secretion through activating transcription factors such as nuclear factor kappa-B (NF- κ B), activator protein-1 (AP1) and activating transcription factor 2 (ATF2) [13]. It is speculated that after novel coronavirus infection, immune cells are activated, tumor necrosis factor- α (TNF- α), interleukin (IL)-1, interferon and chemokines are released, a large number of mediated immune cells are aggregated and infiltrated to the lung tissue. Simultaneously, the intracellular signal transduction pathway is activated, the waterfall inflammatory cascade reaction starts and a large number of cytokines are released. Additionally, much more inflammatory cells are activated constantly and a vicious cycle is formed. Eventually, cytokine storm results [14]. In one research, the expressions of inflammatory immune response cytokines are detected in the plasma of 41 patients with COVID-19. It is shown that the plasma concentrations of IL1B, IL1RA, IL7, IL8, IL9, IL10, basic fibroblast growth factor (basic FGF), granulocyte colony stimulating factor (GCSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon gamma (IFN γ), interferon-inducible protein 10 (IP10), monocyte chemoattractant protein 1 (MCP1), macrophage inflammatory protein-1 A (MIP1A), macrophage inflammatory protein-1 B (MIP1B), platelet derived growth factor (PDGF), TNF- α and vascular endothelial growth factor (VEGF) in the patients are all significantly higher than those in healthy adults. For the patients in intensive care unit (ICU), the plasma concentrations of IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A and TNF- α are higher significantly than those in the patients not in ICU. It is suggested that inflammatory storm is closely related to disease severity [15].

Moxibustion plays an anti-inflammatory role by regulating the level of inflammation-related cytokines. For example, in the model mice with viral pneumonia, moxibustion at “Fèishū(肺俞 BL13)” can effectively control the inflammatory edema in the lungs and

reduces the pulmonary indexes by regulating the relevant inflammatory factors, TNF- α and IL10 [16]. Mild moxibustion with moxa stick can significantly decrease the mortality of mice with staphylococcus aureus infection, reduce bacterial infection and alleviate inflammatory damage, displaying its protective role. Moxibustion exerted after bacteria devour by macrophages, can significantly improve the bactericidal activity of macrophages, with significant anti-bacterial infection and anti-inflammatory effects [17]. By reducing the level of peripheral and central pro-inflammatory factor, IL-6 and increasing the level of anti-inflammatory factor, IL-10 and the ratio of IL-10/IL-6, moxibustion alleviates the peripheral and central inflammatory responses and relieves the secretion imbalance of pro-inflammatory factors and anti-inflammatory factors so as to reduce peripheral and central inflammatory responses in the rats with exercise fatigue [18]. In treatment of rheumatoid arthritis, with moxibustion combined, the anti-inflammatory effect of western medication is obviously improved. Treated with moxibustion in combination, the levels of hypoxia inducible factor-1 α (HIF-1 α), VEGF, NIK and NF- κ B in serum are reduced significantly in the patients and the concentration of transforming growth factor- β 1 (TGF- β 1) is increased significantly. Additionally, visual analogue scale (VAS) score, tenderness index, swelling index, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and IL-1 β are better improved as compared with the control group with western medication [19,20]. In the treatment with moxibustion and infrared irradiation for community-acquired pneumonia, the results of purulent sputum disappearance time, fever relief time, rale absorption time, inflammation absorption time in chest X-ray test, the time length of hospital stay and the changes in serum inflammatory indexes, as well as immune function indexes are all better than those in the control group with western medication, indicating a better therapeutic effect and the improvement of immune functions in the patients [21].

Moxibustion improves the lung functions and inhibits the progress of pulmonary fibrosis

With the increasing cases of cured patients with COVID-19, for some patients in the recovery stage, the results of viral nucleic acid test have turned negative, but the patients still have fatigue, cough, poor mental state, etc. In particular, the changes in chest CT scanning are not coincident with the clinical symptoms, meaning that there is still unabsorbed inflammation in the lungs when the patients are discharged from the hospital [22]. However, compared with coronaviral infectious atypical pneumonia, the incidence of diffuse interstitial pulmonary fibrosis is relatively high in the sequelae after treatment [23]. Although it has not been clinically verified whether COVID-19 will lead to the similar sequelae as atypical pneumonia, pulmonary fibrosis may be a high-risk sequelae due to the lesions involved in the lungs [24]. cess of pulmonary fibrosis. Moxibustion at “BL13” and “Gāohuāngshū (膏肓俞 BL43)” can inhibit the pulmonary fibrosis process in the rats of pulmonary fibrosis induced by bleomycin A5 (BLMA5) and its mechanism may be related to the increase of the expression of E-cad gene in pulmonary epithelial cells, the decrease of the levels of α -smooth muscle actin (α -SMA) and vimentin and the decrease of alveolitis degree [25,26]. In terms of lung function improvement, the isolated moxibustion at CV8 combined with *qiānglǐ zhīkèning* capsule effectively improves the lung function and the quality of life in the patients with chronic bronchitis [27]. *Yang-supplementing fire* moxibustion improves the lung function, delays the progressive decline of lung function, obviously improves the body constitution in the chronic obstructive pulmonary diseases (COPD) patients in stable phase with yang deficiency, increases the quality of life and effectively improves the comprehensive effect

of treatment in the patients with chronic obstructive pulmonary disease in stable stage [28].

Application of moxibustion in infectious disease

In history, moxibustion has been applied for many times to prevent and treat infectious diseases. Epidemic cholera was introduced into the Lingnan region of China in 1820. and plague was introduced in 1867. Both of these two diseases caused high fatality rates before 1911. The medical masters of the Lingnan region believe that epidemic cholera is a *yin* and cold disease and the ginger-isolated moxibustion is applicable. Plague refers to “heat and toxin in blood and obstruction due to blood stagnation”, hence, the garlic-isolated moxibustion is applicable [29].

At the end of 1985, without hindering the management with western medicine (WM), Meisheng ZHOU adopted moxibustion and fire needling therapy at the tender points on the back, Dàzhū (大椎 GV14), Sānyīnjiāo (三阴交 SP6), Jùquē (巨阙 CV14), Zhìyáng (至阳 GV9), etc. in 79 patients with epidemic hemorrhagic fever, with the effective rate of 97.47% [30]. The studies have further found that moxibustion shortens the duration of scanty urine and urinary retention, promotes the conversion of urine protein to be negative, reduces the content of urea nitrogen and protects renal function to some extent in the patients with renal insufficiency of epidemic hemorrhagic fever [31].

A study has reported that the lamp-fire moxibustion is used in the treatment of infectious condyloma acuminatum by the direct cauterization at the foci. The total effective rate is 100% [32]. This therapy is firstly found in *Wūshíèr Bìngfāng* (《五十二病方》 *Formulas for Fifty-two Diseases*), unearthed from the Han Tomb in Mawangdui, Changsha. Besides, this moxibustion method is often used in treatment of mumps.

In a retrospective analysis on the medical cases of hepatitis B treated by Xiliang XIE, the contemporary master of moxibustion, with moxibustion of grain-size cone during 30-year clinical practice, moxibustion of grain-size cone is exerted at Gānshū (肝俞 BL18) and Píshū (脾俞 BL20), with Shēnzhù (身柱 GV12) combined in children and Zúsānlǐ (足三里 ST36) in adults. The improvement rate of clinical symptoms and physical signs is 100%. Hepatomegaly, splenomegaly, liver cirrhosis and ascites are relieved definitely. The negative conversion rate of hepatitis B surface antigen is 28.85% and the conversion rates of e antigen and core antibody are 38.46% and 36.54% respectively [33].

For pulmonary infectious diseases, the garlic-isolated moxibustion is used in treatment of pulmonary tuberculosis and the effective rate is up to 65%. Besides, this therapy can rectify the impaired cellular immune function [34].

The latest research results show that the genetic sequences of COVID-19 and severe acute respiratory syndrome-Cov (SARS-Cov) are similar by 79.5% [35]. In the process of diagnosis and treatment of SARS, 9 patients with SARS in recovery stage had been treated in Guang’anmen Hospital, China Academy of Chinese Medical Sciences. In treatment, moxibustion is applied to GV14, BL43 and ST36, combined with the medication of WM and TCM. After treatment, the symptoms are all relieved, such as low fever, chest oppression, fatigue, headache and general soreness, distending pain in the chest and the abdomen, poor appetite and constipation. Moreover, the percentage of CD4⁺ is increased as compared with that before treatment, suggesting that moxibustion can enhance the partial immune function in SARS patients [36].

In the fight against COVID-19, 42 patients with COVID-19 of common type were treated in the Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, Fusheng Branch (Jiangxi Heat-Sensitive Moxibustion Hospital) and its assisted Qichun County People’s Hospital, Hubei Province. The heat-sensitive moxibustion is applied at CV8 and Tiānshū (天枢 ST25). Each moxibus-

tion lasts for 40 min to 60 min till the heat sensation penetrates to the deep and distal areas, as well as the patient feels feverish sensation in the body and sweating on the forehead. The treatment is given once daily. This therapy effectively alleviates the negative emotions of patients and relieves the symptoms such as chest oppression, poor appetite, etc. [37].

Summary

According to the transmission and pathogenic characteristics of COVID-19, professor Chen WANG, the Academician of Chinese Academy of Engineering, once proposed that it is possible that this virus may be transferred to be chronic and existed for a long term. It means that the prevention, control, diagnosis and treatment of COVID-19 will likely be sustainable. Acupuncture-moxibustion plays a regulatory role in the respiratory system and systemic immune inflammatory response [38]. Hence, it is quite necessary for us to fully display the effect of acupuncture-moxibustion in improving the body immunity, in which, moxibustion is undoubtedly a non-invasive, convenient and effective approach.

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