



Short Commentary

Impact of COVID-19 on Obese Patients with Diabetes Mellitus and Integrative Medicine

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Currently, Novel coronavirus (Coronavirus disease 2019, COVID-19) infection has been defined as a global pandemic by World Health Organization (WHO). The origin and transmission chain of convergent evolution, cross species transmission and covert communication are gradually clear [1-2]. As of August 13, 2020, 20529875 people have been diagnosed in the world, and it is still showing a rapid growth trend [3].

Recent studies [4-5] have reported the epidemiological investigation and disease characteristics of covid-19. Elderly people with underlying diseases are more susceptible to 2019-nCoV. Among the 40000 confirmed patients, 5276 have underlying diseases, of which 1102 are diabetic patients, accounting for 20.9%, and the mortality rate is 7.3%, which is much higher than the average crude mortality rate of 2.3% [6].

In the study of Yang et al., [7], diabetes accounted for 22% of the 32 patients who died of COVID-19 in the intensive care unit of Wuhan Jinyintan hospital. In the study of Guan et al., [8], 1099 patients with confirmed COVID-19 were included in the study, 81 cases (7.4%) were complicated with diabetes mellitus, among them, 173 critically ill patients were complicated with diabetes, 28 cases (16.2%) had diabetes mellitus, and 67 cases had endpoint events (including entering ICU, using mechanical ventilation or death), including 18 cases (26.9%) with diabetes. In another study, 12% of 140 patients admitted to hospital with COVID-19 had diabetes. Diabetes is a disease characterized by absolute or relative deficiency

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of insulin [9]. According to the latest report of the International Diabetes Federation (IDF), in 2019, about 463 million adults aged 20-79 years in the world suffered from diabetes (1 out of 11 individuals was diabetic) [10]. Diabetic patients with high glucose metabolic load can lead to inflammatory injury, immune imbalance, local tissue immune microenvironment disorder, and increase the risk of covid-19 infection. As doctors and researchers, we not only face the difficulty of designing new therapies for covid-19, but also, as global citizens, we also face the task of redesigning our existing health infrastructure, and how we can provide resources for the prevention and treatment of integrated traditional Chinese and Western medicine to people diagnosed with diabetes in the global period of continuous spread of covid-19.

Impaired Body Function and Susceptibility to Covid-19 in Diabetic Patients

Metabolic load induced by high glucose promotes immune imbalance and is more susceptible

With the prolongation of the course of disease, the target of drug therapy is the metabolic load caused by high glucose. The long-term metabolic load in the body will lead to other organ and tissue lesions, such as immune system dysfunction [11]. The immune system plays an important role in the body's resistance to external pathogenic microorganisms, recognition of self cancerous cells and maintenance of autoimmune homeostasis. Immune system imbalance can lead to immune monitoring disorder, unable to play a normal immune effect, more vulnerable to virus infection, the formation of autoimmune diseases. Studies [11] showed that the proportion of T lymphocytes in the blood of diabetic patients decreased, the proportion of CD4 + T / CD8 + T was unbalanced, the differentiation of CD4 + T cells was abnormal, the killing ability of CD8 + T cells to virus was weakened, and the activation of natural immune cells such as macrophages caused virus infection, and the organs were damaged more seriously after infection.

Diabetic complications / comorbidities aggravate covid-19 injury

2019-nCoV is mainly transmitted through respiratory droplets. After infection, it replicates in respiratory tract and lung tissue, causing lung injury. Severe cases can lead to Acute Respiratory Distress Syndrome (ARDS) and Multiple Organ Dysfunction Syndrome (MODS). Respiratory failure is the main cause of death [6]. The study [12] found that 30% of covid-19 patients had varying degrees of renal injury, such as increased proteinuria, creatinine and urea nitrogen, which led to renal failure and was also one of the causes of death. Under high glucose metabolic load, diabetic patients have common complications such as kidney disease and Chronic Obstructive Pulmonary Disease (COPD), resulting in multiple organ immune disorder, reduced immune monitoring ability to external pathogenic microorganisms, more susceptible to the same covid-19 exposure conditions, causing severe lung and kidney tissue damage, in the infection state in a high stress state, promoting blood glucose

rise, further metabolic disorders and negative It can induce hypertonic coma and DKA, and then affect the clinical treatment and even endanger life.

Our study [13] found that AGE-RAGE signaling pathway can not only cause glucose and lipid metabolism disorder, increase oxidative stress, but also induce the activation of MAPK, JAK-STAT, PI3K Akt signaling pathways, promote inflammatory response and promote the development of diabetes. At the same time, the activation of ages- rage signal axis can be caused by the production of oxygen free radicals, the activation of NF - κ B and the increase of the expression of inflammatory factors It can be inferred that AGE-RAGE is the key pathway in the pathological process of covid-19 lung cell apoptosis and lung tissue injury.

Homeostasis of innate immune system in diabetic patients

More than 10 kinds of acute inflammatory markers such as complement C3 in blood biochemical indexes of diabetic patients were significantly higher than those of healthy group, and some of them were important predictors of T2DM [14], It indicates that the body is infected by some bacteria or viruses. With the clearance of pathogenic microorganisms, the above indexes decrease significantly, indicating that the body completes the stress response to external stimulation. However, the persistence of some chronic diseases leads to the non physiological chronic inflammation. The hematological study of clinical patients and diabetic mouse models [14,15] showed that the proportion and absolute number of innate immune cells such as monocytes, macrophages and neutrophils in blood increased in varying degrees, while IL-6, TNF - α and complement components in serum were also significantly increased. In addition to the presence of these inflammatory manifestations in the blood and tissues, macrophages and other mononuclear cells were also found in the kidney, which were localized around the injured renal tubules and some apoptotic cells, and released a large number of Pro fibrogenic and anti angiogenic factors, which activated the inflammatory signal pathway [16-18]. Under the infection of 2019-nCoV, the healthy body can produce a more sensitive recognition and inflammatory response to the external pathogenic microorganisms in time. The chronic inflammation of diabetic patients makes the innate immune cells in the body bear the load and exhaustion state for a long time, so it is unable to effectively recognize and monitor the pathogen, and cannot respond and activate the disease in time The effective transmission of toxic information to acquired immune cells can produce specific humoral and cellular immune responses, which makes 2019-nCoV more likely to infect diabetic patients. At the same time, due to multiple organ dysfunction and chronic inflammation in diabetic patients, apoptosis and necrosis of local tissue cells, strong vascular permeability and abnormal immune microenvironment in organs lead to virus infection and large number of replication, resulting in more serious tissue damage in patients with diabetes.

Diabetic patients are more prone to “cytokine storm”

Recent studies [18] found that the main cause of death of covid-2019 is the occurrence of cytokine storm in the late stage, which leads to circulatory shock, disseminated intravascular coagulation, ARDS, systemic inflammatory syndrome and multiple organ dysfunction syndrome. “Cytokine storm” is a systemic inflammatory disease. The main clinical manifestation is that a large number of proinflammatory factors in the blood increase rapidly in a short period of time, which

is often seen in some viral infections and cellular immunotherapy. Proinflammatory factors mainly include IFN - γ , IL-1, IL-2, IL-2Ra, IL-6, sIL-6R, IL-10, IL-12, TNF - α , IFN - α , human monocyte chemoattractant protein 1, etc [19]. IL-6 and TNF - α are the early activators of cytokine storm. Blocking IL-6 can effectively inhibit the activation of downstream pro-inflammatory factors. IL-6 antibody is also an effective drug for the treatment of “cytokine storm”.

In our study [20], we found that the related target of Yiqi Qudu Recipe on “inflammatory cytokine storm” is IL-17. As an inflammatory factor regulatory protein, IL-17 can regulate the activation of T cells and stimulate epithelial cells, endothelial cells and fibroblasts to produce a variety of cytokines The early initiation factor of cell-induced inflammatory response can amplify the inflammatory response by promoting the release of Pro inflammatory cytokines from lung epithelial cells, forming an “inflammatory cytokine storm”, resulting in leucopenia and dyspnea in patients with asymptomatic covid19 infection. It can be seen that IL-17 is a key factor in the early pathological process of covid19.

Some studies [14] showed that the level of IL-6 in diabetic patients was significantly higher than that in healthy people, and the expression levels of ifnr and TNF - α were relatively high, which were the key proinflammatory factors in the cytokine storm. High level of IL-6 can lead to cytokine storm more easily in patients with diabetes mellitus. In addition, patients with chronic inflammation of multiple organs can cause more serious histopathological damage. At the same time, fewer Treg cells and lower function can enhance the pathogenicity of cytokine storm.

Abnormal changes of angiotensin converting enzyme 2 (ACE2) in diabetic patients

Study [21] found that ACE2 is the receptor of 2019-nCoV infection. Under physiological conditions, ACE2 is the key enzyme of Renin Angiotensin System (RAS), which is a humoral regulatory system, composed of a series of peptide hormones and corresponding enzymes. Its main function is to regulate and maintain the balance of blood pressure, water and electrolyte, and maintain the relative stability of human body environment. RAS plays an important role in the pathogenesis of hypertension. On the one hand, the proportion of diabetic patients with hypertension and hyperlipidemia was higher. On the other hand, even in diabetic patients without hypertension, the expression of ACE2 in serum and some tissues of such patients were higher than that of normal group [21]. High expression of ACE2 is an important factor of susceptibility to 2019-nCoV in diabetic patients. The interaction of ACE2 and ace can maintain vasoconstriction and relaxation to maintain blood pressure stability. Under normal conditions, ace can change angiotensin I (at I) into at II, constrict blood vessels and raise blood pressure. ACE2 can change ang II into ang1-7, relax blood vessels and improve blood pressure. In some diabetic patients with elevated blood pressure or other cardiovascular diseases, the compensatory increase of ACE2 promotes vasodilation. In the case of infection, as the receptor of 2019-nCoV, the virus may be more likely to infect other tissues and organs. At the same time, due to the compensatory relaxation of blood vessels, proinflammatory factors are more easily released into tissues, resulting in secondary immune damage in tissues [22]. All of the above are one of the critical factors of diabetes mellitus patients susceptible to 2019-nCoV.

Prevention and Treatment Strategy of Integrated Traditional Chinese and Western Medicine in Patients with Diabetes during Covid-19 Global Pandemic

Positive self monitoring of blood glucose

Self blood glucose monitoring is also an important link to control blood glucose, which plays an important role in guiding blood glucose control, reasonable diet and scientific exercise. All diabetic patients need to carry out self blood glucose monitoring [23]. In the extraordinary period, the masses are affected by the epidemic situation and abide by the provisions of epidemic prevention and control, which may cause insufficient attention to self blood glucose monitoring; At the same time, diabetes education is not enough, economic factors, the tension and discomfort of blood glucose monitoring are also the important factors leading to the failure of self blood glucose monitoring. Therefore, the diabetes management team should strengthen the health education of self blood glucose monitoring to improve the compliance of patients.

Self blood glucose monitoring is also an important part of blood glucose control, Proper frequency of self blood glucose monitoring can help diabetic patients to understand their own blood glucose control situation, and timely adjust their lifestyle and hypoglycemic drugs to help blood sugar to stabilize. The low frequency of blood glucose monitoring may indicate that patients pay less attention to self blood glucose during the epidemic period, and cannot adjust their own hypoglycemic program according to blood glucose. In addition, due to the special situation of the COVID-19 epidemic, it cannot be ruled out that it is related to the inconvenience of obtaining blood glucose test paper.

Make full use of internet medical treatment

During the outbreak of the epidemic, the residential areas in Wuhan were completely closed, the traffic control in the urban area made it difficult for the citizens to go out of the city, and to seek medical treatment in the outpatient department of the hospital caused greater living difficulties and infection risks for diabetic patients. In recent years, with the rapid development of Internet social network and the popularity of smart phones, mobile medical resources are also gradually developing. Blood glucose management in the Internet era has become the development trend of hospital or personal blood glucose management [24,25], therefore, in the special period, we should make full use of the Internet platform to solve the above problems. Due to the insufficient publicity of the Internet platform, the difficulty in popularizing the network operating system and the insufficient trust of diabetic patients on the network platform, it may be difficult to carry out online consultation and drug purchase.

In this case, doctors and nurses can give professional guidance to the problems raised by patients from the perspective of medical treatment and nursing. Diabetes specialist nurses can provide more accurate and standardized guidance in the operation of specialized injection technology and lifestyle intervention [26]. According to the data, the average praise rate of patients for medical consultation is as high as 100.0%. Therefore, the management of patients with diabetes needs endocrinologists and specialist nurses to give full play to their respective strengths and give professional guidance and help to patients.

Pay attention to lifestyle intervention

Lifestyle intervention is the basic treatment of diabetes. Many studies have shown that exercise can improve the number and sensitivity of glucose transporters. Long term aerobic exercise can also increase the number and sensitivity of insulin receptors on adipocyte level muscle cells, and improve the sensitivity of peripheral tissues to insulin, thus reducing blood glucose [27]. Domestic and foreign guidelines recommend that adult patients with diabetes should adhere to at least 150 minutes of aerobic exercise per week [28]. It can be seen that lifestyle intervention is an important part of diabetes health management, which should run through the whole process of diabetes treatment. The study found that 32.9% and 12.5% of the respondents were faced with two difficulties: insisting on moderate exercise and reasonable diet. The reasons for the above problems may be the limited exercise of patients and the difficulty in purchasing food in the closed community. Moreover, the diabetic patients who stay at home may eat too much or do not eat properly. Therefore, diabetic patients should adjust measures to local conditions and choose appropriate home-based exercise methods; at the same time, they should also maintain self-discipline, adhere to dietary intervention, reasonably arrange meals, and ensure balanced nutrition.

Give correct psychological guidance in time

During the outbreak of COVID-19, due to the spread of information on the development of the epidemic, long-term isolation, inconvenient medical treatment and drug purchase, fear of COVID-19 and other factors, diabetes patients were depressed and nervous, which affected the good control of blood glucose. It is found that about 25% - 30% of diabetic patients have depressive symptoms or depressive disorders [23]. Long term depression can lead to dysfunction of neuroendocrine system, decrease of compliance to diabetes treatment, and increase of blood glucose. The reason why diabetic patients are prone to depression is that diabetes and its complications will bring physical discomfort to patients, and it cannot be cured. Therefore, it is necessary to strictly control diet, exercise and drug intervention for a long time, which will cause life and economic pressure to patients [29].

Family members and our medical staff need to pay attention to their psychological status. If the patients have abnormal behaviors compared with the past, they should consider the possible need for psychological rehabilitation intervention. Remember not to be harsh, blame, or be too tolerant to cause patients to do what they want. Patients can be advised to listen to relaxed music, regular work and rest, patiently listen to the patient's demands. At the same time, the family should create a good environment, give understanding and care to ease the tension and fear of patients.

Strengthen the prevention and treatment of integrated traditional chinese and Western medicine

In the long-term clinical practice, metformin, insulin and other Western medicine play an important role in the prevention and treatment of diabetes, and antiviral western drugs such as acyclovir are also widely used in the early stage of COVID-19. In the case of tension and fear, many patients have more serious adverse drug reactions, and many patients are inconvenient to seek medical treatment and purchase drugs because of the closed management in the area. Faced with this situation, diabetic patients in the COVID-19 transmission

area can actively try the integrated Chinese and Western medicine prevention and treatment. An evidence-based medicine study has confirmed that Chinese massage in the treatment of adult diabetes can safely and effectively reduce or replace the use of metformin tablets, while reducing drug side effects [30]. At the same time, another study is that Lianhua Qingwen combined with conventional antiviral western medicine can effectively control COVID-19.

At the same time, Taijiquan, baduanjing and other fitness Qigong can enhance the body's immunity, strengthen glucose and lipid metabolism, promote blood circulation and relieve tension. Lianhua Qingwen, Qingfei Decoction and other traditional Chinese medicine tea drinks have good anti-inflammatory and bactericidal effects, and can alleviate the inflammatory reaction caused by diabetes to a certain extent. At the same time, a large number of clinical cases have confirmed that it has a good prevention and treatment effect on COVID-19. In the special period of COVID-19 global pandemic, it is an important way of healthy life to strengthen the understanding of prevention and treatment of integrated traditional Chinese and Western medicine, and actively seek the way of integration of Chinese and Western medicine.

How to help diabetic patients manage their blood glucose well, enhance immunity, reduce the risk of infection, and pass the special period of COVID-19 global pandemic healthily is a major medical challenge.

Competing Interests

The authors declare that they have no competing interests.

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