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Mechanisms of Pulmonary Complications after Spinal Cord Injury

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Abstract: Background: Pulmonary complications caused by spinal cord injury (SCI) pose a serious threat to patients' health and quality of life. Understanding the potential injury mechanism of pulmonary complications caused by this destructive disease is necessary for the study of SCI and the guidance of clinical treatment. This article reviews the current situation and progress of exploring the mechanism of pulmonary complications caused by SCI.

Keywords: Spinal Cord Injury, Pulmonary Complications, Mechanism

Introduction

Spinal cord injury (SCI) is a serious disease of the center nervous system (CNS). SCI causes irreversible axonal damage and neuronal death, resulting in permanent disability. SCI can seriously affect the quality of life and puts heavy economic and social burdens on the families and society [1]. By 2016, there are an estimated 282000 individuals who sustain an SCI in the United States, and approximately 550 000 new cases of SCI are diagnosed annually. Whether it is congenital spinal cord injury or acquired spinal cord injury, it will cause a series of dysfunction, SCI will cause functional changes or disorders of the trunk and limbs, as well as defecation and defecation below the injury level, including sensory, limb movement, normal reflex, anal sphincter and autonomic nerve dysfunction, accompanied by pathological reflex, etc [2]. Since the establishment of the National Spinal Cord Injury Database in 1973, patients with SCI have been followed up for 40 years. During this period, it was found that the mortality rate of patients with spinal cord injury caused by cancer, heart disease, stroke, vascular disease, pulmonary embolism, urinary system disease, digestive system disease and suicide was decreasing. The mortality rates caused by neurological diseases, musculoskeletal diseases, mental disorders and septicemia have not changed significantly in the past 40 years. The death rates caused by endocrine, metabolic and nutritional diseases and accidents are increasing. The diseases that have the greatest impact on the life expectancy of patients with spinal cord injury are pneumonia and septicemia [1]. Respiratory dysfunction and related diseases, such as pneumonia, can be complicated with septicemia or pulmonary embolism, which are common causes of death in patients with spinal cord injury[3], Posed a special challenge to medical care [6-10]. In recent years, extensive studies have been carried out on the mechanism, diagnosis and prognosis of pulmonary complications caused by spinal cord injury. Pulmonary complications caused by spinal cord injury pose a serious threat to patients' health and quality of life. Understanding the potential injury mechanism of pulmonary complications caused by this destructive disease is necessary for the study of spinal cord injury and the guidance of clinical treatment. Therefore, this article reviews the current situation and progress of exploring the mechanism of pulmonary complications caused by spinal cord injury caused by various causes.

1. Respiratory muscle paralysis and decreased pulmonary compliance

The spinal cord receives sensory information from the somatic and visceral receptors through the posterior root, and then transmits information to the higher brain tissue through the ascending fibre bundle, and only through the descending fibers and anterior roots to the somatic and visceral target organs. The spinal cord is an important structure that transmits information to the brain and regulates motor and autonomic nervous functions. Spinal cord injury may lead to partial or complete loss of sensory-motor function below the injured segment, resulting in respiratory function involvement. pulmonary dysfunction is closely related to the level and degree of spinal cord injury. in general, the higher the injury level, the more complete the injury, the more obvious the decline in function [4]. When the spinal cord injury segment reaches C2 or above, the diaphragm function is completely lost, the intercostal muscle, scalenus muscle and abdominal muscle lose innervation, The patients can not breathe autonomously, and need ventilator-assisted respiration for a long time. In the acute stage of spinal cord injury, ventilator-assisted breathing is needed, diaphragm function exists in part, auxiliary respiratory muscle is involved, and it is easy to fatigue. Severe respiratory muscle dysfunction leads to respiratory insufficiency [5]. This will cause the lungs not to produce enough vital capacity, and the respiratory muscles are not strong enough to produce a cough, the supine position will further cause the diaphragm to shift, and the abdominal contents will push the loose diaphragm to the side of the head [6-8]. In patients with injury to the C5~C8 segment, the diaphragm function is normal, the intercostal muscle and abdominal muscle are weak, and there is no ability to produce cough; when the T1~T5

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segment is injured, the diaphragm function is normal, part of the intercostal muscle function is preserved, and the cough ability is weak; when the T6~T10 segment is injured, the function of the diaphragm, intercostal muscle and rectus abdominis muscle basically exists, but the cough ability is OK. Damage to T11~T12 segment can carry on effective cough, diaphragm, intercostal muscle, abdominal muscle function exist; injury to L1 segment and below, respiratory muscle function is normal, diaphragm, intercostal muscle and rectus abdominis function exist, cough ability is OK; injury to T11~T12 segment, can carry on effective cough, diaphragm, intercostal muscle, abdominal muscle function exist; injury to L1 segment and below, respiratory muscle function is normal. Inspiratory muscle weakness can lead to chronic alveolar hypopnea (CAH). The risk of lung morbidity and mortality is associated with the severity of hypercapnia, at least for patients with restrictive lung disease, where inadequate peak cough expiratory flow (PCEFs) is difficult to clear airway secretions due to decreased expiratory muscle strength. For patients with neuromuscular disease, hypercapnia usually occurs when vital capacity (VC) drops to 40% to 55% of the predicted normal value. Myelopathy affects respiratory muscles such as intercostal muscles and abdominal muscles, resulting in respiratory disorders. When the function of intercostal muscles changes, contradictory breathing of ribs moving inward will occur during inhalation [9]. Under normal circumstances, exhalation is passive. When ventilation per minute increases, and when effective coughing is needed to remove secretions, the expiratory muscles become important [10]. The main expiratory muscles are rectus abdominis, transverse abdominis, internal oblique abdominis and pectoralis major, as well as a few intercostal muscles. Abdominal muscles are innervated by both thoracic and lumbar nerves (T7-L1). Complete spinal cord injury at and above T6 leads to ineffective cough, difficulty in clearing secretions and mucus thrombus formation. Due to the loss of abdominal muscle strength, the vital capacity of quadriplegic patients was affected by posture. Compared with the supine position, the vital capacity of patients in the upright position decreased by 15%, and weak abdominal muscles placed the diaphragm in a position with lower respiratory efficiency. increasing residual capacity [11-13]. Patients may also damage the function of a motor root segment upward because of spinal cord oedema or bleeding within a few days after spinal cord injury [14]. Impaired cough function can lead to respiratory infections and the accumulation of secretions from tracheostomy tubes. Even patients with T12 injury may have impaired cough function due to bleeding. In patients with a higher level of nerve injury, the ability to produce sufficient cough is lacking due to the loss of function of the abdominal and intercostal muscles. Low cough flow is associated with increased mortality and extubation failure[15]. The cervical vertebra is the most active part of the spinal cord, and it is also the most common injury site in spinal cord injury [16-18]. Patients with cervical spinal cord injury are likely to inhale stomach contents and cause aspiration. Factors such as intake of food or alcohol, changes in mental state, impaired airway reflex and reduced gastric peristalsis can increase the risk of reflux and aspiration of gastric contents. Acute aspiration of gastric contents can lead to serious consequences, such as respiratory failure, bronchospasm, chemical pneumonia, bacterial pneumonia and adult respiratory distress syndrome (ARDS). Acute aspiration of gastric contents usually occurs in the early stage of admission. Of course, patients in the rehabilitation stage of spinal cord injury are also at risk of mistakenly inhaling mouth or stomach contents, which is caused by speech and swallowing dysfunction after cervical spinal cord injury. The spinal cord injury of the seventh cervical vertebra can lead to the interruption of the sympathetic innervation of the airway, which originates from the upper thoracic vertebra (T1 to T6). The loss of sympathetic nerve function can not antagonize cholinergic bronchoconstriction, which will lead to an increase in bronchial tension [19]. Previous studies have suggested that the decrease in lung compliance in spinal cord injury is caused by chronic lung injury caused by repeated infection [20-25]. However, Scanlon[10] found that there was a significant decrease in lung compliance within one month after spinal cord injury, but there was no significant change in lung compliance within one year after spinal cord injury. This cannot be explained by previous views.

2. Neurogenic pulmonary edema

The respiratory complication is one of the most common complications of acute spinal cord injury, and it is also the main cause of death. Neurogenic pulmonary oedema (Neurogenic pulmonary oedema, NPE), first reported in 1908, is acute respiratory distress caused by severe sympathetic excitation caused by acute injury of the central nervous system [26, 27]. Neurogenic pulmonary oedema is an urgent and life-threatening complication caused by encephalitis, cerebral hemorrhage, traumatic brain injury, spinal cord injury, epilepsy, stroke, brain or spinal surgery. It is characterized by pulmonary vascular congestion, protein-rich edematous fluid exudation and intra-alveolar haemorrhage in patients with no cardiovascular or pulmonary pathological changes in the past [023][28]. The main clinical manifestations are dyspnea, shortness of breath, tachycardia, cyanosis and rales. Blood examination showed hypoxemia (low PaO2), PaO2/PiO2 ratio < 200and mild leukocytosis. Chest X-ray often showed bilateral alveolar opacity, no enlargement of the heart, with diffuse bilateral alveolar infiltration [29]. Although neurogenic pulmonary oedema was recognized by people many years ago, it has been ignored in clinical practice for a long time. Because we do not fully understand its pathophysiology and differential diagnosis, it is often misdiagnosed. Most clinicians always pay more attention to spinal cord nerve injury than lung problems,

and before all emergency interventions, this explosive and fatal complication often leads to sudden death, as a result, the serious clinical problem of neurogenic pulmonary edema is often ignored by doctors.

Although a large number of studies have been carried out, little is known about the pathogenesis of NPE. About the pathophysiological mechanism of NPE, the most frequently popularized theory is that excessive sympathetic stimulation causes a catecholamine storm and leads to systemic vasoconstriction. This theory is also known as blast theory[30]. The blast theory refers to the sudden increase of intracranial pressure caused by central nervous system injury, which leads to the dysfunction of the hypothalamus and nucleus of the solitary tract of the medulla oblongata, and the stress of the body leads to sympathetic nerve excitation. the content of catecholamine (epinephrine, norepinephrine, etc.) in the blood increased, and then the systemic vasoconstriction and hemodynamics changed sharply; the arterial blood pressure increased sharply, and a large amount of blood from the systemic circulation entered the pulmonary circulation. The effective filtration pressure of pulmonary capillary bed increased sharply, and a large amount of body fluid remained in the pulmonary tissue space, thus forming pulmonary oedema; at the same time, blood flow shock caused vascular endothelial cell injury, and due to the massive release of vasoactive substances (such as histamine and bradykinin) in the body, vascular permeability increased, and a large amount of plasma protein extravasation led to the further aggravation of acute pulmonary oedema [31].

In recent years, permeability defect theory has been gradually recognized. permeability defect theory holds that the occurrence of NPE is mediated by the sympathetic nervous system. Normally, α receptors (mainly α 1 receptor) in the lungs mediate the contraction of swollen micro-vessels and bronchial smooth machines, promoting the release of inflammatory mediators by mast cells and the secretion of respiratory glands. β-adrenoceptor mediates pulmonary microvascular and bronchiectasis, inhibits the release of inflammatory mediators, and promotes the secretion of surfactant by type II alveolar epithelial cells, thus increasing swelling compliance, dilating surrounding blood vessels and reducing heart load. accelerate the clearance of lung tissue fluid. In the process of NPE, pulmonary vascular α 1 receptor binds to agonists, which on the one hand mediates pulmonary vasoconstriction, causes the increase of pulmonary vascular hydrostatic pressure and vascular filtration pressure, and on the other hand increases the concentration of Ca2+ in pulmonary vascular endothelial cells, acting on the contractile components of the cytoskeleton, causing cell contraction and enlargement of cell junction space. At the same time, the cell membrane is damaged by a series of pathophysiological changes, which leads to the relaxation and shedding of endothelial cell junction, which leads to the increase of pulmonary capillary permeability. The mechanism of β-adrenoceptor reducing pulmonary vascular permeability may be the increase of cAMP content in pulmonary capillary endothelial cells, preventing the increase of intracellular Ca2+ concentration, inhibiting the activation of myosin light chain kinase, increasing the content of intracellular fibronectin, promoting cell relaxation, preventing endothelial cell space from expanding or narrowing the enlarged intercellular space, thus reducing pulmonary vascular permeability. When the sympathetic nerve is excited, the proportion of them is out of proportion, the excitability of α 1 receptor is increased and that of β receptor is decreased, which leads to NPE [32]. NPE not only has the advantages of acute onset, difficult treatment and high mortality but also provides a susceptible environment for pulmonary infection after spinal cord injury, which directly leads to the disturbance of pulmonary oxygen diffusion, which leads to severe hypoxemia and can further develop into acute respiratory distress syndrome (acute respiratory distress syndrome, ARDS).

A large number of studies at home and abroad generally believe that NPE is the result of the joint action of these two theories.

3. Remote effect

The remote effect refers to all kinds of injuries and reactions in the tissues or organs far away from the wound tract after the body is hit by projectiles. It is the result of the direct or indirect action of strong pressure waves. It may be related to the severe disturbance of body fluid caused by strong pressure waves acting on the circulatory pipeline. A naked eye examination is mostly patchy bleeding of organs, which is different from secondary miliary haemorrhage caused by neurohumoral factors after trauma [33, 34]. After the rapid invasion of the body, local high pressure is generated at the front end of the body, which spreads to the distance in the form of pressure waves, acting on the tissues or organs far away from the injury tract, causing damage. The degree of damage depends on the energy transferred to the tissue and the characteristics of the injured site. The ways of pressure wave transmission are usually as follows: ①Blood vessels. After the pressure wave acts on the blood vessel wall, the blood in the tube can be strongly disturbed by shock and vibration, and the energy can be transmitted to a distance, resulting in a sharp increase in the pressure of the blood vessels in the distant parts, bleeding in the distant organs and so on. ②Gastrointestinal tract. When the projectile penetrates or scrapes the gastrointestinal tract containing gas or liquid, the pressure wave can be transmitted to a distance through the gas or liquid in the organs, resulting in bleeding or perforation of the distal intestinal mucosa. ③Soft tissue. The pressure wave can radiate directly to the surrounding soft tissue, but the propagation distance is generally not very far. Some studies have suggested that the far-reaching effect plays

a secondary role in the occurrence of lung injury in spinal cord injury [34].

4. Immunodeficiency

Some studies have suggested that the cellular immune function of patients with spinal cord injury is suppressed, which can cause lung-specific and specific immune dysfunction. In specific immunity, the injury of cellular immune function is especially important. It is mainly due to the inhibition of the function of T cells and natural killer cells (NK cells), which is characterized by the decrease of the transformation and activation of T lymphocytes in peripheral blood, the decrease of proliferation response to cytokines, the increase of soluble IL-2 receptor, the decrease of the number and cytotoxic activity of NK cells, and so on. These changes may be the main causes of infection after injury. The loss of innervation of secondary lymphoid organs (such as the spleen) can induce secondary immunodeficiency (also known as immune paralysis), increasing susceptibility to infection [35].

As an organ with the functions of respiration, barrier defence, immunity, metabolic secretion and so on, the lung is often vulnerable to injury in the systemic effects of severe burns, trauma, spinal cord injury, cerebral ischemia and other diseases. The incidence of acute pulmonary dysfunction in MODS patients is as high as 83% - 100%. When SIRS occurs, the lungs are often the first to be involved, and severe cases can develop into ARDS. As one of the important complications affecting the prognosis of patients with spinal cord injury, pulmonary complications have high mortality, which has been paid great attention by scholars. Although the pathogenesis of this complication is still not very clear and there is a lack of effective treatment methods and means, with the further study of its mechanism, we can find effective prevention and treatment measures to deal with the complication. improve the survival rate and quality of life of patients.

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