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Research Progress on Metabolic Reprogramming in Cancer Cachexia and Intervention with Traditional Chinese Medicine Formulations

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Abstract: ***As a common complication of cancer, cachexia has a high prevalence and significantly affects patients' quality of life and prognosis. It is closely associated with sarcopenia, leading to decreased muscle mass and dysfunction. The metabolic mechanism of cachexia sarcopenia is complex, involving glucose, lipid, amino acid, nucleotide metabolism and other aspects. Traditional Chinese Medicine believes that sarcopenia belongs to the category of 'flaccidity syndrome', while tumor cachexia sarcopenia belongs to asthenic fatigue and thinness. The occurrence and development of this condition are believed to be caused by a deficiency of vital qi, which is thought to be related to a corresponding decline in the function of the spleen, liver, kidney and viscera function. With regard to the treatment of ailments, Traditional Chinese Medicine is founded upon the principle of invigorating the spleen, combined with the methods of benefiting qi and stomach, soothing liver and promoting qi, detoxifying and resolving masses, nourishing yin and activating blood circulation to alleviate the symptoms of sarcopenia. At present, Chinese patent medicines such as Kanglaite Injection, Kangai Injection, Zilongjin Tablets and Traditional Chinese Medicine compound have made progress in improving the symptoms of cachexia and sarcopenia, regulating metabolic mechanism and improving the quality of life. These studies provide new reference and ideas for the treatment of cancer cachexia and sarcopenia with Traditional Chinese Medicine.***

Keywords: Metabolic reprogramming, Cachexia; Sarcopenia, Chinese medicine compound, Chinese patent medicine**.**

1. Metabolic Reprogramming Mechanism of Cancer Cachexia Sarcopenia

As we all know, the existence of tumors can affect the metabolism of the whole body. Furthermore, metabolic switching represents a pivotal attribute of proliferative neoplasms [1]. The main function of this pathway is to facilitate the rapid growth and proliferation of tumour cells by regulating energy metabolism. The pathway primarily provides ATP rapidly through the glycolytic pathway, or obtains macromolecular substances through the gluconeogenesis pathway (PPP) [2]. Additionally, malignant cells can also promote their own proliferation through amino acid metabolism (such as glutamic acid, serine, arginine, branched-chain amino acids) and lipid metabolism in tumor cells [3].

1.1 Glucose Metabolism in Tumor Cachexia Sarcopenia

The energy required for rapid proliferation of cancer cells is mainly obtained through glucose metabolism [4]. This process involves the utilisation of glucose oxidative phosphorylation (OXPHOS) and glycolysis as metabolic pathways [5]. The Warburg effect (aerobic glycolysis) postulates that malignant cells utilize the glycolysis pathway to acquire energy under aerobic conditions. The high expression of a variety of oncogenes (such as MYC, HIF-1α, NF-κB and OCT1) and their targeted metabolic enzymes, such as hexokinase (HK), pyruvate kinase (PKM2), phosphofructokinase (PFK), lactate dehydrogenase (LDHA) [6] can promote the glycolysis process and provide energy for tumor cell growth [4]. Tan X et al. found that the incidence of sarcopenia was inversely proportional to muscle glycogen metabolism in subjects with diffuse large B-cell lymphoma (DLBCL) [7]. The demand for glucose by tumour cells is significantly higher than that observed in non-tumour cells [8]. Therefore, most tumor cells uptake glucose at high speed by up-regulating the level of glucose transporter (GLUT) [9] LI. B et al. found that GLUT1 and GLUT3 were markedly overexpressed in tissues from patients with head and neck squamous cell carcinoma (HNSCC) [10]and increased the rate of glucose conversion to lactic acid. The initial stage of the glycolytic pathway is the activation of glucose through phosphorylation by hexokinase (HK), resulting in the formation of glucose-6-phosphate (G6P). PFK-1 is a catalyst for the conversion of fructose 6-phosphate (F6P) to fructose 1, 6-bisphosphate (F1, 6-BP). PK transfers highly energetic phosphorus from phosphoenolpyruvate (PEP) to ADP to produce ATP and pyruvate [11]. Zambrano A et al. found that hexokinase 2 (HK2) was also up-regulated during glucose phosphorylation, and pyruvate was reduced to lactic acid by LDHA in the cytoplasm, or converted into acetyl coenzyme A (CoA) to enter the mitochondria for the Krebs cycle and provide ATP according to OXPHOS [12]. Also of note is another pathway of glycolysis, the pentose phosphate pathway (PPP). Under aerobic conditions, PPP produces both reduced nicotinamide adenine dinucleotide phosphate (NADPH) and ribulose 5-phosphate (Ru5P). In a series of reversible reactions under anaerobic conditions, PPP produces pentose phosphate for ribonucleotide synthesis. Olaechea et al. found a direct correlation between tumour glucose uptake and cancer-related weight loss in a 18F-FDG cancer-related weight loss experiment in non-small cell lung cancer [13]. There is also metabolic crosstalk between glucose, amino acid and lipid metabolism, complicating the metabolic reprogramming mechanism Figure 1.

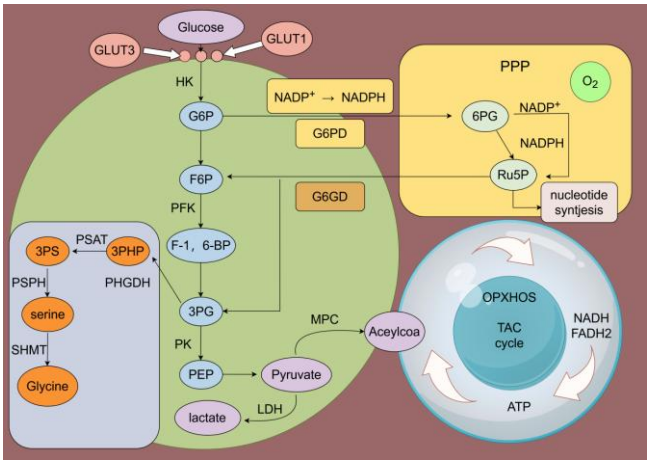

Figure 1: Metabolic reprogramming of glucose. 1. Glucose; 2. GLUT1 - Glucose Transporter 1; 3. GLUT3 - Glucose Transporter 3; 4. PPP - Pentose Phosphate Pathway; 5. HK - Hexokinase; 6. NADP+ - Nicotinamide adenine dinucleotide phosphate; 7. NADPH - Nicotinamide adenine dinucleotide phosphate (reduced form); 8. G6P - Glucose-6-phosphate; 9. 6PG - 6-Phosphogluconate; 10. G6PD - Glucose-6-phosphate dehydrogenase; 11. F6P - Fructose-6-phosphate; 12. Ru5P - Ribulose-5-phosphate; 13. G6GD - Glucose-6-phosphate dehydrogenase; 14. nucleotide; 15. PFK - Phosphofructokinase; 16. synthesis; 17. PSAT - Phosphoserine aminotransferase; 18. F-1, 6-BP - Fructose-1, 6-bisphosphate; 19. 3PS - 3-Phosphoserine; 20. 3PHP - 3-Phosphohydroxypyruvate; 21. PSPH - Phosphoserine phosphatase; 22. PHGDH - Phosphoglycerate dehydrogenase

1.2 Lipid Metabolism in Tumor Cachexia Sarcopenia

Cancer-associated cachexia (CAC) involves crosstalk between fatty tissue and other systems (such as muscle tissue and the immune system) [14]. Fat metabolism is dominated by the oxidation of fatty acids (FAOs), the synthesis of fatty acids (FAs) and the esterification of cholesterol [5]. FAO is an important part of lipid metabolism. Di Lu et al. confirmed in the correlation experiment between sarcopenia and hepatocellular carcinoma (HCC) that CHI3L1 disrupts lipometabolism by promoting lipid peroxidation and fatty acid oxidation, and found that the level of CHI3L1 increased in atrophic muscle tissue [15]. Fatty acid synthesisIn the secondary stage of the glycolysis process, PPP makes the active metabolites necessary for lipid metabolism [16]. Cancer cells often exhibit remodeling of lipid metabolism, including fatty acid transport, de novo synthesis (DNL), storage in lipid droplets (LD), and β-oxidation to produce ATP [17]. Cancer cells meet their high metabolic needs with DNL. DNL pathway begins with acetyl CoA, which is activated by acetylCoA carboxylase to produce malonylCoA, and then forms saturated fatty acids (SFA) under the influence of fatty acid synthase. SFA can be extended by the very long chain fatty acid gene family (ELOVL), and then desaturated by stearoyl CoA desaturase or fatty acid desaturase to form monounsaturated fatty acids, such as oleic acid (OA) and palmitoleic acid [18]. Cancer cells rely on specific transporters (such as fatty acid translocase, fatty acid transporter family, plasma membrane fatty acid binding protein) to uptake exogenous FA, and the up-regulation of these proteins will increase cell SFA, polyunsaturated fatty acid (PUFA) and cholesterol levels [17]. Cholesterol synthesis relies on acetyl-CoA to synthesize related enzymes such as HMG-CoA reductase in cells to activate the mevalonate pathway [19] Figure2.

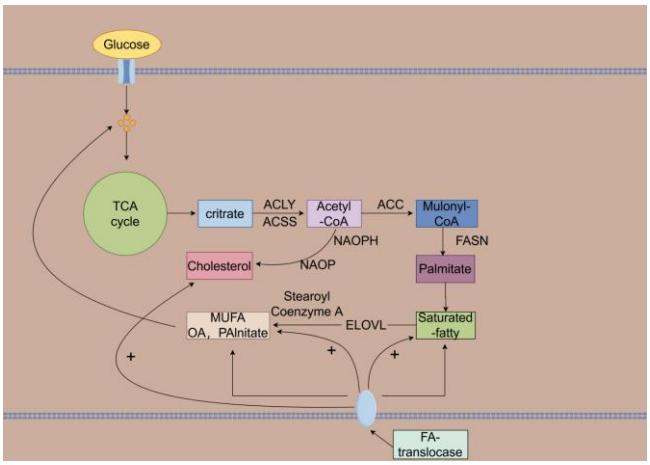

Figure 2: Metabolic reprogramming of lipids.

1.3 Sarcopenia and Amino Acid Metabolism Related to Tumor Cachexia

The metabolism of amino acids varies from tumor to tumor. In branched-chain amino acids (BCAA), leucine is a protein decomposition product, and isoleucine and valine provide carbon precursors for the synthesis of glucose or other precursor molecules. BCAA is transaminated to α-ketoglutarate, glutamic acid and branched α-ketoacids (BCKAs) by branched aminotransferases (BCATs). After decarboxylation and dehydrogenation by the branched-chain α-keto acid dehydrogenase (BCKDH), BCKAs are oxidised into substrate for biosynthesis or energy production [20]. Elevated levels of BCAA in both plasma and tumour tissue and abnormal activation of the mTORC1 signalling pathway have been observed in HCC, mammary cancer, leukaemias, advanced pancreatic cancer (PDAC) and kidney cancer [21]. An experiment has shown that BCAAs can enhance ATG5 levels in the rats and increase the rate of autophagic degradation to induce the onset and evolution of squamous cell lung carcinoma (SCLC) [22]. Leucine metabolite, β-hydroxy-β-methylbutyrate (HMB), can reduce protein degradation and relieve muscle loss. It is composed of supplements with arginine and glutamine to intervene in the nutritional status of cancer cachexia patients and improve body weight [23]. However, one study compared the weight of patients with refractory cachexia and found that this improvement was not obvious. HMB may be used as a nutritional intervention agent for clinical low-grade cancerous sarcopenia. In addition to BACC, the metabolic relationship between aspartic acid and glutamic acid in stromal cells, especially cancer-related fibroblasts and cancer cells, has been paid more and more attention.

In cancer cells, glutamine drives the tricarboxylic acid cycle to maintain ATP production [24, 25], and glycine, serine, glutamine, and aspartic acid extract carbon and nitrogen to maintain purine biosynthesis. In muscle, the L-isoform of aspartic acid acts as a carrier of BCAA amino groups to ensure the synthesis of alanine and glutamine. This is a process in which cancerous cells use the carbonic backbone and reducing nitrogen of glutamine to produce a variety of substances (nonessential aminos, hexosamine, reducing enzyme glutathione, nuclear nucleotides, proteines and

lipoids). The aspartic acid and malic acid in the cell membrane are used for the production of NADPH [26]. See Figure 3.

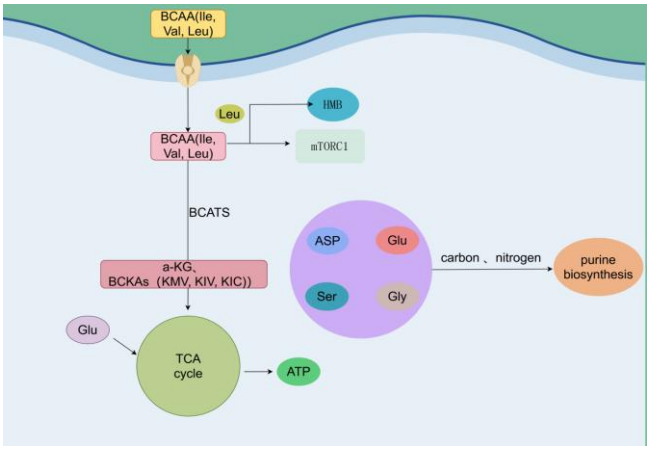

Figure 3: Amino acid metabolism reprogramming. 1. BCAA(Ile, Val, Leu): Isoleucine, Valine, Leucine; 2. BCATS: Branched-chain amino acid transaminase; 3. BCKAs(KMV, KIV, KIC): Branched-chain keto acids: (Alpha ketoisovaleric acid, alpha ketoisobutyric acid, alpha ketoacetic acid); 4. ASP: Aspartic acid; 5. Glu: Glutamic acid; 6. Gly: Glycine; 7. HMB: Beta-Hydroxy Beta-Methylbutyrate; 8. Leu: Leucine; 9. a-KG: Alpha-ketoglutarate; 10. Ser: Serine; 11. TCA: Tricarboxylic acid cycle; 12. ATP: Adenosine triphosphate

2. Progress in the Research of Traditional Chinese Medicine in the Treatment of Sarcopenia Due to Tumour Cachexia

At present, the mainstream clinical treatment of cancer is still surgery, radiotherapy, chemotherapy, immunotherapy, targeted treatment. Traditional Chinese Medicine (Traditional Chinese Medicine) has been used for thousands of years to treat cancer. It is used as an alternative or adjuvant therapy for cancer [27]. According to Traditional Chinese Medicine syndrome differentiation, sarcopenia belongs to the categories of 'flaccidity syndrome', 'flesh flaccidity', 'consumptive disease', 'thinness' and so on. 'huangdi neijing' Cloud 'The muscle of the spleen governing the body... Muscle is not benevolent, hair for meat flaccidity', more 'treatment of flaccidity alone take Yangming' point of view. In Traditional Chinese Medicine, the onset and development of cancer is considered to be 'healthy qi deficiency' by Traditional Chinese Medicine. 'Huangdi Neijing' cloud 'healthy qi is stored in the body, and the evil cannot be done; the evil of the together, the gas will be virtual. Reveals the general principles of the disease. Most of the internal injury flaccidity syndrome is caused by deficiency, which is primarily connected with the function of the spleen, liver and kidneys. Sarcopenia associated with tumor cachexia is more appropriate. Sarcopenia is first seen in 'Synopsis of the Golden Chamber', which refers to the collective term of chronically weak disease with weak visceral function caused by long-term illness or old and weak body, and lack of qi, blood, yin and yang. Some scholars of Traditional Chinese Medicine believe tumor cachexia is more in line with the characteristics of sarcopenia than deficiency and fatigue in Traditional Chinese Medicine. In clinical treatment, the adjuvant therapy of Traditional Chinese Medicine injection and Traditional Chinese Medicine compound still has great potential, which is worthy of attention and research.

2.1 Clinical Research of Traditional Chinese Medicine Injection

Several studies show that Traditional Chinese Medicine can effectively enhance the patient's quality of life and reduce the side effects of anti-tumour treatment, which has unique advantages. As a kind of Traditional Chinese Medicine injection, Kanglaite injection is a type of Traditional Chinese Medicine formulation of coix seed, which is widely used in the supportive management of NSCLC, HCC and GC or cancer complications (such as malignant pleural effusion). Research has shown that muscle wasting in people with wasting due to cancer is mainly caused by the activation of NF-κB, which stimulates the expression of MuRF-1, leading to degradation of proteins in muscle tissue. [28]. Excessive reduction of fat is also often accompanied by muscle loss [29]. Coix seed oil inhibits muscle atrophy and systemic inflammation through the NF-κB pathway, and inhibits adipose tissue atrophy through the AMPK-HSL pathway [30]. In recent years, the Chinese patented medicine Aidi Injection has also been used as an adjunctive drug to chemotherapy. It has the effects of benefiting qi, dispersing knots and consolidating the root. It has been used to treat primary liver cancer, lung cancer, gastric cancer, colon cancer, lymphadenoma, breast cancer, etc. Wu C et al. found that breast cancer patients with Aidi injection combined with chemotherapy and chemotherapy cycles > 3 and non-significant heterogeneity had significantly improved physical status and reduced chemotherapy toxicity [31]. The aglycone contained in Astragalus membranaceus can promote muscle hypertrophy in vitro, inhibit the excretion of TNF-α and IL-6, and quickly restore muscle strength [32]. Formononetin, as a bioactive isoflavone compound derived from Astragalus membranaceus, can also improve muscle atrophy [33]. Experiments have confirmed that ginseng extract (ginsenosides, ginseng total protein, Gintonin) has a powerful protective effect against in vitro and in vivo muscle atrophy. It affects cachexia sarcopenia by interfering with the secretion of TNF-α and IL-6 factors and the Akt / mTOR pathway [34]. Inhibition of NF-κB signaling reduces oxidative damage to myoblasts and restores mitochondrial function [35]. This may be another mechanism of Aidi injection in the treatment of tumor cachexia sarcopenia. Kang 'ai injection contains extracts of ginseng, astragalus and sophora flavescens. Oxymatrine can promote the differentiation of mouse myoblasts and reduce myotube atrophy [36]. Many experiments have proven that Kang'ai can improve the clinical efficacy of targeted drugs, decrease toxicity and improve the weight of cancer patients [37]. Shenmai injection Yiqi Yangyin, thereby improving cancer fatigue. ZhengZ et al. found that Shenmai injection can inhibit the levels of TNF-α and IL-6 inflammatory factors and improve the function of rat myocardial endothelial cells [38]. Studies have confirmed that it is an inhibitor of cell proliferation and a regulator of glycolysis through the AKT-mTOR-c-Myc signal path [39]. Shenqi Fuzheng injection improves cancer fatigue by inhibiting IL-2, IFN-γ and TNF-α [40], and fatigue-related muscle mass loss [41].

2.2 Oral Chinese Patent Medicine Clinical Trial

For treating cancer, oral Chinese patent medicine is convenient and can be used as a supplementary treatment. For example, Cinobufotalin capsules in combination with XELOX chemotherapy can markedly reduce the overall clinical discomforts and improve the quality of life of patients with locally advanced rectal cancer. Wu Q and other research has confirmed Cinobufotalin inhibits the development of G6 PD to affect the formation of NADPH and the manufacture of fatty acids and nucleic acids in liver tumour cells [42]. Some studies have shown that cinobufotalin reduces the side effects of chemotherapy, induce apoptosis, inhibit the inflammatory microenvironment and affect the malignant progression of tumors in the treatment of breast cancer, colorectal cancer, gastric cancer, lung cancer, liver cancer and other tumors [43]. Zilongjin tablets also have obvious anti-tumor effects on multiple cancers (lung cancer, adenocarcinoma, bladder cancer, kidney cancer, gastric cancer, etc.), reduce tumor intake of nutrients, and relieve the energy metabolism pressure of normal cells. The Zhenyuan capsule has the effect of tonifying the qi and the spleen, tonifying the kidneys and filling the essence, regulating the qi and dissolving the phlegm, softening the hardness and dissolving the masses. In combination with paporizumab in advanced lung cancer, improve glycogen level in muscle and liver, relieve cancer fatigue and improve survival rate. The main component of Shenyi capsule is ginsenoside Rg3. Clinical trials have shown that Shenyi Capsule taken in connection with the SOX regimen in the therapy of primary liver cancer can effectively improve the cancer effects such as fatigue, anorexia and emaciation. Sheng et al. found that Babaodan can reduce the levels of TNF-α and IL-6, activate AMPK pathway and affect lipid metabolism [44]. These Chinese patented medicines are widely used to treat malignant tumours. However, their mechanism of action in cancer cachexia and cancer sarcopenia is still the subject of further investigation.

2.3 Clinical Study of Chinese Herbal Compound

Tumor-related muscle atrophy or reduction has become a dangerous sign of poor prognosis in cancer patients. According to the research of many ancient physicians and scholars on the disease, it is believed that the root cause is the loss of spleen and stomach in the middle energizer, resulting in insufficient fine metaplasia of water and grain, and the lack of qi and blood. It is difficult to replenish muscles. As ‘Taiping Shenghui Fang’ said : ‘The spleen and stomach, the essence of water and grain, into qi and blood, qi and blood, nutrient and defensive circulation, nourishing body shape, glory in muscle also ‘. The treatment of Traditional Chinese Medicine is based on the method of invigorating spleen, including invigorating spleen and stomach, invigorating spleen and detoxification, invigorating spleen and soothing liver and promoting qi, invigorating spleen and nourishing yin and activating blood, aiming at restoring spleen and stomach function and tonifying qi and blood to improve the symptoms of muscle atrophy.

2.3.1 Invigorating spleen and stomach qi

Tumor cachexia is a disease of continuous energy consumption. With the development of the disease, the side effects of surgery, radiotherapy, chemotherapy and other treatment methods have led to poor appetite and serious lack of energy intake in patients with tumor cachexia. Weight loss, muscle loss, fatigue, weakness, loss of appetite, etc. [45]. In recent years, people ‘s understanding of the physiological mechanism of appetite regulation in patients with tumor cachexia has been continuously improved. The arcuate nucleus (ARC) is an important region in the hypothalamus, which is strongly linked to the control of appetite and energy homeostasis, and promotes cocaine-amphetamine to regulate the release of transcription peptides and promelanin to inhibit feeding. Several other neuropeptides such as melanin-concentrating hormone, orexin, Nesfatin-1, and the role of the brainstem in controlling appetite have also been confirmed [46]. Neuropeptide Y (NPY) and agouti-related peptide (AgRP) have also been shown to be inhibited by leptin and insulin, another group of neurons controlled by ARC to stimulate appetite. Auxin-releasing peptides can stimulate appetite and have a synergistic effect on Y (NPY) / AgRP. The external compression of the tumour leads to physical blockage of the gastrointestinal system, which can immediately result in symptoms such as fatigue, dysphagia, gastric spasm, and poor absorption, leading to nutritional intake disorders. The systemic inflammatory response promotes the excessive catabolism of fat and protein. Activation of NF-κB has also been shown to be the main pathway leading to skeletal muscle atrophy and emaciation [47]. The above reasons, Traditional Chinese Medicine can be summarized as spleen and stomach injury, less qi and blood deficiency. Sijunzi Decoction has been a famous formula for treating spleen and stomach qi deficiency symptoms in China for hundreds of years. It is widely used in gastrointestinal diseases. At present, Sijunzi Decoction and its modified prescriptions Liujunzi Decoction and Xiangsha Liujunzi Decoction have been proved to be used in colorectal adenoma (CRA), NSCLC, GC, HCC and other tumor diseases. By restoring mitochondrial function in gastrointestinal tract muscle contraction, it can relieve spleen and stomach symptoms [48], control glycolysis, inhibit EMT and induce cancer cell apoptosis [49]. Liujunzi decoction can promote the secretion of auxin release peptide, improve tumor-associated anorexia and cancer cachexia and emotional stress caused by loss of appetite, weight loss and so on [50].

2.3.2 Spleen soothing liver qi

Anxiety and depression are common in cancer patients. Cancer patients have a heavy burden of thinking, ‘Huangdi Neijing’ cloud: ‘thinking is Qijie.’ The poor qi movement makes the stomach poor, the spleen is not healthy, and the patient’s mood is depressed, which also mentions: ‘Sorrowful, gas occlusion and no line. Liver depression and qi stagnation have an effect on the transport and transformation of the spleen and stomach, so that water and grain can not produce qi and blood, muscle dystrophy, which is not conducive to the prognosis of tumors. Related studies have shown that [51], physical dysfunction, depression, fear, and cancer-related fatigue (CRF) may have an impact on the quality of life of cancer patients. Qiu et al [52]. found that Xiaoyao Powder improved depression-like behavior and inhibited the LepR-STAT3 / PI3K pathway to improve glucose intolerance and enhance the expression of AGRP and NPY [53].

2.3.3 Jianpi Jiedu Sanjie

Traditional Chinese Medicine believes that the occurrence of

cancer cachexia sarcopenia is also closely related to cancer toxin, which belongs to the syndrome of deficiency in origin and excess in superficiality. Its aetiology is usually due to weakness of the spleen and stomach. With the prolongation of the disease, it affects other organs, resulting in imbalance of yin and yang, qi and blood, deficiency of healthy qi, phlegm, blood stasis, dampness and other pathological products condensed into cancer toxin in the body. Zhang Y et al [54] demonstrated that Baoyuan Jiedu Decoction prevents atrophy by downregulating the expression of E3 ubiquitinase atrogin-1 and MuRF-1, and can inhibit atrophy of lipid droplet area, inhibit weight loss, and regulate mitochondrial synthesis and function through the p38 MAPK / PGC-1α pathway to slow myotube atrophy [55]. In addition, Fuzheng Xiaoji Recipe can effectively alleviate the symptoms of pain, muscle and fat loss in patients. It plays a role in reducing toxicity and increasing efficacy in the treatment of tumours with combined traditional therapies. Chinese and Western medicine, reducing the level of inflammatory factors, improving nutritional status, alleviating poor appetite, less food, mental fatigue and other adverse conditions [56], and improve patients' quality of life.

2.3.4 Invigorating the Spleen, Nourishing the Yin and Activating the Blood Circulation

Due to the development of the tumour, the excessive consumption of qi and blood in the person's body has caused atrophy of the muscles. On the other hand, pathological products such as phlegm, blood stasis, and dampness are condensed into cancer toxins in the body to hinder the operation of qi and blood, long-term depression and fire, consumption of qi and coagulation, damage of yin fluid, and aggravation of body metabolism. Taohong Siwu Decoction is a classic blood circulation and yin nourishment formula. Clinical studies have confirmed its anti-aging, anti-tumor, immune regulation, anti-fatigue and other effects [57]. It is widely used in the adjuvant chemotherapy of breast cancer [58]. By regulating the expression of MYC, BIRC5, EGF and PIK3R1, it inhibits tumour cell proliferation and induces apoptosis. A kind of Jianpi Yangyin Huoxue decoction made up of a multitude of Traditional Chinese Medicine is based on a large number of outpatient and clinical accumulation, aiming at cancer cachexia, which is formulated after dialectical theory of Traditional Chinese Medicine. It is mainly composed of nine Traditional Chinese Medicines such as Astragalus membranaceus, ginseng, Atractylodes macrocephala, Scutellaria baicalensis, safflower, Polygonum cuspidatum and Lycii Fructus. We have proved that Jianpi Yangyin Huoxue Decoction can inhibit the level of inflammatory factors, improve appetite, alleviate tumor cachexia muscle atrophy and inhibit protein hydrolysis. Tassinari et al. confirmed that thalidomide can significantly inhibit muscle atrophy [59]. This drug combined with Jianpi Yangyin Huoxue Decoction can effectively reduce side effects such as gastro-intestinal reactions and bone-marrow suppression, and improve the nutritional status of patients. 'Blood stasis does not go, new blood does not grow ', correct the imbalance of yin and yang, qi and blood in patients, ensure the filling of qi and blood, in order to alleviate or even reverse the emaciation and muscle atrophy of tumor cachexia.

3. Discussion

Tumor cachexia sarcopenia is an important complication of cancer treatment. It is very important to study its metabolic mechanism to seek treatment. Tumor cells meet energy needs by regulating glycolysis and aerobic oxidative phosphorylation, while affecting muscle tissue metabolism. Changes in lipid metabolism affect energy balance and immune response, and aggravate cachexia. Amino acid metabolism involves the metabolic pathways, signaling pathways and metabolites of glutamic acid, aspartic acid, branched-chain and other amino acids. In addition, nucleotide metabolism is very important for the immune response, which is involved in the release of IL-12 by adenosine produced by tumour immune cells. The content of ATP, ADP, AMP and adenine nucleotides in the muscle tissue of patients with cancer cachexia sarcopenia is reduced, which is not related to nutritional intake. The use of xanthine oxidase inhibitors can reduce muscle atrophy. However, only from the three perspectives of glucose, amino acid and lipid metabolism, the description of the metabolic mechanism of cell microenvironment is not sufficient. We discussed the progress made in clinical research using Traditional Chinese Medicine to treat cancer cachexia sarcopenia, especially the potential and practical application of Traditional Chinese Medicine injection, oral Chinese patent medicine and Traditional Chinese Medicine compound in adjuvant therapy.

First of all, starting from the system of theory of Traditional Chinese Medicine, sarcopenia is classified as 'flaccidity syndrome', 'flesh flaccidity' and other categories, while sarcopenia related to cancer cachexia is asthenia, fatigue and thinness. Its occurrence and development are considered to be caused by 'deficiency of vital qi', which is strongly associated with deficiency of the spleen, liver, kidneys and other viscera functions, which provides theoretical support and medication guidance for the diagnosis and treatment of Traditional Chinese Medicine. Tumor cachexia sarcopenia is closely related to spleen and stomach function. The overall treatment principle takes the spleen-invigorating method as the core, restores the body function, and relieves muscle atrophy. In the later stage of the disease, anorexia and other symptoms lead to qi and blood deficiency. The clinical treatment of Traditional Chinese Medicine adopts the method of invigorating spleen and stomach qi, such as Sijunzi decoction, Qifuzheng injection, Shenyi capsule, Zhengyuan capsule, etc., to restore the function of spleen and stomach and fill qi and blood. In view of the liver depression and spleen deficiency caused by emotional factors, the method of invigorating the spleen, soothing the liver and promoting qi is adopted, such as Xiaoyao Powder, regulating qi movement and improving mood. For cancer toxin condensation, the technique of strengthening the spleen, detoxifying and dissipating knots is adopted, such as Fuzheng Xiaoji Prescription, Kanglaite Injection, Kangai Injection, Zilongjin Tablets and so on. In the later stage of the disease, the deficiency of qi and blood caused by long-term consumption of qi and blood leads to endogenous heat evil. The spile invigorating, yin nourishing and blood circulation activating method is adopted, such as Taohong Siwu Decoction, Yangyin Huoxue Decoction, Shenmai Injection, Babaodan and so on.

This paper reviews the research on metabolic reprogramming of cancer cachexia sarcopenia at home and abroad, the theoretical understanding of cancer cachexia sarcopenia in

Traditional Chinese Medicine and the application of clinical Traditional Chinese Medicine, so as to provide new ideas for the treatment of cancer cachexia sarcopenia. At present, although the use of Traditional Chinese Medicine in cancer treatment has made remarkable progress, there are still some problems. Firstly, the medical research of Traditional Chinese Medicine in the management of tumour cachexia sarcopenia is inadequate, and its mechanism of action and therapeutic mechanism need to be further elucidated, and lack of rich experimental studies and practical data. Second, the unification of standardisation and treatment of Traditional Chinese Medicine has not yet been achieved, which affects the universality of its clinical application.

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