

Commentary

Current concept of Spleen-Stomach theory and Spleen deficiency syndrome in TCM

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INTRODUCTION

Spleen-Stomach theory is an important constituent of the theoretical basis of Traditional Chinese Medicine (TCM), the Spleen here is not synonymous with the Spleen in western medicine anatomically, physiologically or pathophysiologically. Conceptually, Spleen-Stomach theory is a comprehensive one, it mainly involves the digestive system, its vegetative nervous system, immunologic function, hemopoiesis, muscle metabolism, endocrine function (thyroid, adrenal cortex and medulla), hepatic metabolic function, protein, nucleotide, energy, water and salt metabolism. Experimental researches on animal models and clinical studies on Spleen deficiency syndrome have yielded fruitful results in this field which lead to a better understanding of its mechanism and help open a new avenue for treatment of diseases relevant to Spleen deficiency.

Physiology of Spleen-Stomach^[1]

The Spleen-Stomach has various physiologic functions as follows: Spleen governs transport and transformation. Spleen-Stomach transforms food into nutrients which are the sources of Qi and blood. The nutrients include glucose, amino acids, lipid, cations-anions and trace elements. Stomach is considered a reservoir which empties into the intestine. Water and salt absorption depends also on the transportating function of Spleen-Stomach. Qi and blood are both vital to life, Qi means energy, blood points to circulating blood and its formed elements, blood and nutrients furnish nourishment to all organs and tissues of the body.

The up- and down-bearing function of Spleen-Stomach

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Stomach governs down-bearing function and Spleen governs up-bearing which signify the motility, secretory, assimilative, absorptive and dispersing functions of upper digestive tract, among which, gut hormones and functional activities of vegetative nervous system of the gut are involved. Dysfunction of up- and down-bearing function of Spleen-Stomach can cause gastrointestinal disturbances and various Spleen deficiency syndromes; furthermore, they may also affect the functions of other organs.

Spleen governs the flesh or muscles

Transport and transformation function of Spleen-Stomach provided nutrients for muscle and energy metabolism. When Spleen-Stomach is diseased, muscles will be atrophied and become asthenic.

Spleen governs thought

Brain activities depend normally on furnishing the nutrients, Qi (energy), blood, Yin and Yang. With adequate Qi and blood and normal function of Spleen-Stomach, brain activities can proceed normally.

Spleen manages blood

Spleen has hemopoietic functions; the blood encased within the vessels of all solid and hollow organs is managed by Spleen.

Relationship between Spleen-Stomach and other solid and hollow organs

Spleen and Heart The heart governs blood vessels and blood circulation. The lung is related to oxygen uptake. Dispersion of nutrients over the whole body depends on heart, lung and brain function which can also affect Spleen-Stomach motility and function.

Spleen and Kidney In TCM, the Kidney stores the body's essence, and its function also depends on the nutrients transformed by Spleen-Stomach. The transport and transformation function of Spleen-Stomach is also influenced by warming and nourishing functions of Kidney. The two are interrelated and mutually potentiating. The Kidney in TCM involves the genital-urinary system, sexual glands and hormones, immunologic function, nervous system and the heart in terms of western medicine. Spleen and Kidney are both

involved in water and salt metabolism. The Kidney-Yang denotes the hypothalamic-pituitary-adrenal, thyroid and gonadal axes, secretion of the corresponding hormones, sodium pump activity of red blood cells, caloric energy production and immunomodulating functions. The Kidney-Yin involves cAMP/cGMP activity.

Diagnostic approach and preventive treatment of Spleen-Stomach diseases^[2]

Spleen-Stomach theory forms the basis of diagnostic approach and treatment of Spleen-Stomach disease, according to the presence or absence of Stomach-Qi. Poor appetite signifies grave prognosis and absence of Stomach-Qi; good appetite signifies good prognosis and presence of Stomach-Qi. By looking at the complexion and feeling the strength of pulse, one can predict the prognosis of the patient. Sallow face is the usual manifestation of Spleen disease. Color of skin over thenar muscles reflects Cold or Heat. Cyanotic hue of vein over thenar region indicates Cold in the stomach, whereas redness shows Heat in the stomach. During convalescence from postoperative state or infectious diseases, doctors should prescribe those herbal medicine for replenishing and modulating the Spleen-Stomach function.

Spleen deficiency syndrome is a multi-system and multi-organal functional impairment, but mainly manifests as digestive tract disturbance. It can be classified into Spleen-Qi deficiency, Spleen-Yang deficiency and Spleen-Yin deficiency. The diagnostic criteria in common are poor appetite, abdominal fullness after meal, loose bowel movements, pale or sallow complexion. The characteristic features of Spleen-Qi deficiency are fatigue, asthenia, atrophied muscle, pale tongue with thin white coating and moderate, weak pulse. Spleen-Yang deficiency is characterized by cold limbs, fear of cold, puffy pale tongue with slippery coating and slow fine pulse. Spleen-Stomach-Yin deficiency has dry mouth, low urine output, dry stool, shrunken smooth bare, red tongue and rapid fine pulse.

Pathophysiology of Spleen deficiency^[1]

Clinical and animal studies were conducted with controls and statistical analysis made in the past years.

Changes in secretory and absorption functions of gastrointestinal tract

Salivary flow and salivary amylase activity. Salivary gland activity is related to Spleen function. In patients with chronic gastritis, gastric or duodenal ulcer or chronic colitis with Spleen deficiency syndrome, the salivary flow of parotid glands on citric acid stimulation decreased together with decrease in amylase activity. After Spleen-fortifying treatment, the condition was improved and normalized.

Gastrin and acid secretion. Serum gastrin level was found significantly lowered in Spleen deficiency syndrome but elevated after treatment. In peptic ulcer patients with Spleen deficiency, BAO and MAO were both significantly higher than normal. In chronic gastritis patients with Spleen deficiency, the day and night and 24h uropepsin activities were much decreased.

Pancreatic exocrine function, BT-PABA test. In peptic ulcer patients with Spleen deficiency, urine excretion of BT-PABA diminished. On treatment with Spleen-fortifying drugs, urine BT-PABA and amylase activity in chronic atrophic gastritis patients were increased.

Xylose excretion test. Decrease in xylose excretion in chronic atrophic gastritis patients with Spleen-deficiency syndrome indicated impaired absorption function of small intestine. After treatment, the xylose excretion rate was increased.

Motilin and gastrointestinal motility. In patients after major surgery on digestive tract with Spleen deficiency, serum motilin level was significantly higher than normal. The gastric tone was decreased with retention of fasting gastric juice but transit time of small and large intestine was reduced, resulting in rapid emptying, these motility disturbance led to loss of appetite and epigastric fullness after meal.

Structural and biochemical changes in gastric mucosa. In Spleen deficiency syndrome patients, the turnover rate of epithelial cells was hastened, showing a short life span. In the mucosal lamina propria of superficial gastritis with Spleen deficiency, the glandular atrophy was more severe, intestinal metaplasia more frequent, whereas in disharmonic Liver and Stomach type, the metaplasia was modest. Ultrastructural studies revealed reduced microvilli of epithelial cells, increased junctional width, membrane damage, swollen mitochondria with disrupted cristae and dilated endoplasm in parietal cells^[4] decreased pepsinogen granules within chief cells; increased plasma cell infiltration in lamina propria. These changes were not seen in disharmonic Liver and Stomach type. Substance P and VIP were found increased in sigmoid colon, correlated with loose bowel movement. Elevated cAMP levels in gastric mucosa and plasma of Spleen deficiency syndrome were found, and plasma cAMP/cGMP ratio was decreased markedly in those patients with intestinal metaplasia. Likewise, gastric mucosal SOD content and plasma LPO also decreased significantly; these might correlate with metaplasia.

Dysfunction of vegetative nervous system of GI tract

Cerebral cortical function is extensively suppressed, presented with unstable somatic evoked potential, diminished amplitude and poor reproducibility. The hypofunction of sympathetic nervous activity

manifested a decrease in skin electric potential activity, reactivity of peripheral vessels to cold, urine VMA contents as well as plasma dopamine hydroxylase level; all of them increased after adequate treatment. In these patients, blood acetylcholine level was elevated, usually accompanied by bradycardia and lower systolic and diastolic blood pressure; these indicated presence of relative hyperfunction of parasympathetic nervous activity.

Motility and secretion modulating functions of GI tract are relevant to gut hormones. Besides, they are also related to modulating function of the vegetative nervous system of GI tract. Deficiency of Spleen in chronic diarrhea and peptic ulcer patients have overactive parasympathetic nervous system in the majority and hyperactivity of both parasympathetic and sympathetic nervous system in a minority of the patients.

Immunologic functional changes

In Spleen deficiency patients, peripheral blood lymphocyte count is lower than normal. In patients with chronic hepatitis B with liver depression and Spleen deficiency, it is also lower than normal, but can be restored to near normal after Spleen-fortifying therapy. T cell subset study revealed significantly decreased total T cell and TH lymphocytes. Among cancer patients with Spleen deficiency, CD4 was lower than normal, whereas CD8 had no change. On treatment with astragalus and atractylodes, CD4 was elevated significantly.

Immunoglobulin G changed very little but the content of secretory IgA in GI disease with Spleen deficiency decreased significantly. After treatment with the Si Jun Zi decoction, these can be restored to the level of controls. Some Spleen-fortifying prescriptions can enhance proliferation of mice splenic cells and increase significantly the mice specific antibody secretory cell number, antigen-induced delayed allergic reaction and mixed lymphocytic reaction; they also enhance cytotoxic action of lymphocytes and promotes ConA-stimulated mice splenic cells to secrete IL-2. Phagocytic function of monocyte-macrophages also increase as seen by the clearance of carbon particles. In cancer-bearing patients, NK activity and TK activity are lowered but can be restored by Spleen-fortifying therapy. With Hp infection, these patients have a weaker lymphocyte and plasma cell infiltration and local SIgA response. It was believed that red blood cells also have the function of clearing circulatory immune complex and phagocytosis. Astragalus and Si Jun Zi decoction can restore the immunologic function of red blood cells, probably through their promoting effect on C₃b receptor expression and the activity on the red cells surface.

Recently, it was found that Spleen-deficiency

patients had a high frequency of HLA-B₁₂-whereas disharmony of Liver and Stomach patients had a high frequency of HLA-B15. These showed that immune response is closely related with vulnerability to disease.

Endocrine changes

Urine 17-ketosteroid was found significantly lower than normal but there was no significant change in 17-hydroxysteroids as compared with normals. In patients with Spleen deficiency the level of catecholamine was also low. There was thyroid hypofunction in Spleen deficiency patients, with total T₃ and fT₃ significantly lower than normals, whereas rT₃ was significantly higher; low metabolic rate, low skin temperature, poor tolerance to cold and lack of adaptation to environmental changes were also present. This poor tolerance to cold is a special feature of Spleen-Yang deficiency. Asthenia and loss of weight might also be due to hypofunction of thyroid.

Changes of fecal bacteria flora and *Helicobacter pylori*

In Spleen deficiency mice *Lactobacillus bifidus* and other lactobacilli were decreased but could be restored to normal after the Si Jun Zi decoction treatment. The enterobacteria pathogens were increased but could be reduced after treatment and *Helicobacter pylori* was also decreased in amount. Spleen-fortifying therapy lowers the rate of detection and amount of Hp^[3].

Changes of trace elements in blood

In chronic hepatic disease with Spleen-deficiency the blood Zn was significantly lower than normal, but Cu was on the reverse. Zn is important in enzymatic action, nucleic acid synthesis, membranous function of red blood cells, hemopoiesis and cell respiration. In Spleen-Yang deficiency serum Mg was increased, whereas in Spleen-Yin deficiency it was extremely low. Fe was elevated in Spleen Qi deficiency, and Spleen-Yang deficiency patient at the age of 50 to 60 years, and ten years after it was elevated. In Spleen-Qi deficiency Mn and Cr were both increased significantly^[4].

Muscle metabolism

The muscle glycogen and CPK activity in the quadriceps and plasma were all decreased significantly. The resulting asthenia, and muscular weakness were primarily due to energy depletion from lowered hepatic and muscle glycogen content. Besides, ATP, ADP and AMP contents were also much lowered, and LDH and succinyl dehydrogenase activities significantly elevated because of anaerobic glycolysis; those ions relevant to muscle contraction were decreased^[5].

Serum total free amino acids and essential

amino acids including branch chained amino acids were all decreased; lysine, valine, glycine, threonine, tryptophan, isoleucine, serine, alanine and histone were all lower than normal. These may all contribute to muscle emaciation.

Treatment of Spleen-deficiency syndrome^[1,6]

Many GI diseases, such as chronic atrophic gastritis, chronic pancreatitis with diarrhea, inflammatory bowel disease, coeliac disease may present Spleen-deficiency at certain stage of the disease. Because they have similar pathophysiology, they can be treated by the same principle but with emphasis on different aspects.

The Si Jun Zi decoction is the major Spleen-fortifying therapy for Spleen-deficiency syndrome, including Ginsen or Codonopsis, Atractylodes, Poria, Glycyrrhiza. It promotes absorption and dispersion of nutrients to the whole body, increases physical strength and mental activity, and has multiple effects on the digestive organs, immunity, hemopoiesis, blood circulation, hepatic synthetic function, muscle metabolism, etc. By adding Astragalus, the immunologic function and small intestinal muscular tone can also be increased.

Motility and absorptive function of GI tract

The Si Jun Zi decoction inhibits the small intestinal activity, presented with decrease of amplitude and spasmodic contraction of small intestine. It possesses anticholinergic effect as well as antihistaminic response. The inhibitory effect on intestinal tract is both neurogenic and myogenic. It also has modulating effect on the function of vegetative nervous system. In Spleen deficiency and Qi deficiency, there are inhibition of transport and sodium pump on the epithelial cells which can be restored by the Si Jun Zi decoction. Codonopsis-Poria-Atractylodes powder can promote absorption of water and chloride ion so as to improve the diarrhea of Spleen deficiency.

Immunologic function

The Si Jun Zi decoction promotes cellular immunity, enhances peritoneal macrophagic phagocytosis, corrects the immunosuppressive effect of cyclophosphamide and corticosteroids, and reduces the inhibitory effect on bone marrow and atrophy of thymus, Spleen by cyclophosphamide. Experimental study revealed that abundant extramedullary erythroblasts and active proliferation of lymphoblast control the atrophic effect of cyclophosphamide in adrenal cortex and testes, also decreases the toxic adverse effect of chemotherapeutic drugs. It also increases the humoral immunity by increasing antibody production for infected patients with Spleen deficiency, it ameliorates and restores the weight

loss of thymus in undernourished mice as well as the structure within the thymus such as the thickness of cortex/medulla ratio and the diameter of thymus cell nucleus to normal.

Hemopoietic action

Ginsen promotes marrow cell DNA and protein synthesis, and codonopsis promotes red blood cell formation. If ferrous sulfate is given concomitantly, restoration can be hastened.

Hepatic synthetic function

It can increase plasma albumin, hepatic RNA and glycogen contents in favor of tissue repair and hepatic detoxification.

Effect on skeletal muscle

In Spleen-Qi deficiency, the mitochondria decreases in number with decrease of oxidase, and increase of anaerobic glycolysis. The Si Jun Zi decoction can restore muscle glycogen, lipid, ATP synthesis and the ultrastructures of mitochondria to near normal; food consumed, body weight, physical strength and mental spirit all improved.

Blood circulation of gastric wall and mesentery

On the basis of the Si Jun Zi decoction, the addition of *Astragalus*, *Cinnamon Twig*, *Saussure*), *Tangerine Peel*, may dilate arterioles, increase capillary blood flow and tissue perfusion, and promote tissue repair.

Action of individual component of the Si Jun Zi decoction:

① Ginsen, small dose stimulates central nervous system and large dose inhibits it. Ginsen increases mental reactivity and the contents of dopamine, nor-epinephrine in the brain, promotes brain RNA and protein synthesis, increases blood supply, and blood oxygen to the brain; all these are the pharmacologic basis for increasing brain activity. Besides, it has anti-fatigue action and increases tolerance to cold. Ginsen enhances both cellular and humoral immunity, also activates the phagocytic function of macrophages and activity of NK cells, and in addition, it also induces interferon formation.

In the endocrine system, it enhances the hypothalamic-pituitary-adrenal cortical, thyroid and gonadal axis function. It increases cardiac contractility by inhibiting the sodium pump on cardiac muscle cell membrane. It promotes release of insulin and elevates blood insulin level, enhances the synthesis of protein, RNA and DNA, lowers blood lipid, and improves hepatocytic function. As a therapeutic drug for Spleen deficiency, emphasis should be laid on its systemic effect.

② Codonopsis, it also enhances immunologic function, both cellular and humoral immunity, and increases response to stress and

tolerability to hypoxemia. Codonopsis is important for Spleen-fortifying. It can antagonize the decrease in gastric mucosal content of prostaglandin E₂ and aminohe-xose induced by indomethacin and aspirin, and inhibits acid secretion, hence being useful for combating ulceration and mucosal damage. It can also modulate GI motility, and has bidirectional effect on intestinal motility. It can decrease blood viscosity by inhibiting platelet aggregation, and also has some vasodilating action. Furthermore, it has varying degrees of inhibition on the cyclo-oxygenase pathway, TXA₂ synthetase; and these are dose dependent.

③Atractylodes, being a representative of Spleen-fortifying drug, it modulates intestinal motility bidirectionally, increases smooth muscle tone of GI tract, improves the white slippery coating of tongue, and cellular and humoral immunity and protein synthesis. Moreover, it acts on the hypothalamic-putuitary-adrenal cortical axis.

④Poria, trelaxes smooth muscle of GI tract, diminishes the contraction amplitude, reduces acid secretion, and has anti-necrosis and anti-degenerative actions on hepatocytes in hepatitis. Its polysaccharide enhances cellular immunity, increases the weight of thymus and lymph node, and hence is used in treatment of cancer of GI tract.

⑤ Glycyrrhyza, having acidity lowering and antipasmodic actions, it diminishes the smooth muscle tone of the intestine, amplitude of contraction, and inhibits ileal contraction induced by acetylcholine. It also has anti-inflammatory and anti-allergic effects. It can increase the cytochrome P-450 content of hepatocytes, and detoxification effect. Besides, it has corticosteroidal effect.

⑥Astragalus, when added to the Si Jun Zi decoction, it can potentiate the immuno-enhancing effect, including induction of interferon production and increase in antibody formation. Astragalus also increases cardiac contractility, in particular, the ejection fraction, promotes blood cells formation and maturation, restores the reticulocytes and megakareocytes to normal. Through activation of phosphorylase mediated by cAMP, it can promote mitosis, differentiation and growth of marrow cells. Furthermore, it increases the RNA, DNA and protein synthesis of the liver. It has an antioxidant action. Moreover, it may increase corticoid secretion and elevates the plasma level of cortisol. It has long been used in treatment of atrophic gastritis, peptic ulcer and other gastrointestinal diseases with Spleen deficiency by increasing cAMP content for gastric mucosal repair. It is also used in chronic hepatitis with Spleen deficiency to increase hepatocytic RNA, DNA and protein synthesis.

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