

Research Progress on the Correlation between Gut Microbiota-Mediated Spleen-transportation Dysfunction and Endocrine-metabolic Disorders and Regulation by Traditional Chinese Medicine

Jiamin Li¹, Mingli Yang^{2,*}

¹The First Clinical Medical College, Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

²Shaanxi Provincial Hospital of Chinese Medicine, Xi'an 710003, Shaanxi, China

*Correspondence Author

Abstract: *Endocrine-metabolic diseases with high morbidity and frequent comorbidities severely threaten human health, and gut microbiota dysbiosis is closely involved in their pathogenesis. The TCM theory of “the spleen governs transportation-transformation” is highly consistent with intestinal microecology. A bidirectional regulatory relationship exists between spleen-transportation dysfunction and gut microbiota imbalance. Spleen deficiency disrupts microbiota homeostasis, and microbial dysbiosis further impairs spleen-stomach function, mediating chronic low-grade inflammation and insulin resistance via the intestinal barrier and gut-metabolic axis, thereby inducing type 2 diabetes mellitus, obesity, metabolic syndrome and polycystic ovary syndrome. With the core strategy of spleen-tonifying and microbiota-regulating, traditional Chinese medicine improves metabolic disorders by regulating gut microbiota and repairing intestinal barrier through herbal compounds, active ingredients and non-pharmacological therapies, showing unique advantages in preventing and treating metabolic diseases. Current studies are limited by unclear syndrome biomarkers, insufficient high-quality clinical evidence and incomplete mechanistic interpretation. Future standardized research combined with multi-omics techniques is required to explore spleen deficiency-related microbial characteristics, clarify TCM regulatory mechanisms, and promote clinical translational application.*

Keywords: Spleen-transportation dysfunction, Gut microbiota, Endocrine-metabolic diseases, Spleen-tonifying and microbiota-regulating, Gut-metabolic axis.

1. Introduction

Endocrine-metabolic diseases include glycolipid metabolic disorders, obesity, metabolic syndrome, polycystic ovary syndrome (PCOS), and others. These diseases frequently co-occur in clinical practice, with insulin resistance, chronic low-grade inflammation and gut microbiota dysbiosis as their shared pathological bases [1] [2] [3], and have become a major public-health concern [4]. Modern studies have confirmed that gut microbiota imbalance participates in metabolic disorders by modulating the production of short-chain fatty acids (SCFAs), disrupting the intestinal mucosal barrier and triggering chronic low-grade inflammation. The gut-islet axis and gut-gonadal axis have become research hotspots in the field of endocrinology [5] [6] [7].

Traditional Chinese medicine (TCM) does not possess the modern concept of “gut microbiota”. Nevertheless, the TCM theory of “the spleen governs transportation and transformation” covers the whole processes of food digestion, nutrient absorption and distribution, as well as waste excretion, which is highly consistent with intestinal digestion and microecological homeostasis [8]. Improper diet, excessive intake of fatty-rich foods, physical-mental overstrain and emotional disturbance can impair the spleen-stomach. Spleen-transportation dysfunction prevents food-grain nutrients from generating qi and blood, and gives rise to phlegm-dampness and turbid grease, which constitutes the core pathogenesis of metabolic diseases [9]. The spleen-deficiency state is often accompanied by decreased microbiota diversity, reduced abundance of beneficial

bacteria and proliferation of pathogenic bacteria [10] [11]. Most existing reviews focus on the microbiota-regulating effects of Chinese herbal medicines for single diseases, while few sort out the common mechanisms by which gut microbiota mediates multiple comorbid endocrine-metabolic diseases from the pathogenesis of “spleen-transportation dysfunction”. Centering on the logical chain of “spleen-transportation dysfunction-gut microbiota dysbiosis-endocrine-metabolic disorders”, this paper summarizes evidence from both TCM and modern medicine, reviews the research status of “strengthening the spleen to regulate gut microbiota”, analyzes existing limitations, and provides research ideas for TCM intervention on comorbid metabolic diseases.

2. Tracing the Origin of “The Spleen Governs Transportation and Transformation” and Its Modern Connotation

2.1 Traditional Understanding of “The Spleen Governs Transportation and Transformation”

The theory of “the spleen governs transportation and transformation” originates from *Huangdi Neijing* (Huang-Di's Internal Classic), which includes two aspects: transportation-transformation of food-grains and transportation-transformation of water-dampness. The spleen-stomach is the acquired foundation and the pivot for qi movement ascent-descent. Sound function of the spleen-transportation ensures abundant qi and blood; spleen-transportation dysfunction leads to stagnation of water-

dampness and endogenous generation of phlegm-turbidity [12]. The “spleen” in traditional Chinese medicine is not an anatomical entity but a functional system integrating digestion, substance metabolism and energy metabolism [13].

2.2 Extension of Spleen Theory from a Metabolic Perspective

Modern physicians have extended the spleen theory and proposed that the spleen governs both qi movement and grease-lipid transportation [14]. Grease-lipids belong to food-grain essence. Spleen-transportation dysfunction results in disordered grease-lipid metabolism and internal accumulation, which may induce obesity, lipid turbidity and wasting-thirst disorder. The theory of “the spleen stores nutrient-essence” in *Lingshu · Benshen* states that the spleen possesses dual functions of “transporting” and “storing” nutrients; dysfunction of transportation-storage corresponds to modern-concept energy imbalance and ectopic lipid deposition [15].

2.3 Gut Microbiota: Hypothesis on Microcosmic Carrier of Spleen Transportation-transformation Function

The intestine pertains to the spleen system, and spleen transportation-transformation is dependent on the physiological activities of the intestine [10]. Gut microbiota participates in food degradation, the production of SCFAs and bile acids, and regulates the intestinal barrier and systemic inflammatory responses, which is highly consistent with the spleen’s functions of “transforming food-grains, transporting nutrient-essence and excreting waste residues” [16]. Accordingly, a hypothesis is put forward: gut microbiota homeostasis serves as the microcosmic substance carrier of spleen transportation-transformation function. Sufficient spleen-qi maintains balanced microbiota structure; spleen-transportation dysfunction triggers microecological disturbance and abnormal metabolites, thereby inducing systemic metabolic diseases [17].

3. Intrinsic Association between Spleen-transportation Dysfunction and Gut Microbiota Dysbiosis

3.1 Spleen-transportation Dysfunction, Waste Excretion Disorder and Disturbed Microbiota Homeostasis

Spleen-deficiency-induced transportation-transformation dysfunction alters the intestinal microenvironment and directly disturbs the microbiota composition. Clinically, patients with spleen deficiency show an elevated Firmicutes/Bacteroidetes ratio in feces, decreased abundance of SCFA-producing beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, increased opportunistic pathogens, and reduced microbiota diversity [18]. Spleen-transportation dysfunction with internal retention of water-dampness creates an intestinal damp-turbid microenvironment that inhibits beneficial bacteria and promotes the proliferation of pathogenic bacteria, which represents the microcosmic manifestation of the TCM principle “spleen deficiency generates dampness, and damp-turbidity disturbs the intestine” [19]. Rats with spleen-deficiency model induced by high-fat diet plus senna extract exhibit gut microbiota dysbiosis, accompanied by

intestinal mucosal villus atrophy and down-regulated expression of tight-junction proteins [20].

3.2 Gut Microbiota Dysbiosis Impairs Spleen-Stomach Function and Forms a Vicious Cycle

Gut microbiota dysbiosis is not a passive consequence of spleen deficiency; instead, the two form a bidirectional vicious cycle. Massive proliferation of Gram-negative bacteria releases lipopolysaccharides, which disrupt the intestinal mucosal barrier, trigger chronic low-grade inflammation, interfere with gastrointestinal hormone secretion and inhibit gastrointestinal motility, thereby producing spleen-deficiency manifestations such as poor appetite, abdominal distension and loose stools [21]. Abnormal metabolites enter the bloodstream, disturbing energy metabolism, consuming spleen-qi and aggravating phlegm-turbidity, which leads to recurrent and persistent metabolic diseases [22].

3.3 Intestinal Mucosal Barrier and Gut-metabolic Axis as Connecting Bridges

The intestinal mucosal barrier serves as the structural basis for the interaction between the spleen and gut microbiota. Sufficient spleen-qi maintains intact and compact intestinal mucosa; spleen-transportation dysfunction damages tight junctions, increases intestinal permeability and gives rise to “leaky gut” [23]. Gut microbiota and their metabolites enter the bloodstream through the impaired mucosa, acting on the liver, pancreas, adipose tissue and gonads via the generalized gut-metabolic axis. They mediate insulin resistance as well as glycolipid-sex hormone disorders, constructing the pathological pathway of “spleen-transportation dysfunction-gut microbiota dysbiosis-systemic endocrine-metabolic disorders”. As critical branches of the gut-metabolic axis, the gut-islet axis and gut-gonadal axis provide modern biological interpretation for the TCM theory that “spleen disease involves multiple zang-fu organs” [24] [25].

4. Common Endocrine-metabolic Diseases Induced by Gut Microbiota-Mediated Spleen-transportation Dysfunction

4.1 Type 2 Diabetes Mellitus and Insulin Resistance

Type 2 diabetes mellitus falls under the categories of “wasting-thirst disorder” and “spleen-thirst” in traditional Chinese medicine, with spleen deficiency and phlegm-turbidity as its core pathogenesis. Gut microbiota dysbiosis induced by spleen deficiency leads to insufficient production of SCFAs. Lipopolysaccharides released by Gram-negative bacteria activate the TLR4/NF- κ B pathway, trigger chronic low-grade inflammation, inhibit the IRS-PI3K-Akt insulin signaling pathway, and induce insulin resistance. SCFAs promote GLP-1 secretion via GPR41/43 receptors to protect islet function. In the state of spleen deficiency, the level of SCFAs declines, and this protective effect is impaired, which further aggravates glucose metabolic injury.

4.2 Obesity and Metabolic Syndrome

Excessive intake of fatty-sweet foods impairs spleen

transportation-transformation, resulting in disordered grease-lipid transportation and accumulation of phlegm-dampness and turbid lipids, which further leads to obesity and metabolic syndrome. Under spleen-deficiency conditions, the abundance of Firmicutes increases while that of Bacteroidetes decreases. The gut microbiota enhances energy extraction from food, promoting lipid synthesis and ectopic lipid deposition [26]. Dysregulated gut microbiota accelerates hepatic lipogenesis via the gut-liver axis, triggers adipose tissue inflammation, and induces insulin resistance. According to the theory of “the spleen stores nutrient-essence”, dysfunction of the spleen-stomach qi-transformation pivot acts as the initiating factor of metabolic syndrome [15].

4.3 Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology. From the perspective of traditional Chinese medicine, its pathogenesis is mostly attributed to spleen deficiency and phlegm-dampness. Gut microbiota dysbiosis reduces intestinal androgen inactivation capacity through the gut-gonadal axis. Chronic inflammation aggravates insulin resistance, and hyperinsulinemia further stimulates ovarian androgen secretion, forming a vicious cycle of “insulin resistance-hyperandrogenism” [27]. Patients with PCOS of spleen-deficiency-phlegm-dampness type exhibit decreased beneficial bacteria and enrichment of pro-inflammatory microbiota, which provides microcosmic evidence for treating PCOS from the spleen [25].

5. Research Status of TCM “Spleen-Tonifying and Microbiota-Regulating” Intervention for Endocrine-metabolic Diseases

Traditional Chinese medicine takes tonifying spleen-qi and activating the spleen to resolve turbidity as the core strategy. It remodels gut microecology, repairs intestinal barrier, modulates SCFAs, alleviates chronic inflammation and ameliorates endocrine-metabolic disorders through compound prescriptions, active components of Chinese materia medica and non-pharmacological therapies. Representative compound prescriptions include Sijunzi Decoction, Shenling Baizhu Powder, Linggui Zhugan Decoction, Cangfu Daotan Pill and Erchen Decoction, which are capable of regulating microbiota composition and improving insulin resistance, hyperandrogenism and ovulatory dysfunction. Active components from spleen-tonifying herbs such as astragalus polysaccharide, poria cocos polysaccharide, atractylenolide and Chinese yam polysaccharide exert metabolic regulatory effects mainly via host-gut microbiota interaction [28]. Acupuncture -moxibustion, medicinal-food homologous dietary therapy and acupoint application can improve microbiota structure and inflammatory status in patients with spleen deficiency, yet high-quality mechanistic researches are still scarce.

6. Existing Problems in Current Researches

Obvious limitations exist in current studies: there is no universally-recognized specific microbiota characteristic

spectrum for each syndrome-differentiation subtype of spleen deficiency. Confounding factors such as sequencing platforms, geographical regions and age lead to substantial heterogeneity of results, which restricts the application of microbiota indicators in objective TCM syndrome differentiation. Most studies are based on animal experiments, lacking multi-center, large-sample RCTs and long-term follow-up; hence conclusions from animal experiments can hardly be directly translated into clinical practice. The majority of researches focus on single disease, while comparative studies on the commonalities and differences of “spleen deficiency-microbiota dysbiosis” under metabolic comorbidities are insufficient. The interactive network among Chinese herbal compound prescriptions, microbiota and host remains unclear, and studies on combined microbiota metabolome analysis as well as dose-microbiota-efficacy dose-effect relationship are inadequate.

7. Summary and Prospect

Spleen-transportation dysfunction acts as a vital TCM pathogenesis of endocrine-metabolic diseases, and gut microbiota dysbiosis serves as its key microcosmic manifestation. The two interact bidirectionally, driving insulin resistance and chronic low-grade inflammation via the gut-metabolic axis, and further inducing type 2 diabetes mellitus, obesity, metabolic syndrome and PCOS. The “spleen-tonifying and microbiota-regulating” strategy can remodel gut microecology and repair intestinal barrier, possessing unique advantages in the prevention and treatment of metabolic comorbidities. Future researches should screen microbiota-metabolite biomarkers of spleen-deficiency syndrome by multi-center clinical trials combined with multi-omics technology; carry out metabolic comorbidity cohorts to observe the long-term intervention effects of spleen-tonifying formulas; clarify the herb-microbiota-host interaction network with metagenomics and metabolomics; strengthen researches on non-pharmacological therapies including acupuncture-moxibustion and dietary therapy, so as to promote the translational application of traditional Chinese medicine in the field of metabolic diseases.

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