

Therapeutic Potential of Shugan Jieyu Capsule and Group Psychological Counseling for Alexithymia and Neuroimmune Dysfunction in Hemodialysis Patients

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	Abstract
<p>Article history:</p> <p>Received: 18 Oct 2025 Accepted: 8 Dec 2025 Available online: 13 Dec 2025</p> <p>Keywords:</p> <p>Hemodialysis Alexithymia Depression Anxiety, Shugan Jieyu Capsule Group Psychological Counseling Neuroimmunology Biomarkers</p>	<p>Background: Patients with end-stage renal disease (ESRD) on maintenance hemodialysis (HD) experience a high psychological burden, with frequent occurrences of alexithymia, anxiety, and depression. These psychological issues are increasingly associated with disruptions in neuroimmune and neuroendocrine pathways. This review examines the basis and supporting data for using a combined approach of Shugan Jieyu Capsule (SJC) and group psychological counseling (GPC) to target both the psychological and biological aspects of this complex condition.</p> <p>Methods: A synthesis of existing literature was conducted, focusing on the pathophysiology of alexithymia in HD patients, the pharmacological effects of SJC, the therapeutic mechanisms of GPC, and the role of biomarkers such as Orphanin FQ (OFQ), Interleukin-2 (IL-2), Corticotropin-Releasing Hormone (CRH), Neurogranin, and soluble Fractalkine (sCX3CL1).</p> <p>Key Findings: Recent evidence indicates that a combined strategy of SJC and GPC is more effective than standard care alone. This integrated approach has been found to significantly reduce symptoms of alexithymia, anxiety, and depression; enhance sleep quality, self-care capacity, and social functioning; and improve overall quality of life. Importantly, these psychological improvements are associated with changes in key biomarkers, including decreased serum levels of OFQ, IL-2, CRH, Neurogranin, and sCX3CL1, suggesting a positive effect on stress response, synaptic function, and neuroinflammation.</p> <p>Conclusion: The combination of Shugan Jieyu Capsule and group psychological counseling represents a promising, multi-targeted strategy for managing the psychosomatic challenges in hemodialysis patients. This method not only improves clinical symptoms but also appears to address underlying neuroimmune and neuroendocrine imbalances, offering a holistic approach to enhancing patient outcomes in ESRD care.</p>

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Introduction

A compelling area of research involves the use of advanced imaging technologies to objectively measure acupuncture's effects. While body weight and BMI are common outcome measures, they do not distinguish between fat and muscle mass or reveal the distribution of adipose tissue. Visceral fat, in particular, is a key

driver of metabolic dysfunction. Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are non-invasive, high-resolution modalities that provide precise quantification of visceral and subcutaneous fat deposits (7, 8). The integration of this imaging data offers a more nuanced understanding of how

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acupuncture may influence body composition beyond simple weight reduction.

Hemodialysis is a life-sustaining treatment for more than 3 million patients globally with end-stage renal disease (ESRD) [[1]]. However, the prolonged and demanding nature of this therapy—typically involving 4-hour sessions three times weekly—often results in considerable physical discomfort, reduced quality of life, and a significant psychological burden [[2], [3]]. The uremic syndrome itself, marked by an accumulation of inflammatory cytokines, creates a persistent state of systemic inflammation that can directly impact the central nervous system [[4]]. Beyond the physical effects, repeated invasive procedures, dietary limitations, loss of independence, and constant confrontation with mortality often lead to psychological conditions such as anxiety and depression, which can negatively affect treatment adherence and overall prognosis [[5]]. In modern nephrology care, evaluating treatment success now extends beyond survival rates to include the patient's psychological state and health-related quality of life, recognizing the interconnection between mental and physical health [[6], [7]].

A particularly common yet underdiagnosed issue in this population is alexithymia—a concept first described by Sifneos, involving difficulties in identifying, describing, and processing emotions [[8]]. Studies suggest the prevalence of alexithymia in chronic illness groups can reach 30-50%, much higher than in the general population [[9]]. Patients with alexithymia often confuse emotional distress with physical symptoms, leading to somatization and impaired communication with healthcare providers, which can result in poorer management of the primary illness [[10]]. This condition frequently coexists with heightened levels of anxiety and depression, creating a complex psychosomatic profile that complicates clinical management [[11]]. Therefore, understanding and addressing alexithymia is crucial for optimizing holistic care in HD patients.

Recent progress in psychoneuroimmunology has begun to clarify the biological foundations of emotional dysregulation, shifting alexithymia from a purely psychological concept to one with a plausible neurobiological basis [[12]]. Key biomarkers have been linked to the stress and inflammatory responses associated with chronic illness. Orphanin FQ (OFQ), an endogenous neuropeptide, influences serotonergic and dopaminergic pathways and is elevated in mood disorders, possibly contributing to the blunted emotional experience seen in alexithymia [[13]]. Pro-inflammatory cytokines like Interleukin-2 (IL-2) are also dysregulated in individuals with alexithymia and depression, suggesting a connection between the immune activation in ESRD and psychological symptoms [[14]]. Expanding on this, newer biomarkers

offer a more integrated view: Corticotropin-Releasing Hormone (CRH), a central regulator of the hypothalamic-pituitary-adrenal (HPA) axis, is chronically elevated under sustained stress [[15]]; Neurogranin, a protein essential for synaptic plasticity and cognitive-affective integration, may indicate impaired neural circuitry for emotion processing [[16]]; and soluble Fractalkine (sCX3CL1), a chemokine involved in neuron-glia communication and neuroinflammation, is increasingly recognized as a key factor in the pathophysiology of depression and anxiety [[17]]. Together, these markers provide insight into the disrupted neuroimmune-endocrine communication in emotionally distressed HD patients.

Pharmacological and psychological interventions targeting these pathways are of significant interest. Shugan Jieyu Capsule (SJC), a Chinese patent medicine derived from *Hypericum perforatum* and *Radix Acanthopanax Senticosi*, has shown effectiveness in soothing the liver, relieving depression, and modulating neurotransmitters like serotonin [[18], [21]]. Its potential anti-inflammatory properties are also a growing area of research [[22]]. Concurrently, group psychological counseling (GPC) offers a structured environment for emotional expression, social support, and coping skill development, with demonstrated benefits in various chronic disease populations [[19], [24]]. While studies have examined these interventions separately, their combined potential in addressing the multifaceted nature of alexithymia in HD patients, particularly regarding biomarker profiles, warrants a thorough review.

This article aims to consolidate current knowledge on the effects of combined SJC and GPC therapy on alexithymia, psychological distress, and related neuroimmune biomarkers in hemodialysis patients. We will assess the clinical and biochemical evidence supporting this integrated approach and discuss its implications for future research and clinical practice in nephrology and psychosomatic medicine.

Methods

This comprehensive review was conducted through a systematic search and analysis of available scientific literature to synthesize evidence on the psychological and biological effects of SJC and GPC in hemodialysis patients.

Search Strategy

A literature search was performed using electronic databases, including PubMed, Web of Science, Cochrane Library, and CNKI (China National Knowledge Infrastructure), for articles published from January 2000 to June 2024. The search used a combination of keywords and MeSH terms: ("hemodialysis" OR "end-stage renal disease") AND ("alexithymia" OR

"depression" OR "anxiety") AND ("Shugan Jieyu" OR "Chinese medicine") AND ("group therapy" OR "group psychological counseling") AND ("biomarkers" OR "Orphanin FQ" OR "IL-2" OR "CRH" OR "Neurogranin" OR "sCX3CL1" OR "fractalkine").

Study Selection

The initial search aimed to identify randomized controlled trials (RCTs), observational studies, and meta-analyses relevant to the topic. Given the novelty of the specific biomarker panel, studies investigating these biomarkers in the context of chronic kidney disease, depression, or stress-related disorders were also included to provide mechanistic background. Extracted data from selected studies included: author and publication year, study design, patient population, intervention details, outcome measures (psychological scales), biomarker levels, and key findings.

Results

Clinical Efficacy of the Combined Intervention

Synthesizing available evidence, primarily from recent clinical trials, reveals a consistent pattern favoring the combined SJC and GPC approach. Compared to control groups receiving standard care (e.g., estazolam and routine nursing), the intervention groups demonstrated:

- **Significant Reductions in Alexithymia and Mood Disorders:** TAS-20 scores showed marked decreases at 4 and 8 weeks post-intervention, with the combined therapy group outperforming the control group [[25]]. Similar substantial reductions were observed in HAMA and HAMD scores, indicating alleviation of both anxiety and depressive symptoms [[26], [27]].
- **Improved Functional and Quality of Life Metrics:** Patients receiving the combined intervention reported significantly better sleep quality (lower PSQI scores), enhanced personal and social performance (higher PSP scores), greater self-care agency (higher ESCA scores), and a superior overall quality of life (higher WHOQOL-BREF scores across physical, psychological, social, and environmental domains) [[25], [26]]. These improvements were consistently greater than those seen in control groups receiving only conventional therapy.

Impact on Serum Biomarkers

The most compelling findings relate to objective biological changes associated with psychological improvements.

- **Reduction in OFQ and IL-2:** Studies reported a significant decrease in serum levels of OFQ and IL-2 in the intervention group compared to both baseline levels

and the control group [[25]]. This supports the hypothesis that SJC and GPC can modulate neuropeptide and inflammatory pathways involved in alexithymia.

- **Modulation of Advanced Biomarkers:** The intervention led to significant downregulation of other key biomarkers. CRH levels were reduced, suggesting normalization of the dysregulated HPA axis commonly seen in chronic stress [[15], [28]]. A decrease in Neurogranin was noted, potentially indicating stabilized synaptic function and improved neural communication in brain regions responsible for emotional regulation [[16]]. Furthermore, a marked reduction in sCX3CL1 pointed toward attenuated neuroimmune activation and microglial-mediated inflammation, a pathway increasingly implicated in the pathogenesis of depression [[17], [29]].

Safety and Satisfaction

The reviewed studies reported no significant increase in adverse reactions (such as dizziness, sleepiness, or thirst) in the combined intervention group compared to controls, suggesting a favorable safety profile [[25]]. Additionally, patient-reported nursing satisfaction was significantly higher in the group receiving integrated SJC and GPC therapy [[26]].

Discussion

This review consolidates evidence supporting the integrated use of Shugan Jieyu Capsule and group psychological counseling as a multifaceted strategy for managing the profound psychosomatic challenges faced by hemodialysis patients. The convergence of clinical symptom relief and normalization of a panel of neuroimmune biomarkers provides a strong, biologically plausible rationale for this approach.

Managing ESRD requires a paradigm that equally addresses physical and psychological health. The high prevalence of alexithymia in this population acts as a major barrier to effective care, impairing communication and emotional coping [[10], [11]]. The interaction between alexithymia, mood disorders, and systemic inflammation in ESRD creates a vicious cycle where psychological distress worsens physiological dysregulation and vice versa [[4], [12]]. The reviewed evidence positions the combination of SJC and GPC as a powerful, integrative strategy to break this cycle. SJC targets biological underpinnings by modulating neurotransmitter systems (e.g., inhibiting serotonin reuptake) and potentially reducing inflammation, while GPC addresses psychosocial components by fostering emotional awareness, reducing isolation, and building resilience [[18], [19], [22]].

The correlation between clinical improvement and normalization of a panel of biomarkers (OFQ, IL-2, CRH, Neurogranin, sCX3CL1) is particularly compelling. It

advances the field beyond subjective reporting toward objective, biological validation of treatment efficacy. The reduction in OFQ and IL-2 directly supports the "monoamine" and "cytokine" hypotheses of alexithymia and depression [[13], [14]]. The decrease in CRH indicates successful attenuation of the chronic stress response, crucial for long-term health in HD patients [[28]]. Novel findings regarding Neurogranin and sCX3CL1 are especially significant. The reduction in Neurogranin may seem counterintuitive, as it is generally associated with synaptic health; however, in chronic stress, its release into serum may reflect synaptic breakdown or stress-related shedding. Therefore, its decrease post-intervention could indicate stabilized neuronal integrity [[16], [30]]. Similarly, the decline in sCX3CL1 strongly suggests reduced neuroinflammatory signaling, linking the intervention to a key pathological process in mood disorders [[29]]. This multi-biomarker approach could potentially be used in the future to stratify patients or personalize treatment plans.

Conclusion

In conclusion, integrating Shugan Jieyu Capsule and

group psychological counseling offers a comprehensive and synergistic approach to a challenging clinical problem. By simultaneously targeting psychological symptoms of alexithymia, anxiety, and depression and associated dysregulation in neuroimmune and neuroendocrine pathways, this combined therapy holds significant promise for improving holistic well-being and quality of life in patients undergoing hemodialysis. The alignment of improved patient-reported outcomes with objective biomarker modulation provides a strong evidence base for this integrative model, representing a critical step toward truly person-centered, biopsychosocial care in nephrology.

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Authors Contributions

The authors contributed to the data analysis. Drafting, revising and approving the article, responsible for all aspects of this work.

Conflict of Interest

None

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