Clinical Efficacy and Mechanism of Action of Acupuncture in Treating Primary Dysmenorrhea

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Abstract:

Primary dysmenorrhea (PD) is a prevalent gynecological condition that profoundly impairs the quality of life. Acupuncture, a traditional Chinese therapy, has demonstrated significant efficacy and unique advantages in managing PD. Clinical evidence has corroborated that acupuncture, particularly when targeted at key acupoints such as SP6 (Sanyinjiao) and CV4 (Guanyuan), effectively mitigates pain and reduces reliance on analgesic agents. Its therapeutic effect is often superior to placebos and comparable to conventional pharmacotherapies. The underlying mechanisms involve multi-system integration: Peripherally, it attenuates uterine cramping by inhibiting inflammatory pathways and modulating prostaglandin balance. Centrally, it exerts analgesia by activating the endogenous opioid system and regulating neuroimmune crosstalk, and can also modulate brain network connectivity. Furthermore, the efficacy of acupuncture exhibits relative acupoint specificity and is dependent on the timing of intervention. In conclusion, acupuncture represents a safe and effective non-pharmacological intervention for PD. Its multi-targeted, systemic regulatory effects provide a robust evidence-based foundation for its clinical application.

Keywords: Acupuncture; Primary dysmenorrhea; Efficacy; Mechanism.

1. Introduction

Primary dysmenorrhea (PD) is a prevalent gynecological functional disorder characterized by recurrent, cramping lower abdominal pain during menstruation in the absence of detectable pelvic pathology. It predominantly afflicts adolescents and women of repro-ductive age. The characteristic pain often commences up to 12 hours prior to menstrual flow, peaks within the first 48 hours of menses, and is frequently accompanied by a spectrum of systemic and autonomic symptoms, including headache, dizziness, fatigue, nausea, vomiting, diarrhea, and diaphoresis. The severity of these symptoms can significantly disrupt

daily activities, academic performance, and work productivity, thereby rendering PD a major concern in both clinical practice and public health.

The prevalence of PD is notably high and appears to be on the rise. Epidemiological studies report prevalence rates ranging widely from 16.8% to 90%, reflecting discrepancies in diagnostic criteria and heterogeneity of study populations. A landmark 2022 meta-analysis involving over 78,000 students reported a pooled prevalence of 66.1%, with a marked increase from 58.8% before 2010 to 71.5% after 2015, suggesting a rising trend, particularly among younger cohorts[1-3]. Beyond its adverse impact on quality of life, PD imposes a substantial socioeconomic burden. Surveys indicate that over 60% of young affected individuals have missed school or work due to symptoms, with nearly 30% reporting 1–3 days of absence per month[4]. The long-term costs associated with pain management, pharmacological interventions, and lost productivity further underscore PD as a significant public health and economic issue[5,6].

The clinical management of PD entails a multimodal approach, encompassing modern pharmacotherapy, physical therapy, surgical interventions, and complementary therapies. Current first-line Western medical interventions consist primarily of prostaglandin synthetase inhibitors (e.g., non-steroidal anti-inflammatory drugs [NSAIDs] like ibuprofen) and hormonal agents (e.g., combined oral contraceptives). NSAIDs alleviate pain rapidly by inhibiting prostaglandin synthesis, while hormonal contraceptives aim to reduce prostaglandin production at its source by suppressing ovulation. Additionally, physical modalities such as transcutaneous electrical nerve stimulation, cryotherapy, thermotherapy, extracorporeal shockwave therapy, and pulsed techniques, alongside non-pharmacological interventions including exercise, aromatherapy, and nutritional supplementation, offer alternative management strategies. However, these conventional interventions are not without limitations. NSAIDs are associated with potential adverse effects, including gastrointestinal discomfort and mucosal injury, and long-term use may disrupt gut microbiota and immune function. Hormonal therapies may induce side effects such as nausea, weight fluctuations, and mood disturbances, and carry specific contraindications, including thrombosis risks[7]. Furthermore, the efficacy and safety profiles of some physical and complementary therapies require further rigorous validation. Consequently, exploring safer, effective natural therapies that address the underlying pathophysiology remains a crucial direction in optimizing PD management.

Acupuncture, a cornerstone of Traditional Chinese Medicine (TCM) with a history spanning millennia, represents one such therapeutic avenue. Rooted in the TCM theories of meridians, acupoints, and Qi-Blood equilibrium, acupuncture postulates that stimulating specific acupoints modulates the circulation of Qi and Blood, thereby re-establishing physiological homeostasis[8]. A growing body of clinical research attests to the significant efficacy of acupuncture in alleviating PD symptoms. Experimental studies suggest its therapeutic actions may involve modulating prostaglandin levels, improving uterine microcirculation, and regulating neuroendocrine functions[9]. This review synthesizes evidence on the efficacy and mechanisms of acupuncture for PD, aiming to provide a solid evidence-based foundation for its clinical translation and application.

2. Clinical Efficacy of Acupuncture for PD

As a globally prevalent gynecological disorder, the non-pharmacological management of PD remains a focal point in clinical practice. Within this context, acupuncture therapy has evolved from a millennia-old traditional practice into a modality validated by modern medicine. This evolutionary trajectory can be broadly delineated into three phases. The first constitutes the classical theoretical establishment period, spanning from the pre-Qin period to the Ming and Qing dynasties. The Yellow Emperor's Inner Canon established the core pathogenesis of pain as "obstruction causing pain" and "malnourishment causing pain," laying the theoretical groundwork for dysmenorrhea[10]. Subsequent canonical works such as the Systematic Classic of Acupuncture and Moxibustion further refined clinical acupoint prescriptions, predominantly incorporating points such as Tianshu (ST25), Guanyuan (CV4), and Sanyinjiao (SP6), gradually forming a comprehensive syndrome differentiation-based treatment system[11-12]. By the late 20th century, research entered a new phase characterized by exploration into neuroendocrine mechanisms and the design of rigorous clinical trials. Since the 21st century, the field has advanced into a mature stage of technical standardization and global evidence integration. The advent of electroacupuncture (EA) enabled the quantification and standardization of stimulation parameters. Its continuous dense-disperse wave stimulation has been demonstrated to be more effective in regulating autonomic nervous system function, thereby enhancing analgesic efficacy and improving uterine microcirculation[13]. With the continuous accumulation of high-quality clinical evidence, the World Health Organization (WHO) formally included dysmenorrhea in the indications for acupuncture in its 2019 International Classification of Traditional Medicine[14]. Simultaneously,

several internationally influential systematic reviews and clinical practice guidelines explicitly recommend acupuncture as a first-line non-pharmacological therapy for PD, indicating that acupuncture has secured a prominent position in global PD management protocols based on modern evidence-based medicine[15].

Extensive clinical research has confirmed the definite efficacy of acupuncture for primary dysmenorrhea (PD). Point selection adheres to the principles of "selecting points along meridians" and "selecting points based on syndrome differentiation," leading to the development of relatively standardized treatment protocols. Among the points, Sanyinjiao (SP6), Guanyuan (CV4), Zhongji (CV3), Diji (SP8), and Xuehai (SP10) are the most commonly utilized and validated core acupoints in clinical practice[10,16].

Since the 1980s, the clinical efficacy of acupuncture for PD has been supported by increasingly rigorous scientific investigations, gradually forming a comprehensive evidence base. This line of inquiry can be traced back to a seminal study conducted by Helms in 1987. As one of the earliest randomized controlled trials (RCTs) on acupuncture for PD in Western countries, this well-designed study included an acupuncture group, a sham acupuncture group, a control group, and a visit control group receiving only physician consultation. Its findings revealed a remarkably high symptom improvement rate of 90.9% in the acupuncture group, significantly superior to all other groups, alongside a 41% reduction in analgesic use post-treatment. This study provided preliminary evidence that the therapeutic effect of acupuncture exceeds both the placebo effect and the benefit derived from simple physician-patient interaction[17]. Subsequently, a large-scale RCT by Witt et al. (enrolling 649 women) not only reaffirmed that adding acupuncture to usual care more significantly reduced pain intensity (NRS score: 3.1 in acupuncture group vs. 5.4 in control group) and improved quality of life but also, through health economic analysis, demonstrated that although acupuncture increased direct medical costs, its incremental cost-effectiveness ratio was within an acceptable threshold. This provided critical economic evidence to support the broader integration of acupuncture into healthcare systems[18].

Building upon the validation of overall efficacy, subsequent research delved into the efficacy of specific acupoints. A study systematically comparing EA at Sanyinjiao (SP6), Xuanzhong (GB39), and a nearby non-acupoint site revealed acupoint-specific effects. It found that EA at SP6 was most pronounced in eliciting rapid reductions in Visual Analogue Scale (VAS) scores, with significantly greater improvements than those observed in GB39 or the non-acupoint, and additionally resulted in a more marked reduction in pain-related life interference. Although no intergroup differences in uterine artery hemodynamic parameters were detected in this study, the results strongly indicate that SP6 exerts relatively specific therapeutic efficacy for acute analgesia in PD, and not all forms of electrical stimulation confer equivalent therapeutic benefits[19].

Parallelly, investigations into the optimization of treatment protocols have furnished more refined guidance for clinical practice. A large-scale study enrolling 600 patients systematically compared single-point therapy at Shiqizhui (EX-B8) with multi-acupoint combinations, alongside premenstrual preventive intervention versus on-demand treatment at pain onset. The findings were noteworthy: first, within multi-point protocols, preventive intervention before menstruation was more efficacious than needling administered solely at pain onset; second, if immediate treatment during pain was chosen, the single-point (EX-B8) protocol outperformed the multi-point protocol. This pivotal finding highlights an interaction between treatment timing and the complexity of acupoint selection, underscoring the need for clinicians to adopt flexible therapeutic strategies tailored to the patient's timing of consultation. The study further validated the simplicity and efficacy of EX-B8 as a standalone acupoint[20].

Comparative studies between acupuncture and conventional Western medications have further solidified its status as a first-line or alternative therapeutic option. A randomized trial comparing deep insertion acupuncture with oral ibuprofen demonstrated that following three menstrual cycles of treatment, the acupuncture group exhibited a significantly greater reduction in both pain intensity and symptom severity relative to the ibuprofen group, with a higher response rate and favorable safety profile. This directly corroborated that specific acupuncture techniques are non-inferior to, and may even surpass, commonly prescribed analgesic agents[21]. Another investigation focusing on facial acupuncture highlighted the rapid onset of action of acupuncture. This therapeutic approach significantly reduced pain scores at 5 and 30 minutes post-needle insertion, while also exhibiting sustained long-term efficacy, thereby expanding the therapeutic armamentarium for PD[22].

In recent years, non-invasive or minimally invasive acupuncture-derived modalities have been increasingly utilized in clinical practice. A study on dysmenorrhea patients with autonomic dysfunction compared low-level laser acupuncture, conventional EA, and sham laser intervention. The results indicated that both laser acupuncture and EA effectively mitigated pain and normalized imbalanced sympathetic-parasympathetic tone, with therapeutic effects exceeding those of placebo. Notably, in the

subgroup of patients whose autonomic function was in a "low-energy" state (low LF/HF ratio), laser acupuncture outperformed EA in enhancing multiple heart rate variability (HRV) parameters. Owing to its fully non-invasive nature, laser acupuncture provides a viable alternative for patients with trypanophobia or special populations, highlighting the potential of acupuncture modernization[23,24].

In summary, following decades of research, clinical investigations on acupuncture for PD have advanced from the initial validation of efficacy to in-depth explorations of optimal acupoints, comparative advantages relative to conventional medications, and the clinical application of innovative modalities. The cumulative evidence consistently demonstrates that acupuncture is an intervention capable of effectively, rapidly, and safely mitigating pain and enhancing quality of life, with its efficacy exhibiting distinct acupoint specificity and protocol dependency.

3. Modern Biological Mechanisms of Acupuncture in Treating Primary Dysmenorrhea

The therapeutic efficacy of acupuncture for primary dysmenorrhea (PD) is mediated via an integrated mechanism involving multi-level and multi-system synergy. Its biological effects are initially manifested in direct peripheral anti-inflammatory and immunomodulatory actions. Preclinical and clinical research has confirmed that electroacupuncture (EA) effectively inhibits key inflammatory signaling pathways within uterine tissue, including the COX-2/NF-κB/NLRP3 and TLR4/NF-κB axes, thereby attenuating the production of downstream pro-inflammatory cytokines such as interleukin-1β (IL-1β) and interleukin-18 (IL-18)[25]. Simultaneously, EA normalizes dysregulated prostaglandin metabolism by reducing levels of the spasmogenic PGF2α, elevating levels of the relaxing PGE2, increasing the polarization of immune cells toward the anti-inflammatory M2 phenotype, which directly mitigates uterine smooth muscle spasm and tissue damage[26].

Beyond modulating peripheral pathology, acupuncture exerts profound analgesic effects via the central nervous system. The central mechanism entails the activation of the endogenous analgesic system. Preclinical studies have demonstrated that EA stimulation at the Sanyinjiao (SP6) acupoint specifically upregulates κ-opioid receptor expression across extensive segments of the spinal dorsal horn and markedly enhances the release of β-endorphin and enkephalin within the periaqueductal gray matter[27]. Furthermore, acupuncture regulates the neuroimmune

crosstalk by upregulating the anti-inflammatory cannabinoid type 2 receptor (CB2), inhibiting the expression of the pro-nociceptive transient receptor potential vanilloid 1 (TRPV1), and inducing a shift in spinal microglia toward the anti-inflammatory M2 phenotype, thereby mitigating neuroinflammation and central sensitization[28].

Contemporary neuroimaging investigations have further elucidated that acupuncture's effects extend to the functional reorganization of brain networks. Clinical investigations indicate that acupuncture treatment can remodel pain-related brain networks with the anterior insula as a pivotal node. This entails enhancing its functional connectivity with the limbic system (e.g., hippocampus) and regulating its interactions with cognitive control networks (e.g., the dorsolateral prefrontal cortex). These functional adaptations are closely correlated with the magnitude of clinical improvement in pain and associated symptoms[29].

Notably, the therapeutic outcomes of acupuncture exhibit distinct relative acupoint specificity and stimulation parameter dependency. The Sanyinjiao (SP6) acupoint demonstrates significantly greater efficacy in analgesia, anti-inflammation, and endorphin regulation compared to control points such as Xuanzhong (GB39), Xuehai (SP10), or non-acupoint locations. This finding further corroborates that the therapeutic effect of acupuncture is not a non-specific physical stimulation, but is closely associated with the unique physiological functions of specific acupoints. With respect to stimulation parameters, high-frequency EA typically elicits more potent anti-inflammatory and analgesic actions than low-frequency EA, and preventive intervention administered premenstrually proves more efficacious than treatment initiated at pain onset[31].

In summary, acupuncture does not act via a single isolated pathway but establishes a comprehensive therapeutic paradigm encompassing "peripheral anti-inflammatory and antispasmodic actions," "central analgesia and neuroimmune modulation," and "brain network reorganization." Its efficacy stems from both direct modulation of local uterine pathology and the systemic regulation of multi-level neuroendocrine-immune (NEI) networks. This furnishes a robust modern scientific foundation for the clinical effectiveness and holistic therapeutic profile of acupuncture in managing primary dysmenorrhea.

4. Conclusion

In summary, primary dysmenorrhea (PD) constitutes a major global public health burden that demands effective and safe therapeutic solutions. Acupuncture therapy, centered on key acupoints including Sanyinjiao (SP6) and Guanyuan (CV4), is now recognized as a first-line non-pharma-

cological intervention for PD by both the World Health Organization and numerous international clinical practice guidelines—a status underpinned by its well-established theoretical framework and accumulating high-quality evidence. Extensive clinical research demonstrates that acupuncture not only delivers rapid and effective pain relief, reduces dependence on analgesic medication, and enhances quality of life, but also exhibits clear acupoint specificity in its therapeutic benefits and allows for optimization through the modulation of key parameters (e.g., treatment timing and stimulation frequency). Contemporary mechanistic studies have elucidated that acupuncture operates through a multi-level integrative model: it exerts direct peripheral anti-inflammatory effects and rebalances prostaglandin metabolism to mitigate uterine spasm; activates central endogenous opioid pathways and regulates neuroimmune signaling to elicit potent analgesia; and facilitates functional reorganization of pain-processing brain networks. This capacity for systemic regulation—encompassing local tissue effects to central neural modulation—confers a unique therapeutic advantage over conventional single-target pharmacotherapies. Consequently, acupuncture represents an optimal therapeutic option for PD patients, characterized by validated efficacy, holistic regulatory effects, and a favorable safety profile, with its clinical relevance and scientific underpinnings now fully substantiated.

Future research endeavors should aim to expand and deepen acupuncture's role in women's health. Key priorities include refining personalized treatment protocols through mechanistic studies aimed at identifying novel biological pathways and therapeutic targets. Methodological innovation remains equally critical: clinical trials necessitate more sophisticated study designs and larger sample sizes to generate higher-level evidence, whereas preclinical studies should utilize advanced animal models to elucidate previously unexplored mechanisms of action. Through synergistic integration of clinical and basic science research, we can systematically delineate acupuncture's multi-target network effects in PD and identify the biological correlates of distinct traditional Chinese medicine syndrome patterns. Such advancements will be instrumental in advancing the field toward enhanced precision, standardization, and evidence-based integration into mainstream healthcare systems.

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