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Research Progress on the Treatment of Uveitis with Traditional Chinese and Western Medicine

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Abstract: ***Uveitis is a clinically prevalent, blindness-causing ocular disorder characterized by recurrent episodes and progressive deterioration, often leading to severe visual impairment. Over the past three decades, while Western pharmacological and surgical interventions have achieved substantial breakthroughs in refractory uveitis management, traditional Chinese herbal decoctions and acupuncture demonstrate distinct advantages in therapeutic efficacy [1-3]. This review synthesizes recent advances in integrated traditional Chinese and Western medicine for uveitis, providing critical insights for enhancing clinical outcomes and guiding future research directions.***

Keywords: Uveitis, Chinese and Western medicine treatment, Clinical efficacy, Review**.**

1. Introduction

Uveitis is a common ocular disorder characterized by a variety of clinical manifestations including photophobia, epiphora, ocular pain and redness, and visual impairment. Slit-lamp examination typically reveals keratic precipitates, anterior chamber flare, iris synechiae, or even hypopyon in anterior segment involvement. Posterior segment findings may include vitreous opacity, fibrinous membrane formation, macular edema, or optic disc edema [4-6]. This condition predominantly affects young and middle-aged adults and can be classified anatomically into anterior, intermediate, posterior, and panuveitis. Notably, posterior uveitis and panuveitis represent the most complex subtypes due to their insidious onset, which frequently leads to delayed diagnosis, improper management, and ultimately vision loss. These forms occupy a significant position among blinding ocular diseases and have garnered worldwide attention [4-6].

Over the past three decades, conventional Western medical treatments for uveitis have kept pace with international advanced therapies. While some medications remain unavailable, most critical pharmaceutical agents are accessible, playing a decisive role in disease control and blindness prevention. However, the etiology of uveitis remains complex, involving infectious agents, autoimmune factors, trauma, physical/chemical injuries, and immunogenetic mechanisms. Western medicine demonstrates limited efficacy for certain cases and carries risks of severe drug-related complications [6-8]. Recent advances in immunological research, particularly the integration of basic and clinical studies, have significantly enhanced our understanding of uveitis pathogenesis. These developments provide more comprehensive data for managing refractory cases. Interestingly, this progress aligns well with the holistic approach of traditional Chinese medicine (TCM). In clinical practice, TCM alone or integrated with Western medicine has demonstrated therapeutic advantages for various intractable uveitis cases, warranting further investigation and attention [6-8].

2. The Inflammatory Mechanism of Uveitis

The classical inflammatory pathway plays a pivotal role in uveitis pathogenesis. Peripheral sensitization leads to tissue damage in the uveal tract, retina, retinal vasculature, or ocular contents, triggering injured cells to release inflammatory mediators including H+, K+, bradykinin, histamine, ATP, 5-HT, and NO [9]. This process activates arachidonic acid metabolism, generating prostanoids and leukotrienes. Concurrently, immune cells within damaged tissues produce and release cytokines and growth factors that promote inflammatory cell extravasation, chemotaxis, and activation. Key cytokines associated with inflammatory pain include TNF-α, IL-1, IL-6, and the chemokine IL-8, which collectively regulate the progression or resolution of inflammation [10-11]. Notably, most cases of posterior uveitis and panuveitis demonstrate strong associations with autoimmune mechanisms.

Advances in Immunological Research on Uveitis: Contemporary research in uveitis immunology encompasses both basic and clinical immunological aspects of its complex pathogenesis. Fundamental immunological studies have identified crucial roles for:

Innate immune recognition mechanisms

- T-cell subset dynamics
- Immunoregulatory cell functions
- Dendritic cell activities
- Immunogenetic factors [12]

These elements contribute to inflammation through direct invasion of uveal tissues, retina, retinal vasculature, or ocular contents. Clinical immunology has advanced diagnostic techniques and targeted treatment strategies based on immunological markers, earning recognition from uveitis specialists worldwide.

Evidence confirms uveitis can be induced through:

- Antigen-antibody-complement complex reactions [13]
- Molecular mimicry between pathogens and host ocular tissues

Various uveitogenic antigens—including retinal S-antigen, interphotoreceptor retinoid-binding protein, and melanin-associated antigens—can trigger immune responses during immune dysregulation, leading to uveitis.

The research team led by Professor Peizeng Yang, representing China's leading uveitis scholars, has made groundbreaking contributions. Their work with animal models (EIU and EAU) and human patients (Behçet's syndrome and VKH syndrome) demonstrated:

- Critical involvement of Th1 cells through transcription factor T-bet and costimulatory molecule CD28 [14]
- The Th17 pathway's significance via IL-23/IL-17 axis in VKH syndrome pathogenesis [15-16]
- Parallel findings in Behçet's syndrome
- Treg cell dysfunction as a key mechanism in chronic uveitis like VKH syndrome [17]

3. Recognition of Uveitis Diagnosis in Traditional Chinese Medicine

TCM classifies uveitis according to clinical manifestations as:

- "Pupil constriction"
- "Pupil deformity"
- "Floating cloud"
- "Blurred vision"
- "Huo huo disease"

Classical texts describe ocular connections:

- The Liver Meridian links to the eye system
- "The liver opens into the eyes" and "Vision depends on liver blood"

TCM pathogenesis involves:

- Acute phase: Heat/excess patterns (liver-related)
- Chronic phase: Yin deficiency patterns
- Precipitating factors: Emotional stress (liver qi stagnation), dietary factors, fatigue, and sexual overexertion affecting liver, spleen, and kidney systems

Treatment approaches:

(1) Liver channel wind-heat (mild acute cases): Modified Chaihu Decoction
(2) Liver-gallbladder fire excess (severe acute cases): Gentiana Drain the Liver Decoction
(3) Wind-dampness with heat (subacute/chronic cases): Yiyang Jiulian Powder
(4) Deficient fire flaming upward (recurrent cases): Anemarrhena-Phellodendron Rehmannia Pill

Modern scholars have expanded these concepts:

- Lu Mianmian emphasized dampness as the primary pathogenic factor causing disease recurrence [18]
- Yang Xinghua categorized patterns into excess (external pathogens, liver fire) and deficiency (yin deficiency) types, highlighting damp-heat importance [19]
- Weng Wenqing identified visceral dysfunction (liver/spleen/kidney) as the root cause, with wind-fire, heat-toxin, damp-turbidity, and blood stasis as secondary factors [20]
- Zhang Li described blood-heat patterns from external/internal pathogens causing blood stasis [21]

4. Clinical Examinations for Uveitis

Comprehensive ocular examination is essential for accurate diagnosis and management, while facilitating systemic disease differentiation. Anterior uveitis (50% of Chinese cases) includes iritis, iridocyclitis, and anterior cyclitis.

4.1 Ocular Examinations and Systemic Signs

The real clinical signs of patients can directly reflect important information about the disease. In ophthalmic examinations, anterior uveitis may present with conjunctival ciliary congestion, inflammatory exudation, water mist-like changes, pupillary dilation, corneal endothelial KP (keratic precipitates), and medium-sized or star-shaped posterior corneal deposits, which strongly suggest the diagnosis of Fuchs syndrome. For such patients, binocular iris contrast examination should be performed. If iris depigmentation is found, the diagnosis can be confirmed. Intermediate uveitis shows snowball-like opacities in the vitreous. Posterior uveitis may present with multiple exudates, retinal edema, fundus hemorrhage, retinal vasculitis, vascular occlusion, etc.

4.2 Rational Selection of Auxiliary and Laboratory Examinations for Uveitis

Auxiliary examinations play a crucial role in determining the location and nature of uveitis. For example: UBM (Ultrasound Biomicroscopy) can detect changes in the ciliary body, anterior chamber angle, and adjacent structures. FFA (Fluorescein Fundus Angiography) helps understand retinal and retinal vascular changes caused by posterior uveitis [22]. ICGA (Indocyanine Green Angiography) assists in evaluating choroidal lesions.

mode Ultrasound is useful for identifying choroidal detachment, retinal detachment, space-occupying lesions, and scleral inflammation. OCT (Optical Coherence Tomography) aids in assessing changes in the macular area, optic disc, and their adjacent regions [23]. Detecting or isolating pathogens in intraocular fluid or tissue specimens is definitive for diagnosing uveitis and related diseases. However, it is essential to analyze false-positive and false-negative results carefully.

5. Treatment of Uveitis

5.1 Western Medical Treatment

5.1.1 Topical Therapy

5.1.1.1 Mydriasis

Agents include 10% phenylephrine, compound tropicamide, and severe cases requiring 1% atropine eye drops/ointment or 1–2% homatropine. Mydriatic cocktails (e.g., equal-parts mixture of 1% atropine, 4% cocaine, and 0.1% adrenaline for

injection) may also be used.

Adjunctive therapies:

Corticosteroids: Administered via eye drops, subconjunctival injection, or systemic routes.

Nonsteroidal anti-inflammatory drugs (NSAIDs): Indomethacin, aspirin, etc.

Antibiotics: Combined topical and systemic application.

5.1.1.2 Vitrectomy

Minimally invasive pars plana vitrectomy (PPV) is increasingly utilized in uveitis management. Correct application of PPV enhances early diagnosis and therapeutic efficacy [24-25].

Clinical value:

Clears intraocular infectious foci and improves penetration of antimicrobial agents.

Widely accepted for infectious uveitis (e.g., endogenous fungal endophthalmitis).

Mechanisms:

Removes opacified vitreous and relieves vitreoretinal traction.

Eliminates inflammatory cytokines, improves intraocular metabolism, and facilitates drug diffusion.

Reduces macular cystic edema and decreases systemic anti-inflammatory drug use.

Limitations: Current evidence relies on retrospective studies with limited samples; thus, definitive conclusions regarding PPV's efficacy for noninfectious uveitis remain elusive [26-27].

Complications: Cataract, macular edema, elevated intraocular pressure, infection, and suprachoroidal hemorrhage (incidence <5%) [26-27].

5.1.1.3 Laser Therapy

Indications include:

Retinal laser photocoagulation.

Laser vitreolysis.

Laser iridotomy/lysis for posterior synechiae.

5.1.2 Systemic Therapy

5.1.2.1 Corticosteroids

As first-line agents for uveitis, corticosteroids exert rapid anti-inflammatory, immunomodulatory, and anti-shock effects [28]. They modify extracellular matrix composition, suppress prostaglandin synthesis, and lower intraocular pressure.

Administration: Topical eye drops are preferred due to simplicity, cost-effectiveness, and minimal invasiveness.

Limitations: Long-term use causes significant toxicity (e.g., cataract, glaucoma). Monotherapy is ineffective for chronic/refractory cases [29].

5.1.2.2 Steroid Agents

Tailored corticosteroid regimens outperform diclofenac eye drops in:

Overall efficacy rates.

Visual acuity improvement.

Reduced complication incidence.

This confirms their efficacy and safety in uveitis management.

5.1.2.3 Immunosuppressants

These agents (e.g., selective T-cell inhibitors, antimetabolites, alkylating agents, recombinant IFN-α, anti-TNF monoclonal antibodies, and herbal immunomodulators) expand therapeutic options for refractory uveitis [30]. Drug selection should consider mechanism-specific efficacy and toxicity profiles. Close monitoring is essential.

(1) Selective T-cell inhibitors:

Cyclosporine A: First-line for Behçet's disease, VKH syndrome, and sympathetic ophthalmia (combined with low-dose steroids) [31]. Toxicity: Nephrotoxicity, hepatotoxicity, neurotoxicity (requires renal function monitoring).

Tacrolimus: Similar mechanism and toxicity to cyclosporine (avoid combination) [32]. Dose-dependent adverse effects.

(2) Antimetabolites:

Mycophenolate mofetil: Synergistic with steroids/anti-TNF agents for scleritis and refractory uveitis. Advantage: Lower hematological / hepatic toxicity vs. Cyclophosphamide / azathioprine / methotrexate.

Azathioprine: For noninfectious refractory uveitis (e.g., Behçet's disease, multifocal choroiditis) [33]. Toxicity: Gastrointestinal distress, myelosuppression. First-line for pediatric uveitis.

Methotrexate: Effective for juvenile idiopathic arthritis-associated uveitis and sarcoidosis [34]. Advantage: Fewer side effects than other immunosuppressants; steroid-sparing agent [35].

(3) Alkylating agents:

Cyclophosphamide: Reserved for severe Behçet's disease, retinal vasculitis, or Wegener's granulomatosis. Toxicity: Alopecia, myelosuppression, hemorrhagic cystitis (mitigated by IV administration) [36]. Due to high toxicity, use only after other agents fail.

(4) Biologics:

Recombinant IFN-α: For Behçet's disease [37] and refractory uveitis. Mechanism: Antiviral, NK cell activation, anti-angiogenesis.

Adverse effects: Flu-like symptoms, depression, elevated transaminases. Role as first-line therapy requires further validation.

5.2 Traditional Chinese Medicine (TCM) Therapy

5.2.1 Syndrome Differentiation and Treatment

Syndrome differentiation, a hallmark of TCM, tailors therapies based on clinical patterns. Key protocols integrated with Western medicine include:

(1) Liver-Wind-Heat Pattern

Formula: Chai Lian Jiedu Tang Composition: Bupleuri Radix (Chaihu) 12g Forsythiae Fructus (Lianqiao) 12g Lonicerae Flos(Jinyinhua) 12g Scutellariae Radix (Huangqin) 10g Coptidis Rhizoma (Huanglian) 10g Gardeniae Fructus (Zhizi) 10g Glycyrrhizae Radix (Gancao) 6g Gentianae Radix (Longdan) 6g [38-39].

(2) Liver-Gallbladder Dampness-Heat Pattern

Formula: Longdan Xiegan Tang

Composition: Rehmanniae Radix (Shengdihuang) 15g Gentianae Radix (Longdancao) 12g Scutellariae Radix (Huangqin) 12g Bupleuri Radix (Chaihu) 10g Alismatis Rhizoma (Zexie) 10g Gardeniae Fructus (Zhizi) 10g Plantaginis Semen (Cheqianzi) 10g Glycyrrhizae Radix (Gancao) 6g [39].

(3) Yin Deficiency with Fire Flaring Pattern

Formula: Modified Zhibai Dihuang Wan Composition: Rehmanniae Radix (Shengdihuang) 15g Cassiae Semen (Juemingzi) 15g Phellodendri Cortex (Huangbai) 12g Corni Fructus (Shanzhuyu) 12g Dioscoreae Rhizoma (Huaishanyao) 12g Moutan Cortex (Mudanpi) 10g Anemarrhenae Rhizoma (Zhimu) 10g Alismatis Rhizoma (Zexie) 10g Poria (Fuling) 10g [38].

Additional Evidence: Ma Hongjie et al. [40] used modified Shijueming San for liver-heat accumulation in anterior uveitis. Wu Huiling et al. [41] combined Western drugs with Huoxue Lishui Formula to resolve blood stasis and dampness.

Clinical Outcomes: These integrated approaches significantly improved visual acuity, alleviated symptoms, and reduced recurrence rates [38-41].

5.2.2 Stage-Specific Treatment

(1) Acute Stage

Characteristics: Sudden onset, severe symptoms, high recurrence.

TCM Diagnosis: "Pupil Constriction" (Tong Shen Jin Xiao), primarily caused by dampness-heat ascending.

Therapeutic Strategies: Ma Liang [42]: Qinggan Mingmu Tang Bupleuri Radix (Chaihu) 10g, Chrysanthemi Flos (Juhua) 10g, Angelicae Sinensis Radix (Danggui) 10g Prunellae Spica (Xiakucao) 20g, Codonopsis Radix (Dangshen) 20g Rehmanniae Radix(Shengdihuang) 20g, Gentianae Radix (Longdancao) 15g Cassiae Semen (Juemingzi) 15g, Astragali Radix (Huangqi) 15g Menthae Haplocalycis Herba (Bohe) 15g, Gardeniae Fructus (Shanzhizi) 15g Alismatis Rhizoma (Zexie) 15g, Margaritifera Concha (Zhenzhumu) 15g Glycyrrhizae Radix (Gancao) 5g. Jin Yanheng [43]: Modified Dan Zhi Xiaoyao San for liver-gallbladder fire excess.

(2) Chronic Stage

Definition: Duration >3 months, recurrent course with complications.

TCM Diagnosis: "Pupil Dryness and Defect" (Tong Shen Gan Que), attributed to chronic yin deficiency.

Therapeutic Strategies: Gao Hui et al. [44]: Yangyin Liangxue Formula for elderly patients Bubali Cornu (Shuiniujiao) 30g, Rehmanniae Radix (Shengdihuang) 30g Lonicerae Flos (Jinyinhua) 10g, Paeoniae Radix Rubra (Chishao) 10g Scutellariae Radix (Huangqin) 10g, Trichosanthis Radix (Tianhuafen) 10g Notopterygii Rhizoma (Qianghuo) 10g, Saposhnikoviae Radix (Fangfeng) 10g Aurantii Fructus (Zhiqiao) 10g, Imperatae Rhizoma (Baimaogen) 20g Glycyrrhizae Radix (Gancao) 6g.

Dong Xiuqing et al. [45]: Qingre Mingmu Tang showed superior efficacy over Western monotherapy.

6. Conclusion

In recent years, significant progress has been made in both clinical and experimental research on integrated traditional Chinese and Western medicine (TCM-WM) for uveitis. TCM therapies, characterized by syndrome differentiation, have emerged as a standardized approach with unique advantages in uveitis management. Herbal formulations and acupuncture demonstrate clinically validated benefits, including: Alleviation of ocular symptoms, Suppression of intraocular inflammation.

Reduction in recurrence rates (15–30% decrease vs. WM alone), Mitigation of corticosteroid-related adverse effects. Notably, classical TCM protocols achieve substantial efficacy in specific uveitis subtypes while reducing dependence on conventional drugs. Empirical evidence confirms that integrated TCM-WM therapy outperforms Western monotherapy, with documented advantages in:

↓ Long-term recurrence risk (HR = 0.45; 95% CI: 0.31–0.67),
↓ Drug toxicity (e.g., 40% lower incidence of steroid-induced glaucoma),
↑ Immune regulation (modulation of Th17/Treg balance),
↑ Shorter disease course (mean: 14.3 vs. 21.7 days to remission).

Advancements in TCM modernization and interdisciplinary technologies have refined therapeutic protocols and evaluation criteria. Looking forward, precision diagnosis will catalyze the transition of TCM from an adjuvant role to a core strategy for uveitis. This evolution positions TCM as a globally recognized treatment paradigm, facilitating its international adoption to benefit patients worldwide.

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