

The Regenerative Frontier: Consolidating the Evidence for Platelet-Rich Plasma in the Management of Mixed Urinary Incontinence

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Abstract

Mixed urinary incontinence (MUI) presents a formidable therapeutic challenge, requiring a strategy that simultaneously addresses the anatomical defect of stress urinary incontinence (SUI) and the functional disorder of urgency urinary incontinence (UUI). While surgical and pharmacological interventions exist, they often target a single component and carry significant limitations. Platelet-rich plasma (PRP), an autologous concentrate of growth factors, has emerged as a promising regenerative therapy. Recent pioneering work has introduced a novel dual-target approach, combining intra-sphincteric injections for SUI with intravesical instillations for UUI. This review synthesizes the current evidence on PRP for urinary incontinence, with a specific focus on the efficacy, safety, and clinical implications of this combined technique for MUI, as recently demonstrated in a landmark prospective trial. The findings indicate that dual-target PRP therapy yields significant and sustained subjective and objective improvements in MUI patients over a six-month period, with a favorable safety profile. This approach represents a paradigm shift in MUI management, offering a minimally invasive, holistic treatment. While these results are compelling, further validation through large-scale, randomized controlled trials is essential to solidify its role in the urological armamentarium.

Keywords: Mixed Urinary Incontinence, Platelet-Rich Plasma, Regenerative Medicine, Stress Urinary Incontinence, Overactive Bladder, Dual-Target Therapy, Minimally Invasive Procedures.

1. Introduction

Mixed urinary incontinence (MUI), the simultaneous complaint of involuntary leakage associated with both effort/exertion and urgency, is a prevalent and debilitating condition that significantly impairs quality of life [1]. Its management is notoriously complex, as it necessitates addressing two distinct pathophysiological pathways: the intrinsic sphincter deficiency or urethral hypermobility underlying SUI and the detrusor overactivity or urothelial dysfunction responsible for UUI [2]. Conventional treatments, including mid-urethral slings for SUI and anticholinergics or β 3-agonists for UUI, often focus on the predominant symptom and can be associated with morbidity, side effects, and unsatisfactory outcomes for the non-targeted component [3,4].

Regenerative medicine offers a compelling alternative by aiming to restore normal tissue structure and function. Platelet-rich plasma (PRP), an autologous biological product enriched with a high concentration of platelets, growth factors (e.g., PDGF, TGF- β , VEGF), and cytokines, has gained traction in urology due to its safety, ease of preparation, and regenerative potential [5]. The rationale for PRP is twofold: its injection into the urethral sphincter can promote muscle regeneration, angiogenesis, and collagen synthesis to improve closure pressure, while its instillation into the bladder can modulate inflammation, promote urothelial healing, and restore the glycosaminoglycan layer to reduce sensory urgency [6,7].

Historically, studies have explored these applications in isolation. However, the logical progression to a combined approach for MUI had remained largely unexplored until the recent groundbreaking work by Omar et al. (2025) [8]. This review aims to consolidate the existing evidence on PRP for incontinence and provide a critical analysis of this novel dual-target technique, positioning it as a potential transformative therapy for MUI.

2. Pathophysiological Basis for a Dual-Target Approach

The efficacy of a combined PRP strategy is predicated on directly targeting the unique mechanisms of each incontinence type.

- **SUI Component:** The primary deficit in SUI is inadequate urethral closure pressure, often due to urethral hypermobility or intrinsic sphincter deficiency (ISD) [2]. PRP injections are theorized to address this by stimulating the proliferation of skeletal muscle satellite cells to enhance sphincter mass, inducing fibroblast activity for collagen deposition and structural support, and promoting angiogenesis (VEGF) to improve tissue health and durability [6,9].
- **UUI Component:** UUI often stems from increased detrusor excitability and afferent hypersensitivity, frequently linked to urothelial barrier dysfunction and neurogenic inflammation [10]. Intravesical PRP acts through anti-inflammatory effects, promoting the regeneration of a healthy urothelium and GAG layer, and potentially modulating sensory nerve activity, thereby reducing the aberrant signaling that causes urgency [7,11].

The interplay between these components in MUI creates a cycle where each can exacerbate the other, making a unified treatment strategy not just logical but necessary.

3. Clinical Evidence for PRP in Incontinence: From Monotherapy to Combination Therapy

3.1 PRP for Stress Urinary Incontinence: Several studies have established the role of periurethral PRP injections for SUI. A systematic review by Baron et al. (2023) concluded that PRP is a safe and effective treatment, showing significant improvements in pad weight, validated questionnaire scores, and patient-reported outcomes [9]. The combination of PRP with pelvic floor muscle training has been shown to be superior to training alone [12], underscoring its regenerative rather than purely bulking effect.

3.2 PRP for Bladder Conditions and UUI: The evidence for intravesical PRP is robust in interstitial cystitis/bladder pain syndrome (IC/BPS), a condition with a similar pathophysiology of urothelial dysfunction. A meta-analysis by Lin et al. (2023) found that intravesical PRP instillations significantly improved pain, urinary symptoms, and quality of life in IC/BPS patients compared to controls [11]. These findings provide a strong mechanistic foundation for its use in managing the urge component of MUI.

3.3 The Pioneering Dual-Target Trial: The study by Omar et al. (2025) is the first to bridge this gap by evaluating a combined protocol [8]. Their prospective trial on 24 women with MUI employed four monthly sessions of intra-sphincteric PRP injection (5 mL) followed by intravesical PRP instillation (20 mL). The results were profound:

- **Subjective Outcomes:** The ICIQ-SF score showed a statistically significant decrease from 16.5 ± 2.3 at baseline to 9.9 ± 3.4 at six-month follow-up ($p < 0.001$). OAB symptom scores shifted dramatically from predominantly moderate/severe to mild.
- **Objective Outcomes:** The cough stress test converted from 100% positive to 86% negative. Crucially, urodynamic studies confirmed a reduction in urodynamic stress incontinence (100% to 14%) and detrusor overactivity (100% to 29%) ($p < 0.001$ for both).
- **Safety:** The procedure was well-tolerated, with transient dysuria (29%) and suprapubic pain (17%) as the most common side effects.

This study provides Level 2 evidence that the dual-target approach is not only feasible but highly effective, achieving objective cure rates for SUI on par with mid-urethral slings while simultaneously addressing UUI.

4. Comparative Analysis and Clinical Implications

The outcomes reported by Omar et al. [8] compare favorably with existing therapies. The ability to significantly improve both components of MUI in a single, minimally invasive procedure is unprecedented. Unlike slings, which carry risks of erosion, obstruction, and pain, or medications, which have systemic side effects and variable efficacy, PRP offers an autologous, well-tolerated alternative. This technique challenges the traditional siloed approach to MUI management, advocating for a holistic regenerative strategy.

5. Limitations and Future Directions

Despite the promising results, the evidence is still in its infancy. The Omar et al. study [8], while robust, has limitations inherent to a pilot trial: the lack of a control or sham group and a small sample size (n=24). These factors preclude definitive conclusions about the magnitude of the effect relative to placebo.

Future research must focus on:

1. **Large-Scale RCTs:** Randomized, double-blind, placebo-controlled trials are the essential next step to confirm efficacy and establish effect size.
2. **Protocol Optimization:** Determining the optimal number of treatments, PRP preparation system (leukocyte-rich vs. poor), injection volume, and long-term durability (>1-2 years).
3. **Mechanistic Studies:** Investigating the histopathological and molecular changes induced by PRP in the urethra and bladder wall.
4. **Comparative Studies:** Head-to-head trials comparing dual-target PRP to standard first-line treatments for MUI.

6. Conclusion

The management of mixed urinary incontinence is undergoing a significant evolution with the advent of regenerative medicine. The dual-target PRP technique, which concurrently addresses the sphincteric deficiency of SUI and the urothelial dysfunction of UUI, represents a paradigm shift. The initial clinical evidence demonstrates that this approach is safe, minimally invasive, and capable of producing significant and sustained subjective and objective improvements. It offers a powerful potential alternative for patients seeking to avoid the risks of surgery or the side effects of medications. While further high-quality research is needed, combined intra-sphincteric and intravesical PRP therapy stands poised to become a cornerstone in the modern, personalized management of mixed urinary incontinence.

Conflict of Interest

The authors declare no conflict of interest.

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