Section: Urology

Original Research Article

A STUDY ON THE EFFECT OF MIRABEGRON IN URETERIC STENT RELATED MORBIDITY, A PROSPECTIVE STUDY AT TERTIARY HOSPITAL

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ABSTRACT

Background: Ureteral stents, though commonly used post-ureteroscopy for urolithiasis, are associated with significant morbidity, including pain, urinary symptoms, and reduced quality of life (QoL). Alpha-blockers like tamsulosin have shown limited efficacy in addressing these issues. Mirabegron, a β3-adrenoceptor agonist traditionally used for overactive bladder, presents a potential alternative with fewer side effects. This study evaluates the efficacy of Mirabegron in reducing stent-related morbidity in patients undergoing ureteral stent placement after unilateral ureteroscopic lithotripsy**. Materials and Methods**: This prospective, randomized study was conducted on 180 patients at Osmania General Hospital between February 2023 and April 2024. Patients were randomized into two groups: Group A received standard post-operative care; Group B received standard care plus Mirabegron 50 mg once daily for 21 days. Symptom burden was assessed using the International Prostate Symptom Score (IPSS), Visual Analog Pain Scale, and QoL indices at baseline and at 3 weeks post-procedure. **Result**: Baseline symptom scores were comparable between groups. At stent removal, Group B demonstrated significantly lower IPSS (5.12 vs 13.37, $p < 0.001$), irritative symptom scores (2.34 vs 8.82, $p < 0.001$), and pain scores (3.10 vs 5.67, $p < 0.001$), along with better QoL scores (2.08 vs 3.43, $p < 0.001$) than Group A. Within-group comparisons confirmed symptom worsening in Group A and significant improvement in Group B. **Conclusion:** Mirabegron 50 mg once daily significantly reduces ureteral stent-related morbidity and improves quality of life, offering a well-tolerated and effective alternative to traditional alpha-blocker therapy in stented patients post-URS.

INTRODUCTION

Double-J (DJ) ureteric stents have become an almost reflex addition to ureteroscopic lithotripsy (URSL) because they secure drainage, prevent early obstruction, and permit passive ureteric dilatation for fragment passage. Unfortunately, up to 80 – 90 % of stented patients develop a spectrum of lower-urinary-tract symptoms (LUTS), flank pain, dysuria and haematuria that collectively impair sleep, work performance and quality of life (QoL).

α-Adrenergic antagonists (eg. tamsulosin) partly alleviate pain and urgency by reducing ureteric peristalsis and bladder-neck resistance. Clinical effect, however, is modest and balanced by dizziness, orthostatic hypotension and ejaculatory dysfunction that limit adherence, particularly in young or hypertensive men.

Mirabegron, a selective β3-adrenoceptor agonist originally licensed for over-active bladder, relaxes detrusor smooth muscle during the filling phase while sparing cholinergic and α-adrenergic pathways; its safety profile is favourable and cardiovascular events are rare at the therapeutic dose (50 mg once daily). Proof-of-concept trials suggest that mirabegron lessens stent-related urgency and frequency, yet the evidence base remains heterogeneous and under-powered.

We therefore prospectively evaluated whether mirabegron 50 mg, daily reduces stent-associated morbidity more effectively than standard care alone among adults undergoing unilateral URS with DJ stenting at a high-volume tertiary centre in South India.

MATERIALS AND METHODS

A single-centre, parallel-group, open-label randomised controlled trial was performed between February 2023 and April 2024 in the Department of

Urology, Osmania General Hospital, Hyderabad, Telangana. The protocol was approved by the Institutional Ethics Committee (IEC/OGH/2022-595) and registered prospectively with the Clinical Trials Registry–India (CTRI/2023/01/049999). Written informed consent was obtained from every participant.

Eligibility criteria

Inclusion

- Age ≥ 18 years.
- Single, uncomplicated ureteric calculus treated by semi-rigid URS with complete fragment clearance.
- Placement of a unilateral 4.5 Fr, 26 cm silicone DJ stent.
- Sterile pre-operative urine culture.
- Ability to complete questionnaires in Telugu, Hindi or English.

Exclusion

- Bilateral stents or solitary kidney.
- Pregnancy or lactation.
- History of benign prostatic enlargement with LUTS, neurogenic bladder, stress incontinence, urethral stricture or bladder malignancy.
- Use of α-blocker, anti-muscarinic or β3-agonist within 4 weeks.
- Bleeding diathesis, uncontrolled hypertension (>160/100 mmHg).
- Hypersensitivity to mirabegron.
- Failure to achieve stone-free status or intra-operative ureteric injury.

Randomisation and masking

A biostatistician generated a computer sequence in blocks of ten (1:1). Allocation concealment employed sequentially numbered opaque envelopes opened after surgery by the ward nurse. Because mirabegron tablets added obvious pill burden, participant blinding was not feasible; outcome assessment and statistical analysis were performed by personnel unaware of group allocation.

Interventions

- Group A (Control) Standard care: ciprofloxacin 500 mg 12-hourly × 3 days + paracetamol 500 mg t.i.d. prn.
- Group B (Mirabegron) Standard care plus mirabegron 50 mg orally once daily from post-operative day 1 to day 21 (inclusive).
- Drug compliance was verified by return-pill count at follow-up.

Outcome measures

Primary outcome

- **Change in total International Prostate Symptom Score (IPSS)** between post-operative day 7 (baseline) and day 21 (stent removal).

Secondary outcomes

1. Irritative (storage) IPSS sub-score, obstructive sub-score.
2. Visual Analogue Scale (VAS 0–10) for flank/suprapubic pain.
3. Single QoL question within IPSS (scale 0–6)
4. Adverse events related to mirabegron (blood pressure, tachycardia, headache, allergy)

Data Collection

Demographics, BMI, stone site (upper/mid/lower ureter), operative time and anaesthetic details were recorded. Baseline symptom assessment was intentionally deferred to post-operative day 7 to avoid confounding by immediate post-surgical pain. The same validated questionnaires were administered on day 21 immediately before cystoscopic stent extraction.

Sample-size justification

A clinically meaningful difference of 3 points in total IPSS (SD=6) was anticipated. With $\alpha = 0.05$ and power = 0.90, 80 patients per arm were required. Allowing 10 % attrition, 180 participants were recruited.

Statistical Analysis

SPSS v26 (IBM, USA) was used. Normality was examined by Kolmogorov–Smirnov test. Continuous variables were compared with independent-sample or paired t-tests; skewed data used Mann–Whitney U. Categorical variables employed χ^2 or Fisher's exact test. Two-tailed $p < 0.05$ was considered significant.

RESULTS

Flow of participants

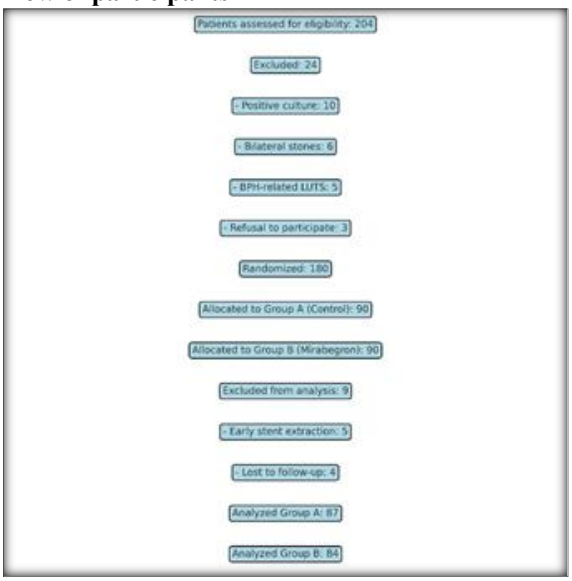

Figure 1: CONSORT diagram

Of 204 screened patients, 24 were excluded (positive culture = 10; bilateral stones = 6; BPH-related LUTS = 5; refusal = 3). One hundred eighty were randomised (90 per arm). Nine were removed from analysis (early stent extraction for haematuria = 5; lost to follow-up = 4). The per-protocol cohort comprised 171 (Group A = 87, Group B = 84). Figure 1 depicts the CONSORT diagram.

Baseline comparability

Groups were well matched for demographics, stone characteristics, operative variables, and baseline symptom scores (Table 1).

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Table 1: Baseline demographic and clinical variables

Characteristic	Group A (n = 87)	Group B (n = 84)	*p*
Age (y), mean ± SD	35.8 ± 10.4	36.6 ± 11.2	0.62
Male sex, n (%)	58 (66.7)	54 (64.3)	0.75
BMI (kg m^{-2})	25.2 ± 3.4	24.9 ± 3.7	0.48
Stone site, n (%)	Upper 25 / Mid 12 / Lower 50	Upper 24 / Mid 10 / Lower 50	0.92
Mean operative time (min)	38.4 ± 8.7	37.9 ± 9.1	0.71
Baseline total IPSS	7.68 ± 2.18	7.91 ± 1.77	0.43
Baseline VAS pain	4.24 ± 1.04	4.31 ± 1.08	0.68
Baseline QoL score	2.89 ± 0.68	3.06 ± 0.61	0.09

Primary endpoint

At day 21, mean total IPSS increased in controls (7.68 → 13.37, $p < 0.001$) and decreased in mirabegron patients (7.91 → 5.12, $p < 0.001$). The between-group difference was −8.25 points (95 % CI: −8.9 to −7.6; $p < 0.001$).

Secondary endpoints

Mirabegron produced significant advantages across all secondary parameters (Table 2; Figure 2)

Table 2: Outcomes at stent removal (day 21)

Outcome	Group A (n = 87) mean ± SD	Group B (n = 84) mean ± SD	Mean difference (95 % CI)	*p*
Total IPSS	13.37 ± 2.13	5.12 ± 0.67	−8.25 (−8.9, −7.6)	<0.001
Irritative sub-score	8.82 ± 1.76	2.34 ± 0.50	−6.48 (−6.9, −6.0)	<0.001
Obstructive sub-score	4.54 ± 0.75	2.78 ± 0.70	−1.76 (−2.0, −1.5)	<0.001
VAS pain	5.67 ± 0.92	3.10 ± 0.70	−2.57 (−2.8, −2.3)	<0.001
QoL score	3.43 ± 0.81	2.08 ± 0.74	−1.35 (−1.6, −1.1)	<0.001

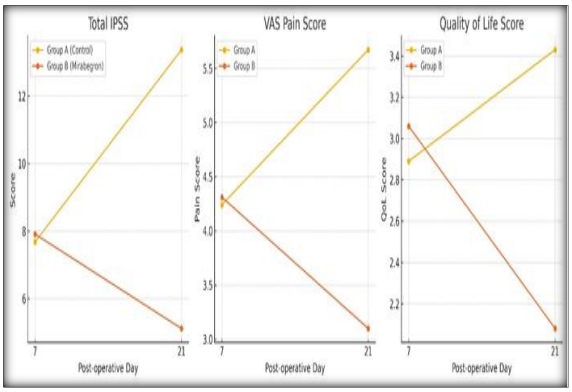

Figure 2: Line graphs showing mean changes in (a) total IPSS, (b) VAS pain and (c) QoL scores from baseline to day 21.

Safety Profile

Mirabegron was well tolerated. Transient headache occurred in 2 patients (2.4 %) and mild palpitations in 1 patient (1.2 %); all resolved spontaneously. No discontinuation or serious adverse event occurred. Blood pressure readings did not differ significantly between groups at any visit

DISCUSSION

Principal findings

In this pragmatic Indian cohort, mirabegron 50 mg once daily for 21 days substantially mitigated LUTS, flank pain and QoL deterioration attributable to indwelling DJ stents when compared with standard care. The 8-point absolute reduction in total IPSS exceeds the minimal clinically important difference (3 points) and mirrors the magnitude of relief patients expect when opting for early stent removal.

Mechanistic considerations

Stent irritation provokes involuntary detrusor contractions and vesico-ureteric reflux during voiding, raising pelvic pressure and producing flank pain. β3-receptor activation by mirabegron relaxes detrusor smooth muscle, augments bladder capacity and blunts urgency without compromising contractile voiding efficacy. Our data – particularly the marked improvement in storage sub-score (−6.5 points) – reinforce this mechanistic rationale.

Comparison with literature

Our results align with Cinar et al. (Turkey) and Tae et al. (Korea), who also observed significant reductions in USSQ or IPSS domains. Yavuz et al. reported equivocal benefit, but noteworthy methodological differences include shorter mirabegron exposure (14 days) and smaller sample size (n = 60). A recent meta-analysis by Lu et al. pooled five trials (n = 309) and confirmed superiority of mirabegron over anti-muscarinics or placebo in relieving stent symptoms; our larger South-Asian dataset adds robust confirmatory evidence.

Strengths and limitations

Strengths

- Prospective randomisation with adequate sample and power.
- Uniform stent calibre/length and single stent material to eliminate hardware confounding.
- Use of validated, language-adapted questionnaires and per-protocol analysis.

Limitations

- Open-label design may introduce expectation bias, though objective pain and QoL measures minimised subjectivity.
- IPSS was selected for literacy practicality; the Ureteric Stent Symptom Questionnaire (USSQ)

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could have captured sexual and work-performance domains.
- Lack of active comparator (tamsulosin or solifenacin) precludes direct head-to-head efficacy conclusions.
- Single-centre setting may limit generalisability; nevertheless, patient demographics reflect typical government hospital caseloads in India.

Clinical implications

Given the simplicity of once-daily dosing, negligible sexual side-effects and sparse cardiovascular events, mirabegron appears an attractive first-line pharmacological option for stent-related morbidity, particularly among:

- Young men wary of tamsulosin-induced retrograde ejaculation.
- Elderly hypertensive patients susceptible to orthostatic hypotension.
- Women intolerant of antimuscarinic xerostomia or constipation.

Routine prescription could reduce unscheduled emergency visits and lost work-days, providing socio-economic benefit in resource-restricted settings.

Future directions

Randomised head-to-head comparisons of mirabegron versus silodosin or combination β3-agonist + α-blocker regimens will clarify optimal pharmacotherapy. Longer follow-up may explore whether benefits persist when delayed stent removal (>4 weeks) is unavoidable, a frequent reality in busy public hospitals.

CONCLUSION

Mirabegron 50 mg once daily for three weeks significantly reduces LUTS, pain and QoL impairment associated with unilateral DJ stents after URSL. Its favourable tolerability and ease of administration justify adoption as frontline therapy for stent-related morbidity in adult Indian patients.

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