Abstract No. 68

Efficacy and Safety of Mirabegron for the Treatment of Low Compliant Acontractile/Underactive Detrusor due to Conus/Cauda Lesions: A Prospective Study

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INTRODUCTION & AIM

•A significant proportion of patients with acontractile/underactive neurogenic bladders will develop high end filling pressures and poor compliance over time, risking the upper tracts.
•Mirabegron has shown efficacy in patients with idiopathic over active bladder.
•However its effects on patients with acontractile/underactive poorly complaint neurogenic bladder remains undefined.
•We present the first prospective study evaluating the clinical and urodynamic efficacy and safety of Mirabegron in patients with low compliant acontractile/underactive detrusor due to Conus/Cauda lesions.

METHODS

•Prospective study, ethical clearance obtained
•**Inclusion criteria:** Adult patients of acontractile/underactive neurogenic bladders with low compliance (defined as <40ml/cmH2O for study purposes) due to conus/cauda lesions.
•**Exclusion criteria:** Patients with symptomatic urinary tract infection, gross hydroureteronephrosis, previous urologic surgery, prior treatment with intradetrusor botulinum toxin injection, history of pelvic radiation, uncontrolled hypertension (systolic >180mmHg and/or diastolic >110mmHg), unstable cardiac disease or abnormal electrocardiogram (ECG), deranged kidney or liver function tests, history of glaucoma, and those unwilling to give consent or unwilling to do clean intermittent catheterization (CIC).
•**Evaluation:** Baseline investigations included urine routine and culture, kidney and liver function tests, ECG, ultrasonography of kidney bladder prostate with post void residual urine estimation, micturating cystourethrography, and invasive urodynamic data pertaining to filling phase .
•Newly diagnosed cases/those who were not employing CIC as the bladder emptying method were instructed to start performing CIC 6th hourly. Those already on CIC were allowed to continue their previous schedule.
•All patients were asked to make a CIC diary of 48 hours duration and this baseline data was also recorded.
•Those patients who were already on an antimuscarinic were advised to continue the drug in the same dosage
•All patients were started on tab mirabegron 50mg once daily for 6 weeks.
•At 6 weeks, all patients made another 48 hour CIC diary and underwent a repeat invasive urodynamic evaluation. Side effects, if any, were noted.
•The **primary outcome** analysis included CIC diary parameters and urodynamic variables (efficacy) whereas the tolerability/side effect profile constituted the **secondary outcomes**.
•Variables at the baseline were compared to that at 6 weeks using the paired t test and a p value of <0.05 was considered statistically significant.

RESULTS

•20 patients included, 17 males and 3 females, mean age 34.1 years
•Mean duration of symptoms was 77.7 months (6-276 months)
•Six patients were already on CIC, the rest 14 were started on CIC after inclusion
•Four patients were already on antimuscarinics.

Primary Outcomes:

a)CIC diary:

After 6 weeks of mirabegron therapy:
•Mean urine volume per CIC was 280.7 ml (36.1 - 711 ml) (compared to 268.2ml (55-495ml) at baseline) (p = 0.8)
•Total 24 hr CIC volume (urine output) was 1735.5 ml (250 -4010 ml) (compared to 1954.5 ml (445-3950 ml) at baseline) (p = 0.1)
•*Only 2 patients recorded leakage in the intervening time between CIC as compared to 7 at the baseline (p value 0.02).*

b) Invasive Urodynamics:

Various urodynamic parameters recorded at the baseline and at 6 weeks follow-up are summarized in Table 1.
•Improvement in compliance noted in all but 3 patients in whom it deteriorated further (from 18 ml/cmH2O to 12.7 ml/cmH2O).
At the 6 week urodynamic assessment:
•None had leak on UDS as compared to 4 at baseline (at mean DLPP of 37.05 cmH2O),
•The end filling pressure exceeded 40cmH2O in two patients (at mean volume of 381ml) (as compared to 8 at baseline at a mean volume of 249.6 ml, p = 0.058).

Secondary Outcomes:

Side effects: none discontinued medication or developed intolerable untoward effects.
•No significant changes in pulse rate, systolic BP or diastolic BP.
•Six patients reported dry mouth at the baseline, which was perceived to be similar in intensity at 6 weeks in 4 and increased in intensity 2 patients.
•Four patients developed new onset dry mouth during the treatment.
•No patient developed new onset constipation.

Failed antimuscarinic subgroup:

Various urodynamic parameters recorded at the baseline and at 6 weeks follow-up are summarized in Table 2.
•The end filling pressures and compliance showed a significant improvement post therapy.

Table 1: Urodynamic parameters at baseline and at 6 weeks post therapy of all patients.

Parameter	Baseline	6weeks	P value
Mean volume at first sensation (ml)	157.9 (42 - 419)	143.3 (38 - 409	0.32
Mean volume at strong desire (ml)	275.1 (88 - 570)	302.5 (105 - 647)	0.72
Mean volume at cystometric capacity (ml)	368.1 (96 - 724)	386.2 (121 - 765)	0.62
Mean End Filling Pressure (EFP) (cmH2O)	*38.2 (19.2 - 97.5)*	*15.5 (0 - 53.6)*	*0.003*
Mean compliance (ml/cmH2O)	*12.5 (0.9 - 33.2)*	*101.5 (5 - 410)*	*0.000*

Table 2: Urodynamic parameters at baseline and at 6 weeks post therapy in the failed antimuscarinic group.

Parameter	Baseline	6weeks	P value
Mean volume at first sensation (ml)	129.3(119-192)	107(82-174)	0.41
Mean volume at strong desire (ml)	235.6(135-298)	332.3(125-638)	1.00
Mean volume at cystometric capacity (ml)	390.5(150-724)	427.5(136-661)	0.71
Mean End Filling Pressure (EFP) (cmH2O)	*46.1(41.7-54.3)*	*15.5(5.6-21.7)*	*0.06*
Mean compliance (ml/cmH2O)	*8.1(3.6-13.3)*	*42.3(13.8-110.1)*	*0.00*

CONCLUSIONS

•Mirabegron is safe and effective in patients with low compliant acontractile/underactive neurogenic bladder.
•It reduces end filling pressure and improves compliance
•It does not significantly affect the cystometric capacity.
•Mirabegron therapy is equally effective and similarly well tolerated when prescribed as add on therapy to patients with inadequate response to antimuscarinics when compared to antimuscarinic naïve patients.

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