An explorative analysis of the effect of a beta 3 adrenoreceptor agonist (Mirabegron) on urethral pressure variations during filling cystometry.

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To evaluate the effect of beta 3 adrenoreceptor agonist on urethral pressure variations during filling phase and to initially explore the possibilities for individualisation of treatment for overactive bladder symptoms.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Urethral disorders (excl calculi)
Study type	Observational invasive

Summary

ID

NL-OMON46848

Source
ToetsingOnline

Brief title
Effect Mirabegron on urethral pressure variation during filling cystometry

Condition

- Urethral disorders (excl calculi)

Synonym
overactive bladder, urgency

Research involving
Human

Sponsors and support

Primary sponsor: Haaglanden Medisch Centrum

Source(s) of monetary or material Support: unrestricted grant Astellas Pharma

Intervention

Keyword: mirabegron, overactive bladder, urethra pressure, urodynamics

Outcome measures

Primary outcome

Number (proportion) of patients with a reduction of significant urethral pressure variations >15cmH2O on urodynamic investigation (two sequential standard filling cystometries until strong desire to void) while on treatment with beta 3 adrenoreceptor agonist.

Secondary outcome

* Difference of total number of urethral pressure variations on urodynamic investigation after treatment, compared to initial urodynamic investigation.

* Difference in volume to first detrusor contraction between *before* and *on treatment*.

* Differences in volume to first sensation of filling, normal desire to void and strong desire to void, between *before* and *on treatment*.

* Difference in volume to first urethral pressure drop between *before* and *on treatment*.

* Difference in largest pressure drop (cmH2O) between *before* and *on treatment*.

* To explore the association of symptoms and voiding diary data before and on treatment with a beta 3 adrenoreceptor agonist with significant urethral pressure variations/ urethral pressure drops during urodynamic investigation (before and on treatment).

* Sexual function as measured with a questionnaire before and on treatment with

beta 3 adrenoreceptor agonist.

Comparison of (grouped average) individual before and on treatment effect(s) of

a beta 3 adrenoreceptor agonist on symptoms and voiding diary and urodynamic

parameters

Study description

Background summary

Patients with overactive bladder symptoms have an increased voiding frequency and a sudden need to urinate (*urinary urgency*). In a large proportion of these patients detrusor (=bladder muscle) overactivity can be demonstrated during the filling (urine-storage) phase of a urodynamic investigation (= investigation to measure bladder function or dysfunction, which explains the pathophysiology of the symptoms). With or without urodynamic diagnosis, the mainstay of treatment for patients with overactive bladder symptoms is oral anticholinergical or antimuscarinergical pharmacotherapy (*bladder muscle relaxants*).
During the filling (urine storage) phase of a urodynamic investigation however, urethral (bladder outlet) pressure variations can be observed in association with detrusor overactivity in a proportion of patients. The clinical relevance and or the role of urethral pressure variations in the pathophysiology are yet not precisely established.
Recently a beta 3 adrenoreceptor agonist is approved for the treatment of overactive bladder symptoms. The beta 3 adrenoreceptor agonist stimulates inhibition of detrusor overactivity (and is clinically and urodynamically effective in this regard). Theoretically beta 3 adrenoreceptor agonists may, apart from inhibition of detrusor overactivity, stimulate the urethra to maintain closure *contraction.
Patients with urethral pressure variations might therefore especially benefit from beta 3 adrenoreceptor agonist since theoretically the treatment might *stabilize* the urethral pressure and therefore reduce symptoms of *urinary urgency*. The effect of a beta 3 adrenoreceptor agonist on the urethral pressure and or on urethral pressure variations during filling cystometry is however unknown.

Study objective

To evaluate the effect of beta 3 adrenoreceptor agonist on urethral pressure

variations during filling phase and to initially explore the possibilities for individualisation of treatment for overactive bladder symptoms.

Study design

Multicentre prospective open label observational cohort study to evaluate the short term urodynamic effect of treatment with a beta 3 adrenoreceptor agonist, in patients with symptoms of overactive bladder.
After initial urodynamic investigation a cohort of patients will be treated for 6 weeks with beta 3 adrenoreceptor agonist to conclude with * endpoint - urodynamic investigation while on medication. The study is an observational cohort with invasive * endpoint- measurement.

Study burden and risks

Treatment with beta 3 adrenoreceptor agonist is clinically safe and effective. Urodynamic testing at the start of treatment is standard in patients resistant to first line treatment. However, also in second line treatment a pragmatic approach on the basis of symptoms without further urodynamic tests is usually the first step of management in many practices. The second urodynamic investigation, and for some patients also the initial urodynamic investigation will be extra, as a consequence of our research question.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Female.
>18 years of age.
Mentally fit to consent.
(Referred with) Bothersome OAB symptoms (standard symptom and bother score)
Voiding diary with total urine production in 24 hour (morning to morning) <2200mL
Treating physician has indicated treatment with B3AA Mirabegron
Signed informed consent
May have had *unsatisfying- treatment with antimuscarinergic medication
Willing to stop medication for lower urinary tract dysfunction 2 days before urodynamic investigation (at entry of study)
Willing to start B3AA *study medication- after initial urodynamic investigation

Exclusion criteria

* Sediment + or clinical signs of UTI at the start of the urodynamic investigation
* Necessity to perform CIC or significant post void residual (>100mL).
* Significant voiding abnormalities; bladder outlet obstruction (UDI >grade 1 or BOOI >20) or underactive or acontractile detrusor.
* Unwilling or unable * according to treating physician- to stop current treatment for lower urinary tract dysfunction.
* Treatment with intradetrusor botulinum toxin less than one year before urodynamic investigation (whether or not symptomatically effective).
* Having a contraindication for treatment with B3AA : severe renal impairment with GFR <15 mL/min/1.73m2 or patients requiring haemodialysis) or severe hepatic impairment (Child-Pugh Class C)
* Pregnancy or breastfeeding.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-05-2015
Enrollment:	75
Type:	Actual

Ethics review

Approved WMO

Date:	14-10-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	11-05-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	26-07-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL48463.098.14

Study results

Date completed:	01-08-2018
Actual enrolment:	49

Summary results
Trial is onging in other countries