Integrale Overactieve Blaas Clinical Trial in de klinische praktijk III.

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27243

Source
Nationaal Trial Register

Brief title
INTACT III

Health condition

overactive bladder
clinical practice
clinical trial
integrated

overactieve blaas
klinische praktijk
klinische studie
integraal

Sponsors and support

Primary sponsor: Maastricht University Medical Center + , P.O.Box 5800, 6202 az, Maastricht, the Netherlands,
Source(s) of monetary or material Support: initiator + sponsor

Intervention

Outcome measures

Primary outcome

1. The proportion of patients who have a treatment response of improvement of at least 2 categories on the PPBC (Coyne 2006). As stated before, the power calculation to define the sample size for this study is based on the PPBC;

2. The mean change from baseline to endpoint in Incontinence Episodes Frequency (IEF) as recorded in the 3 day micturition chart (frequency volume chart).

Related to primary objective 2:

Safety measures:

1. Adverse events;

2. Serious medical events.

To evaluate the safety of the procedure through prospective observation of serious adverse events
and serious adverse device effects.

Endpoint: The analysis of the incidence of serious adverse device effects through the course of the
study. Safety data (vital signs, occurrence and duration of adverse events (AEs), and drop-out/discontinuation during study due to AEs). Measurement of post void residual (PVR) urine volume.

Secondary outcome

1. Intensity of urgency scale (Patient Perception of Intensity of Urgency Sensation (PPIUS)) (Cartwright 2010);

2. Mean absolute change in number of voids/24 hrs (3-days micturition diary);

3. Volume involuntary loss of urine (from 3-days micturition diary);

4. Urinary Incontinence-Specific Quality-of-Life Instrument Dutch (I-QOL) Total score change from baseline, subscale change from baseline;

5. PRAFAB (Impact and severity of urinary incontinence) Total score change from baseline;

6. Patient's satisfaction;

7. Percentage patients with a positive response on "Behandeling Baat Schaal" . (score is 1 or 2, i.e., "fors verbeterd"or "verbeterd".

Study description

Background summary

Rationale:

INTACT III is the follow up study of INTACT II. Participants will be eligible in case they were not successful after or non-responders to conservative treatments as specified in INTACT I and to PTNS as specified in INTACT II. After non-successful first line treatment and the minor invasive intervention PTNS, the urologist can choose between Sacral Neurostimulation (SNS) or botulinum toxin injections in the bladder wall. Based on both randomized and non-randomized studies, investigators concluded that these treatment modalities might offer a safe invasive and effective treatment for managing refractory overactive bladder and/or pelvic floor dysfunction.

Objective:

The realisation of (the implementation of) an effective and efficient protocol and model, useful in first and second line clinical practice for patients with idiopathic OAB in order to differentiate between successfully treated patients and non-successful treated patients who then will be selected for INTACT III.

Study design:

INTACT III is a mono-centre, single-blind, randomized, pragmatic, parallel-group study to assess the efficacy and safety of SNS (Group 1) compared to a single treatment of BOTOX® (Group 2) followed by a second treatment (if applicable) with BOTOX® (Group 2) in patients with idiopathic OAB with urinary incontinence whose symptoms have not been adequately managed with conservative therapy, i.c. anticholinergic therapy or pelvic physiotherapy or PTNS.

Study population:

Adult women and men, living in the region South- Limburg, with symptoms of frequency and/or urgency and urinary incontinence who consulted an urologist, who, after non-successful INTACT I and II or who, after consultation of their general practitioner and/or urologist did not wish to participate in INTACT I or II.

Intervention:

After diagnosing OAB (with urodynamics) subject will be randomized either to SNS or to BOTOX® injections. In case the first BOTOX® injection will not be successful a second BOTOX® injection will be given after 6 months. Six months after each injection and 12 months after the last one outcome will be measured, using the predefined study parameters.

Diagnostics and treatments will be performed at the MUMC+ by especially trained urologists. Normally, treated subject may leave the hospital the same day.

Main study parameters/endpoints:

1. The proportion of patients who have a treatment response of improvement of at least 2 categories on the Patient Perception of Bladder Control (PPBC);

2. The mean change from baseline to endpoint in Incontinence Episodes Frequency per week (IEF) as recorded in the 3 day micturition diary (frequency volume chart).

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

Several published peer-reviewed (non-)randomized clinical trials seems to demonstrate the safety and efficacy for both SNS and BOTOX® injections. None of these studies would report significant adverse events or side effects. Participation in the study means that the patient will undergo a minor invasive surgery, i.c., SNS or will undergo maximally 3 BOTOX® injection sessions, dependent on the success of the former BOTOX® injection. Subjects need to fill out questionnaires at onset of therapy, after 6 months and 12 months. In case of success patients will suffer significantly less of urgency and frequency and eventually urgency urinary incontinence, increasing their often jeopardized quality of life.

Study objective

1. SNS is more effective than BOTOX® 100 U as assessed by the difference between treatment groups in the proportion of idiopathic OAB patients with a positive treatment response on the Patient Perception of Bladder Condition (PPBC) at Week 12 after (first) treatment , 6 months and at 12 months after treatment;

2. SNS is more effective than BOTOX® 100 U improving the symptoms of idiopathic OAB as measured by the difference between treatment groups in the reduction of urinary incontinence episodes at Week 12 after (first) treatment and at Week 52 after treatment.

Study design

Subjects need to fill out questionnaires at onset of therapy, after 6 months and 12 months.

Intervention

Group 1: SNS treatment:

SNS is a rehabilitative treatment to be used to treat selected patients with OAB (Siegel 2000, Aboseif 2007) . In this technique, low-intensity electrical impulses are generated by an implantable neurostimulator (INS) (also referred to as an implantable pulse generator (IPG)), and delivered via a conducting electrode to one of the lower sacral nerves (usually S3) involved in the control of lower urinary tract function. The neurostimulator will be programmed and interrogated externally by the physician with a magnetic programming device. With the use of the hand-held patient programmer, the patient can stop and start the INS, as well as increase and decrease the amplitude of the stimulation. Before the system is permanently implanted, a test with a permanent lead (two-stage procedure) will be carried out to identify whether or not the candidates is suitable for the permanent implant. The test phase will lasts 1-6 weeks. The patient qualifies for permanent implant if during the test phase, the patient reports at least 50% improvement in the micturition diary variables and lower urinary tract symptoms (as recorded in the micturition diary). The permanent implant of the system is by a minimally invasive technique which will be performed at the ‘Dagcentrum” of the MUMC.

Group 2: BOTOX® (Comparator):

Each vial of BOTOX® (Botulinum ToxinType A) Purified NeurotoxinComplex, (formulation no. 9060X), contains: 100 units (U) of Clostridium botulinum toxinType A, 0.5 mg albumin (human), and 0.9 mg sodium chloride in a sterile, vacuum-dried form without a preservative. One unit (U) corresponds to the calculated median lethal intraperitoneal dose (LD50) in mice. The botulinum toxin injections will be administred at the ‘Dagcentrum’ of the MUMC+. A flexible or rigid cystoscope may be used for study treatment administration. BOTOX® injections are administered as a minimally invasive technique which will be performed at the ‘Dagcentrum” of the MUMC. The urologist will receive one 10 mL syringe pre-filled with 10 mL of study medication and one 1 mL syringe pre-filled with saline from the independent drug reconstitutor. The 10 mL of study drug will be administered as 20 injections each of 0.5 mL.

Contacts

Public
Pelvic care Center Maastricht
Maastricht University Medical Center +
P.O.Box 5800
Bary Berghmans
Maastricht 6202 AZ
The Netherlands
Scientific
Pelvic care Center Maastricht
Maastricht University Medical Center +
P.O.Box 5800
Bary Berghmans
Maastricht 6202 AZ
The Netherlands

Eligibility criteria

Inclusion criteria

1. Written informed consent has been obtained;

2. Written documentation has been obtained in accordance with local privacy requirements, where applicable;

3. Patient is male or female, aged between 18 and 75 years old (Amundsen 2005);

4. Patient weighs ≥ 40 kg;

5. Patient has symptoms of idiopathic OAB (frequency and urgency) with urinary incontinence immediately prior to qualification, determined by documented patient history;

6. Patient experiences a mean of 3 episodes of urinary urgency incontinence in the 3-day patient bladder diary completed during the qualification period (qualification day -14 to start treatment day 1);

7. Patient experiences urinary frequency, defined as an average of ≥ 8 micturitions (toilet voids) per day i.e. a total ≥ 24 micturitions in the 3-day patient micturition diary completed during the qualification period (qualification day -14 to start treatment day 1);

8. Patient has a negative pregnancy test result if female and of childbearing potential;

9. Patient has a negative urine dipstick reagent strip test at start treatment day 1 (for nitrites, blood and leukocyte esterase) and, in the investigator's opinion, patient is asymptomatic for UTI on day of treatment;

10. Patient is able to complete study requirements including using the toilet without assistance, is able to collect volume voided per micturition measurements over a 24- hour period, complete micturition diaries and questionnaires, and attend all study visits in the opinion of the coordinating investigator.

Exclusion criteria

OAB patients not eligible for SNS and botulinum toxin type A:

1. Residual urine after micturition > 100 cc determined using sonography or catheterisation;

2. Presence of urinary tract infection (UTI), determined using urinary sticks. (temporarely until UTI has been solved by antibiotics, then still potential candidate);

3. Patient has symptoms of overactive bladder due to any known neurological reason (eg, spinal cord injury, multiple sclerosis, cerebrovascular accident, Alzheimer's disease, Parkinson's disease, etc);

4. Patient has a predominance of stress incontinence in the opinion of the coordinating investigator, determined by patient history;

5. Patient has received anticholinergics or any other medications or pelvic physiotherapy or PTNS to treat symptoms of overactive bladder, including nocturia, within 3 months of start treatment day 1;

6. Patient uses chronic intermittent catheterisation (CIC) or indwelling catheter to manage his or her urinary incontinence;

7. Patient has been treated with any intravesical pharmacologic agent (eg, capsaicin, resiniferatoxine) within 12 months of start treatment day 1;

8. Patient has history or evidence of any pelvic or urological abnormalities, bladder surgery or disease, other than 'overactive bladder', that may affect bladder function including but not limited to:
bladder stones and/or bladder stone surgery at the time of qualification or within 6 months prior to qualification, surgery (including minimally invasive surgery) within 1 year of qualification for: stress incontinence, uterine prolapse, rectocele, or cystocele;

9. Patient has a history of interstitial cystitis/painful bladder syndrome, in the opinion of the coordinating investigator;

10. Patient has an active genital infection, other than genital warts, either concurrently or within 4 weeks prior to qualification;

11. Patient has a history or current diagnosis of bladder cancer or other urothelial malignancy, and/or has un-investigated suspicious urine cytology results. Suspicious urine cytology abnormalities require that urothelial malignancy is ruled out to the satisfaction of the investigator according to local site practice;

12. Patient is male with previous or current diagnosis of prostate cancer or a prostate specific antigen (PSA) level of > 10 ng/L at screening. Patients with a PSA level of ≥ 4 ng/L but ≤ 10 ng/L must have prostate cancer ruled out to the satisfaction of the investigator according to local site practice;

13. Patient has evidence of urethral and/or bladder outlet obstruction, in the opinion of the coordinating investigator at qualification or start treatment day 1;

14. Patient has had urinary retention or an elevated PVR urine volume that has been treated with an intervention (such as catheterization) within 6 months of qualification. Note: voiding difficulties as a result of surgical procedures that resolved within 24 hours are not exclusionary;

15. Patient has a 24-hour total volume of urine voided > 3000 mL, collected over 24 consecutive hours during the 3-day bladder diary collection period prior to treatment day 1;

16. Patient has a history of 2 or more urinary tract infections within 6 months of qualification;

17. Patient has a serum creatinine level > 2 times the upper limit of normal at qualification;

18. Patient has current or previous un-investigated hematuria. Patient with investigated hematuria may enter the study if urological/renal pathology has been ruled out to the satisfaction of the investigator;

19. Patient has hemophilia, or other clotting factor deficiencies, or disorders that cause bleeding diathesis;

20. Patient cannot withhold any antiplatelet, anticoagulant therapy or medications with anticoagulant effects for 3 days prior to start treatment day 1. Note: some medications may need to be withheld for > 3 days, per clinical judgment of the investigator;

21. Patient has a known allergy or sensitivity to any components of the study medication, such as the active ingredients botulinum toxin type A or the inactive ingredients human albumin and sodium chloride or has had a known allergic reaction to any other botulinum toxin product such as Myobloc®, Dysport® or Xeomin® (Allergan Pharmaceuticals 2010), or antibiotics to be used during the study;

22. Females who are pregnant, nursing or planning a pregnancy during the study or females of childbearing potential who are unable or unwilling to use a reliable form of contraception

during the study;

23. Patient is currently participating in or has previously participated in another therapeutic study within 30 days of qualification (or longer if local requirements specify);

24. The urologist first preference is a treatment with anticholinergics/antimuscarinics;

25. Use of anticoagulant medications (eg, warfarin and other coumadin derivatives), antiplatelet
medications (eg, clopidogrel and aspirin [including low dose]) and any other medications with anticoagulative effects (eg, non-steroidal anti-inflammatory drugs [NSAIDs]) within a period 3 days (or longer according to the clinical judgment of the ccordinating investigator) prior to any study treatment.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2011
Enrollment:	144
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL2926
NTR-old	NTR3073
Other	:
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A