Validation of molecular pathways in urgency urinary incontinence

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1) To isolate and cryopreserve human primary bladder muscle and urothelial cells from women with isolated UUI so that we can validate the results from the molecular landscape in vitro.2) To collect and store human bladder biopsy tissues from women...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bladder and bladder neck disorders (excl calculi)
Study type	Observational invasive

Summary

ID

NL-OMON49318

Source
ToetsingOnline

Brief title
Validation of molecular pathways in UUI

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
involuntary leakage of urine, urinary incontinence

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: EFRO Operationeel Programma Oost (OP-Oost)

Intervention

Keyword: cell cultures, molecular pathways, proteomics, urgency urinary incontinence

Outcome measures

Primary outcome

Validation of the significant genes or molecular pathways derived from a molecular landscape on UUI and to perform in vitro tests of possible drug targets.

Secondary outcome

It is expected that, during the study period, more hypotheses will be formulated. They also need to be validated with in vitro assays.

Study description

Background summary

Urinary incontinence (UI) is a common problem among adult women. Around 25% of Dutch women under the age of 65 years has UI-related complaints, which leads to a decreased quality of life. Two types are distinguished: stress (SUI) and urgency (UUI) urinary incontinence. SUI is defined as involuntary loss of urine associated with increased abdominal pressure such as coughing. UUI is defined as the complaint of involuntary loss of urine accompanied by or immediately preceded by urgency. Especially UUI has a significant impact on the quality of life. No effective long-term treatment has been found yet for UUI. It can be treated by medications, but they have bothersome side effects. The present study is part of the DIAgnose en Behandeling van Incontinentie en Prolaps (DIABIP) project, carried out by three departments of the Radboud university medical center (Gynaecology, Urology and Genetics), and two small and medium-sized enterprises: Drug Target ID (DTID) and Nimagen. The DIABIP project combines clinical and physiological data with lifestyle factors and genetic information to improve the diagnosis, prognosis and treatment of women with pelvic floor dysfunctions. The first step is to provide insight into the biological processes that, when impaired, could be involved in the pathogenesis of UI.
Based on GWAS-data and literature research resulted in a concept molecular landscape for UUI. Based on this landscape several biological processes were

identified:
These processes still need to be validated in vitro.
Proteomics, genomics, and in vitro cell culture tests using the samples derived from the bladder biopsies are then used to validate the hypotheses and to test whether 'repurposed' drugs could alter these biological processes in a disease specific manner. To our knowledge there are no cell cultures available at other centres to do the planned testing.

Study objective

1) To isolate and cryopreserve human primary bladder muscle and urothelial cells from women with isolated UUI so that we can validate the results from the molecular landscape in vitro.
2) To collect and store human bladder biopsy tissues from women with UI so that we can perform Omics (proteomics and/or genomic) analyses to corroborate the findings from the molecular landscape at tissue level.

Study design

Observational study.

Study burden and risks

During cystoscopy, which is part of the planned procedure of the regular treatment the patients are undergoing, two additional bladder biopsies will be taken. The risks of bladder biopsies are minimal, but it can cause: transient minor bleeding, transient minor paín and discomfort. ln rare case reports, more severe bleeding or bladder perforation has been described.(1) Cystoscopy increases the chance of urinary infections, but this is not an added risk for patients who are already undergoing a cystoscopy procedure. All women receive antibiotic profylaxis as standard medical treatment.
According to the risk classification of the NFU for patients participating in this study, the risk has been assessed as "moderate". The method (taking bladder biopsies) that we will use in this study is identical as in two previous studies by the department of Urology: 'OAB feasibility; Molecular and cellular characterization of detrusor smooth muscle cells' (CMO 20041053) and 'The role of GAG's in the pathology of interstitial cystitis (|C/PBS)' (CMO 2009/310). ln the previous studies, bladder biopsies were used for immunohistology and Western blotting, whereas in the present study in vitro cell culture tests and omics (proteomics/genomics) will be performed.

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

18 years or older
Diagnosed with urgency urinary incontinence
Requiring cystoscopy under anesthesia

Exclusion criteria

Patients who will or cannot give informed consent (including language barriers)
Patients who are pregnant or actually trying to conceive (i.e. active in fulfilling pregnancy wish)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-03-2021
Enrollment:	5
Type:	Actual

Ethics review

Approved WMO

Date:	08-12-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL67582.091.18