Patient experience and Quality of Life in children receiving percutaneous tibial nerve stimulation (PTNS) in a group setting.

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

DO	Detrusor overactivity
DSQOL	Disease specific Quality of Life
ESPU	European Society for Pediatric Urology
GDPR	General Data Protection Regulation; in Dutch: Algemene Verordening Gegevensbescherming (AVG)
IC	Informed Consent
ICCS	International Children's Continence society
LUTD	Lower urinary tract dysfunction
METC	Medical research ethics committee (MREC); in Dutch: medisch-ethische toetsingscommissie (METC)
OAB	Overactive bladder
PINQ	Pediatric Incontinence Questionnaire
PTNS	Percutaneous tibial nerve stimulation
TENS	Transcutaneous Electrical Nerve Stimulation
UUI	Urge urinary incontinence

SUMMARY

Rationale: Overactive bladder (OAB) as part of lower urinary tract dysfunction (LUTD) is a common condition in otherwise healthy school aged children with a lot of impact on quality of life (QOL). Percutaneous tibial nerve stimulation (PTNS), given in a group setting, is a 2nd line treatment modality for therapy refractory complaints. Previous research suggests group intervention, as given in PTNS, to have a positive effect in QOL in this particular group of patients regardless of the effect of PTNS on the urinary symptoms.

Objective: To gain insight in patient experience and quality of life of children receiving PTNS and their parents in a group setting (PART A) and to study the change in DSQOL throughout treatment and its correlation with the effect of PTNS treatment on urinary incontinence (PART B)

Study design: Qualitative empirical study with semi-structured interviews (PART A), retrospective data analysis, (PART B)

Study population: Children with therapy refractory OAB and their parents receiving PTNS in a group setting.

Intervention (if applicable): Semi-structured interviews

Main study parameters/endpoints: Primary end point is insight in experiences and factors that contribute to QOl in this patient group.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: There are no risks or direct potential benefit for participants. Potential burden for the individual subject is mainly time consummation of approximately 30-45 minutes.

1. INTRODUCTION AND RATIONALE

Overactive bladder syndrome (OAB) as part of lower urinary tract dysfunction (LUTD) is a common condition in children, with a prevalence up to 10-20% in 7-year-old children and 1-6% in 17-year-old adolescents [1, 2]. OAB can significantly impair quality of life (QOL) leading to less self-esteem, social stigmatization and impaired interpersonal interactions [3, 4].

Despite optimal treatment, 20-40% of the children are resistant to standard treatments like urotherapy, psychological counselling and medication (antimuscarinics) [5]. Furthermore, efficacies of antimuscarinics are restricted by their known and unwanted side-effects, like behavioural changes and constipation. Compliance is low and many patients discontinue antimuscarinics on the long term (88% at four years) [6]. Not surprisingly, parents are reluctant to give medication for a long period to their otherwise healthy children.

Second-line treatment options for children with therapy resistant complaints include other types of mainly off-label medication, botulinum toxin, or neuromodulation. Percutaneous tibial nerve stimulation (PTNS) is one of the forms of neuromodulation offered to children. In PTNS, stimulation is offered 30 minutes once weekly for 12 consecutive weeks at the outpatient clinic. In a pilot study conducted at our centre, over 70% showed improvement of their urinary symptoms after 3 months of PTNS (NL 55958.091.15). Scores on Disease specific Quality of Life (DSQOL) questionnaires improved as well throughout the treatment. Surprisingly, improvement of DSQOL was also seen in children not responding to the PTNS treatment itself. As PTNS is given in a group setting, social interaction and peer support is facilitated. This provides both parents and children coping strategies and stimulates for example better acceptance of their condition. This might be one of the factors involved in improved DSQOL despite a response seen in actual reduction of urinary symptoms.

The aim of this study is to gain insight into patient experience and QOL in children and their parents receiving PTNS in a group session for therapy refractory OAB. This helps to get a better idea how group interventions can add to a therapeutic effect in children suffering from LUTD and their parents.

Research questions

- How do parents and children experience PTNS in a group setting?
- How does therapy in a group setting affects DSQOL in children with LUTD and their parents?
- How does DSQOL changes throughout the treatment period?
- How is DSQOL related to treatment outcome of PTNS?

2. OBJECTIVES

The primary objective is to gain insight in how children with therapy refractory OAB and their parents experience PTNS in a group setting (PART A).

Secondary objectives are changes in DSQOL throughout the treatment period, insight in factors that affect DSQOL of therapy given in a group setting and relation between DSQOL and the effect of PTNS on urinary incontinence (PART B).

3. STUDY DESIGN

Qualitative empirical study design with semi-structured interviews of parents with their child or parents alone (PART A)
Retrospective data analysis of DSQOL scores (collected before the start of PTNS and after PTNS as part of standardized care) in all children treated with PTNS in our centre (PART B).

4. STUDY POPULATION

Children between 6-11 years of age and their parents receiving PTNS in a group setting for therapy refractory overactive bladder in our centre.

4.1 Inclusion criteria

- Willingness to be interviewed
- Informed consent for qualitative part of the study, part A

4.2 Exclusion criteria

None

4.3 Sample size calculation

In qualitative research, data saturation determines the number of interviews needed. We expect approximately 10-15 interviews to be needed to obtain sufficient data.[7, 8]

5. TREATMENT OF SUBJECTS

At one of the regular PTNS treatments, children and their parents are asked whether they are willing to be interviewed. Written information is handed over and at the next appointment parents and children are asked again. If they agree to participate, an appointment is made for the interview. As PTNS treatment is given for 30 minutes, every week, for 12 consecutive weeks the interview is planned at the same day just before or after one of the treatments, depending on the preference of child and parents. The interview takes approximately 30-45 minutes. Either one parents is interviewed or both or parent(s) together with their child. No children are interviewed without one or both of their parents. A concept version of the topic guide for the interviews is shown in the attachment.

The interviews are held in the period October-December 2021 and are conducted by a medical student, trained and supervised by a qualified interviewer.

6. ANALYSIS

All interviews are recorded. Recorded data are transcribed and analyzed following a thematic analysis approach[9]. This qualitative analysis method aims to identify themes and concepts in the interviews. This method does not imply testing of predefined hypotheses, but generates codes and a codebook.[10, 11] The program ATLAS.ti 8 is used to analyze the data. The first transcripts are analyzed separately by two researchers and differences are discussed till consensus is reached. The COREQ guideline for qualitative research is used to for the design and reporting of the results.[12]

The data generated by the validated Pediatric Incontinence Questionnaire for parents and children (PIN-Q) are transformed and interpreted according to instructions given [13, 14]. Data are expressed as median and standard deviation.

Treatment outcome is defined as change in urinary incontinence quantified according to Mulders et al. and further classified as: complete response (100% decrease), partial response (50-99%) or no response (<50%) as recommended by the International Children' Continence Society.[15, 16]

One-way ANOVA or Non Parametric tests are used to study the effect of treatment outcome on DSQOL scores. Data will be analysed using SPSS statistics 25.0 (SPSS Inc., Chicago, Il, USA). Differences are considered statistically significant at $p < 0.05$.

7. ETHICAL CONSIDERATIONS

7.1 Regulation statement

The study is conducted according to the principles of the Declaration of Helsinki (2013) ,see also www.wma.net and in accordance with the Medical Research involving human subjects act (WMO) and other guidelines, regulations and acts (AVG/ WGBO) and guidelines for qualitative research[12].

7.2 Recruitment and consent

Children and their parents are asked to participate during the regular appointment at the outpatient clinic where information is given orally and in writing by one of the research members. At the next PTNS treatment (one week later) the subjects are asked again. Subjects can decide themselves whether or not they want to participate – we will stress that participation is voluntary and their decision will not impact their care. When they agree to participate, parent(s) and their child, or one or both parents alone receive an appointment at the outpatient clinic for the interview, preferable before or after one of the PTNS sessions, depending on their preference. Children are not interviewed alone. Parents can sign the informed consent at home and bring it along at the interview or they can sign it at the start of the interview. A copy of the signed informed consent is given to the subjects.

7.3 Objection by minors or incapacitated subjects

The study will be conducted according to the codes of conduct for minors (available on the CCMO site and accepted by the Board of the Netherlands Association for Pediatric Medicine (NVK) on May 21, 2001.

7.5 Benefits and risks assessment, group relatedness

There are no risks or direct potential benefit for participants. Potential burden for the individual subject is mainly time consummation of approximately 30-40 minutes.

8. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

Data from the study participants will be handled confidentially according ICH-GCP regulations. Confidentiality will be maintained at all times. The original signed informed consent forms will be kept in a binder in a locked closet in a locked room of all participating centers.

The protocol, data of recorded interviews, CASTOR data, statistical analyses and reports are stored in a secured Digital Research Environment created and access is password protected and assigned to research members only.

Each subject will receive a unique identifier, after which the treating physician will extract all necessary clinical parameters from the electronic health records into an electronic Case Report Form (eCRF) of Castor EDC. Castor EDC is a browser-based, metadata-driven EDC software solution and workflow methodology for building and managing online databases. The eCRF contains data items as specified in this research protocol. Modification of the eCRF will be made only if deemed necessary and in accordance with an amendment to the research protocol. Access to the eCRF is password protected and specific roles are assigned (e.g. study coordinator, investigator, etc.). The CASTOR database will be supplemented with the outcome of a validated DSQOL questionnaires.

When required, authorized personnel of the study can access this source data for analysis or regular back-ups. A manual (meta)data export in either Excel or SPSS will then be made to the DRE previously mentioned.

For part B of the study a subject identification code list will be used to link data to subjects by the treating physician. The key to the code is stored in a file at a network drive only accessible to the treating physician. Besides the treating physician, study monitors/auditors have access to the study data. No personal data will be transported outside the network drives.

At the end of the study, all generated data will be stored in the DRE. In order to reproduce the study findings and to help future users to understand and reuse the data, all changes made to the raw data, including analysis steps will be documented in an data management analysis plan. Thus the secure DRE will serve at the end of the study as a data package. The data package will be locally archived on the secured research network for 15 years after the study has ended.

8.1 Monitoring and Quality Assurance

Internal audits conform Good Clinical Practice (GCP 5.18.3) are standard procedure at the IQ health department.

8.2 Public disclosure and publication policy

The results are shared with relevant fora and data will be presented at international conferences and published in peer reviewed medical journals

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