Risperidone versus behaviour therapy in the treatment of tic disorders - a randomized single-blinded trial

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In a randomized single-blinded trial we compare two treatments for GTS and CTD patients. The primary aim of this study is to compare the efficacy of the D2-blocking agent risperidone with ERP-therapy in tic reduction. Dropout rates and side effects...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON38252

Source
ToetsingOnline

Brief title
Risperidone versus behaviour therapy for tics

Condition

- Other condition

Synonym
chronic tic disorder, Gilles de la Tourette syndrome

Health condition

neuropsychiatrische aandoening (syndroom van Gilles de la Tourette en aanverwante chronische ticstoornissen)

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis
Source(s) of monetary or material Support: betrokken afdelingen van de 3 centra financieren extra kosten voor onderzoek zelf

Intervention

Keyword: behaviour therapy, Gilles de la Tourette syndrome, risperidone, tic disorder

Outcome measures

Primary outcome

Primary outcome measure will be tic severity according to the Yale Global Tic Severity Scale (YGTSS, Leckman et al, 1989) directly post treatment (after 12 weeks), as measured by trained experts, blinded for the allocated treatment.
The YGTSS is a widely used clinical rating scale that provides information on tic severity for motor and vocal tics in five dimensions: number, frequency, intensity, complexity, and interference. A rating of impairment is added to provide a total Tic severity score that ranges from 0 (no tics) to 55 (severe tics).
The YGTSS has demonstrated satisfactory convergent and discriminant validity and interrater reliability.

Secondary outcome

Secundary outcome measures include ticfrequency at home and at the institute after 12 weeks, and tic severity and frequency at home and at the institute after 6 and 12 months (follow-up). General assessment of functioning and quality of life, cost-effectiveness, severity of premonitory sensations, side

effects and severity of comorbidity will be measured as well, as are effects during half way of treatment (after 6 weeks). Prognostic factors for response on the two treatments will be analysed with the use of multivariate analysis. Ticfrequency at home will be measured by daily registrations by a parent/ partner of the patient. They count the number of tics in a 15 minute interval during a fixed time/ activity. Tic frequency at the institute will be measured by counting tics of videotaped YGTSS measures. Standardized videotaped tic counts of at least 5-minute samples have previously been found to provide reliable and stable measures of tic frequency and are sufficiently correlated with YGTSS ratings (Chapell et al., 2004).
Quality of life is measured by the Gilles de la Tourette Syndrome*Quality of Life Scale(GTS-QOL, Cavanna et al, 2008). The GTS-QOL is a 27-item, patient-reported scale which measures GTS-specific health related quality of life on 4 subscales. The GTS-QOL demonstrated high reliability and test-retest reliability, and supported validity. The economic evaluation will use a societal perspective: we will document mental and general health care utilization (direct medical costs), travel to and from health care providers (non-medical costs) and productivity loss generated by absence from paid work (indirect costs).TIC-P (Trimbos/iMTA questionnaire for costs associated with psychiatric illness, Hakkaart-van Roijen, 2002) will be administered. The TiC-P is a generally applied tool to estimate health care utilisation and production losses by self-report from recipients (patients with mental health problems) in the Dutch health care setting. It is often used to determine costs in economic evaluations.

Premonitory urge severity is measured using the Premonitory Urge for Tics Scale (PUTS, Woods et al, 2005). The PUTS is a brief self-report scale designed to measure tic-related premonitory urges. Side effects are measured by the UKU Side Effects Rating Scale (Lingjaerde et al., 1987) and the Extrapyramidal Symptom Rating Scale (ESR, Chouinard et al, 1980) for measuring parkinsonian and dyskinetic symptoms.
In case of comorbid OCD, the Yale Brown Obsessive Compulsive Scale (Y-BOCS, Goodman et al., 1989) or Children*s Yale Brown Obsessive Compulsive Scale (CY-BOCS, Scahill et al, 1997) is administered. If ADHD is present, the severity is measured in adults with the Conners' Adult ADHD Rating Scales (CAARS, Conners et al, 1999), and in children with the Conners' rating scales-revised (CRS-R, Conners, 1997). Autism is measured with the Adults Social Behavior Questionnaire (VIS-V, van den Bosch et al, 2002) for adults and the Children*s Social Behavior Questionnaire (VISK, Luteijn et al, 2002) for children.

Study description

Background summary

Gilles de la Tourette syndrome (GTS) and chronic tic disorders (CTD) are neuropsychiatric disorders, starting below age 18, and characterized by tics. Tics may have severe impact on daily and social life, may interfere with work, be painful due to the overstraining of muscles or joints, and thus become a severe handicap for patients. Effective treatment of tics is essential to enlarge the quality of life. To date, D2-blocking agents (antipsychotic drugs) are regarded as treatment of first choice, but these drugs are not well tolerated and stopped by up to 70 percent of the patients within the first year. Also, many patients are reluctant to take antipsychotics. Several randomised controlled studies showed behaviour therapy as an effective

treatment method for tics. One of these methods is exposure and response prevention (ERP). In ERP, patients are exposed to the unpleasant sensory sensation, which often precedes the actual tic. By withholding the tic, patients learn to adapt to the sensory sensations, resulting in reduction of tic frequency. We are not aware of any comparative study between D2-blocking agents and ERP in patients with GTS or CTD. The primary aim of the present study is to compare the efficacy of the D2-blocking agent risperidone with ERP in tic reduction in patients with GTS or CTD. We expect ERP to be more effective than medication based on higher effect sizes in earlier studies, fewer side effects, lower dropout rates and better long-term effects. Secondary, we aim at identifying prognostic factors with regard to therapy response. 80 GTS or CTD patients will be randomized to receive either risperidone (2-6 mg. per day) or ERP during 12 weeks. After a baseline of 2 weeks and treatment of 12 weeks, treatment response is measured. The primary outcome measure will be tic severity as measured by the Yale Global Tic Severity Scale (YGTSS, Leckman et al., 1989) directly post-treatment. The YGTSS is scored by trained assessors, blinded for the allocated treatment. Secondary outcome measures include video-taped tic counts, cost-effectiveness, measures of quality of life and general functioning post-treatment. Furthermore, long term effects will be measured by follow-up (week 24 and 52).

Study objective

In a randomized single-blinded trial we compare two treatments for GTS and CTD patients. The primary aim of this study is to compare the efficacy of the D2-blocking agent risperidone with ERP-therapy in tic reduction. Dropout rates and side effects are taken into consideration. Secondary, we want to measure cost-effectiveness and identify prognostic factors with regard to treatment response. At last, long-term effectiveness will be measured by follow-up.

Study design

This study is a randomized, single blinded effectiveness study, in which a comparison is made between two treatment methods: Risperidon and exposure and response prevention. Dropout rates and side effects are included. In 2 groups of 40 patients, assuming a SD of 6 and correlation of .78 between baseline and end of treatment, the power needed for a difference of 2 points between the two groups is .65, for a difference of 2.5 .84 and .94 for a difference of 3 points by analysis with ANCOVA, with baseline YGTSS scores as covariates included. The YGTSS will be the primary outcome measure; the (two-tailed) level of significance will be set at $p<0.05$.

Intervention

Randomization starts after the in- and exclusion criteria are checked. Stratification is applied for patients under and above 18 years of age.

There are two treatment conditions:
1) Exposure and Response Prevention (ERP);
2) Risperidone
Treatment starts 2 weeks after inclusion so a baseline of home tic registration will be available. The ERP condition consists of 12 sessions of 1 hour. In the first two training sessions, patients are taught to systematically suppress their tics (i.e. response prevention). In the 10 consequent sessions, exposure takes place to the unpleasant sensory sensation, which often precedes the actual tic. By withholding the tic, patients learn to tolerate (or habituate to) the sensory sensations. The therapist encourages the patient to suppress all tics and at the same time keep concentration on the premonitory sensations and the corresponding location in their
body. During sessions, information is gathered on the existence, anatomical location, character and severity of premonitory sensations and urges. Every five minutes, the severity of these sensations is asked for on a five-points scale, and pointed out in a graphic. The occurrence of each motor or vocal tic that has not been suppressed is registered. Integrity of treatment is guaranteed by the use of treatment protocols (Verdellen et al, 2004b), intensive training and supervision of therapists and monitoring of videotaped sessions. The effect of ERP has been proven in one randomized controlled trial and some case studies (for a review, see Cook& Blacher, 2007)
The medication condition consist of a flexible dose of risperidone, 2-6 mg a day. Patients in the medication arm will be weekly contacted to get information about effects and side effects. Integrity of treatment is guaranteed by a compliance check with use of a blood draw after 6 weeks. The effect of risperidone has been proven in different studies as well (for a review, see Cath et al., 2008).

Study burden and risks

There are no risks in participation, the only burden is the extra time that is needed for measurements. As far as possible, measurements by independent assessors will be planned when patients have to come for treatment anyway. Furthermore blood draw as a part of compliance check and taping sessions can be felt as a burden. Treatment itself won't cause burden or risks because both treatment conditions are proven to be effective treatment in these illnesses. If patients don't participate in the research they will be offered one of the two treatments.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Patients have to meet DSM-IV criteria for GTS or CTD, and will be included according to the Diagnostic Confidence Index. Both children and adults are included, ranging from 6 to 65 years of age. Written informed consent is necessary to participate in the study by the patient. In case the patient is under age of 16 a written consent of parents is necessary before a patient is included in the study.

Exclusion criteria

Exclusion criteria are: severe major depression, psychosis, addiction, mental deficiency, known cardiovascular disease, family history of QT prolongation, bradycardia, other medication known to prolong QT interval, and inability to read/ speak Dutch. Exclusion criteria will be established
using the Mini International Neuropsychiatric Interview for adults, or the KIDDIE-SADS for children.Patients need to be free of antipsychotic medication for at least four weeks prior to

entering the study.

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-04-2011
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Risperidone
Generic name:	Risperdal
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-07-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	17-04-2012

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

Approved WMO Date:	08-02-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Not approved Date:	07-03-2014
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
EudraCT	EUCTR2009-011134-96-NL
CCMO	NL27245.098.09