Multicentre, randomised, double-blinded, placebo-controlled trial of efficacy of amoxicilline/clavulanic acid in patients affected by tic disorder colonized by GAS. No-proft stidy.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Developmental disorders NEC
Study type	Interventional

Summary

ID

NL-OMON53389

Source
ToetsingOnline

Brief title
AntibioTICS

Condition

- Developmental disorders NEC

Synonym
Tourette Disorder, Tourettes

Research involving
Human

Sponsors and support

Primary sponsor: Azienda Universiaria Policlinico Umberto I di Roma
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: Antibiotics, Infections, Tourette Syndrome, Treatment

Outcome measures

Primary outcome

The main study outcome is tic severity as measured by the Yale Global Tic

Severity Scale (YGTSS).

Secondary outcome

1) Premonitory Urge for Tics Scale (PUTS).

2) Symptoms of OCD as measured by the Children*s Yale Brown

Obsessive-Compulsive Scale (CYBOCS).

3) Symptoms of autism spectrum disorders, ADHD, and internalising and

externalising psychopathology

a. Social Communication Questionnaire (SCQ).

b. Swanson, Nolan, and Pelham, version IV (SNAP-IV) rating scale.

c. Strengths and Difficulties Questionnaire (SDQ).

4) Moderators

- Prenatal and perinatal adversities as assessed by parental self-report.

- Psychosocial stress measured using the Perceived Stress Scale.

- Cortisol levels in hair as biomarker of retrospective chronic stress.

- Microbiological typing of bacterial GAS population

- Anti-Streptococcal Immune Response

Study description

Background summary

The aetiology of tic disorders and associated obsessive-compulsive and behavioural symptoms is poorly understood. It has been postulated that genetic and environmental factors active upon regulatory systems (e.g. immune and endocrine systems) might interact in creating a neurobiological vulnerability to the development of tics and associated behaviours. The largest body of evidence from clinical research has been gathered in support of a role of exposure to psychosocial stress, of pregnancy and delivery adversities and of infections from GAS (Murphy, Kurlan, and Leckman, 2010). The human pathogen GAS is a major cause of common pharyngitis, but also of significant post-streptococcal non-suppurative autoimmune multi-organ sequelae associated with the existence of host autoantibodies against GAS antigens (also known as the Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections [PANDAS]-hypothesis). It has been hypothesized that TS patients colonized by GAS are not merely carriers and that this colonization may promote a sustained anti-streptococcal immune response contributing to the persistence of tic symptoms. If this hypothesis is true, the antibiotic treatment of GAS colonization in patients affected by a chronic tic disorder could modify their symptoms in term of severity and number of exacerbations.

Study objective

This study is an extension of the European Multicenter Tics in Children Studies (EMTICS) Course study for which a separate study protocol exists; its aim is to verify the efficacy of GAS colonization treatment on tic symptoms in term of severity. The primary objective is to test the hypothesis that antibiotic treatment of GAS colonisation compared to placebo is associated with a larger reduction of tic and associated neuropsychiatric symptoms in the short-term (1 month) in patients with a tic disorder colonised by GAS. The secondary objective is to test the hypothesis that antibiotic treatment of GAS colonisation is superior to placebo in the long-term (1 year) reduction of tic and associated neuropsychiatric symptoms in patients with a tic disorder colonized by GAS.

Study design

Multicentre, randomised, double-blinded, placebo-controlled trial. In AntibioTICS, European sites together will recruit 72 children, of which the UMCG will recruit 4 children participating in the EMTICS COURSE study. EMTICS is a longitudinal observational European multicenter study consisting of an ONSET and COURSE study part. European sites together will recruit 700 children in the COURSE study, of which the UMCG will recruit 60 children, thus of which

5 children shall take part in AntibioTICS.

Intervention

Amoxicilline/clavulanic acid, Oral suspension, 25/3.6 mg/kg/day, oral, over the course of 10 days two times daily.

Study burden and risks

The burden for the child will be the use of two daily doses of antibiotics or placebo for 10 consecutive days. Further, there will be four visits at the clinical center (4 x 60 minutes), completion of parent-questionnaires before the visits (4 x 20 minutes) and a short child-questionnaires (4 x 5-10 minutes), and completion of a weekly home diary by the parent (32 x 5 minutes = 20 min), and two telephone interviews (2 x 20 minutes). At the visits, a blood draw by venipuncture, throat swab and collection of hair strands will be taken in the child. Risks and physical or physiological discomfort of these measurements will be negligible or mild. Side effects of antibiotics may involve nausea or dizziness. This research protocol includes the participation of minors as tic disorders have a childhood onset and are most pronounced at that age.

Contacts

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Trial sites

Listed location countries

Germany, Hungary, Israel, Italy, Spain, Switzerland

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Participant and parents willing and able to give informed consent for participation in the study * Male or Female, aged 3-16. * Diagnosis of Tourette Syndrome or another chronic tic disorder according to DSM IV-TR criteria. * Evidence of GAS colonization at any visit of EMTICS Longitudinal Course Study. * Either no current psychotropic medication or on stable anti-tic medication for at least 2 months before the enrolment in the trial. Able (in the Investigators opinion) and willing to comply with all study requirements.

Exclusion criteria

The participant may not enter the study if ANY of the following apply: * Children and/or parents are unable to understand and comply with protocol * Any antibiotic treatment for any reason during the last month before enrolment in the trial. * Clinical manifestations of pharyngitis or other streptococcal infections at moment of enrolment in the trial. * Known or suspected hypersensitivity to penicillin or other *-lactam antibacterials, a history of amoxicillin-clavulanate-associated cholestatic jaundice or hepatic dysfunction. * Known and/or suspected renal or hepatic impairment (due to the potential for drug-related toxicity in patients with such a condition). * Scheduled elective surgery or other procedures requiring general anaesthesia during the study. * Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk because of participation in the study, or may influence the result of the study, or the participant*s ability to participate in the study. Participants who have participated in another research study involving an investigational product in the past 12 weeks

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2013
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Augmentin
Generic name:	amoxicillin/clavulanate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-03-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-09-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	2012-002430-36
CCMO	NL44444.042.13