The effect of glycopyrroniumbromide oral solution for nocturnal drooling due to the use of clozapine.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26368

Source
Nationaal Trial Register

Brief title
QUITSPIT-study

Health condition

English: CIS, clozapine-induced-sialorrhea, hypersalivation, drooling
Nederlands: sialorroe, hypersalivatie, kwijlen

Sponsors and support

Primary sponsor: Mw. Dr. Ingeborg Wilting
ziekenhuisapotheker

Universitair Medisch Centrum Utrecht
ziekenhuisapotheek
Source(s) of monetary or material Support: fonds = verrichter = sponsor
Universitair Medisch Centrum Utrecht
ziekenhuisapotheek

Intervention

Outcome measures

Primary outcome

The percentage of patients showing a clinically significant improvement on the severity of complaints of nocturnal sialorrhea, defined as a score of 1 ("very much improved") or 2 ("much improved") on the PGI-I (Patient Global Impression of improvement questionnaire).

Secondary outcome

The mean score on the PGI-I, PGI-S, NHRS (Nocturnal Hypersalivation Rating Scale) and MSQ (Medication Satisfaction Questionnaire), the occurence of side effects and patients satisfaction with oral glycopyrroniumbromide.

Study description

Background summary

Recruting countries: The Netherlands.

Background of the study:

Hypersalivation or sialorrhea is one of the most frequently occuring side effects of clozapine use with an incidence ranging from 30 to 90%. In most cases it occurs at the start of clozapine treatment, mostly at night and persists during further treatment.

Several symptomatic (farmacologic) therapies exists that reduce sialorrhea by reducing saliva excretion. There is no drug therapy registered for clozapine induced sialorrhea and most of the medications that are used often have central side effects.

Glycopyrroniumbromide is a quaternairy ammonium compound and an effective and potent anticholinergic agent with poor penetration across the blood-brain-barrier, causing less central side effects than other anticholinergics. In a number of relatively small studies oral glycopyrroniumbromide was found to be effective in reducing sialorrhea in children with cerebral palsy, patients suffering from Parkinson’s disease and schizophrenic patients using clozapine.
The effect on nocturnal sialorrhea in patients using clozapine compared to placebo has not been studied yet.

Study design:

Double blind, randomized, cross-over trial with an extended open label phase. The length of the study will be 6 weeks in total. The first phase (week 1 up to and including week 4) of the study will be a randomised, double blind, placebo controlled and cross-over design, where an equal amount of glycopyrroniumbromide oral solution 0,2 mg/ml (1 mg = 5 ml) and placebo oral solution are compared. The second phase (week 5 and 6) is an extended open-label phase, with patients receiving a double dose of glycopyrroniumbromide oral solution 0,2 mg/ml (2 mg = 10 ml) if they well tolerated the oral solution in the first phase of the study. In week 1 there will be baseline-measurements. In week 2 and week 4 the patients will take during 6 days oral
glycopyrroniumbromide 1 mg or placebo before the night. In week 3 and week 5 no studymedication is taken (wash-out period). In a weekly consult in week 2 up to and including week 6 the patient scores the severity and possible improvement of the sialorrhea. Also the occurence of side effects will be questioned. In week 6 the patients who well tolerated the glycopyrroniumbromide oral solution in the first phase of the study receive a double dose glycopyrroniumbromide oral solution 2 mg during 6 days before the night. At the end of week 4 or 6 a concluding visit will take place.

Study objective

Hypersalivation or sialorrhea is one of the most frequently occuring side effects of clozapine use with an incidence ranging from 30 to 90%. In most cases it occurs at the start of clozapine treatment, mostly at night and persists during further treatment.

Several symptomatic (farmacologic) therapies exists that reduce sialorrhea by reducing saliva excretion. There is no drug therapy registered for clozapine induced sialorrhea and most of the medications that are used often have central side effects.

Glycopyrroniumbromide is a quaternairy ammonium compound and an effective and potent anticholinergic agent with poor penetration across the blood-brain-barrier, causing less central side effects than other anticholinergics. In a number of relatively small studies oral glycopyrroniumbromide was found to be effective in reducing sialorrhea in children with cerebral palsy, patients suffering from Parkinson’s disease and schizophrenic patients using clozapine.
The effect on nocturnal sialorrhea in patients using clozapine compared to placebo has not been studied yet.

Main objective: To determine the effect, defined as the percentage of patients that show a clinical relevant improvement on the severity of complaints of nocturnal sialorrhea, of oral glycopyrroniumbromide in comparison with placebo in psychiatric patients treated with clozapine.

Study design

1. % PGI-I score 1 or 2, timepoints: 2 weeks, 4 weeks, 6 weeks;

2. Mean PGI-I, timepoints: 2 weeks, 4 weeks, 6 weeks;

3. Mean PGI-S, timepoints: every week (6 weeks in total);

4. Mean NHRS, timepoints: every week (6 weeks in total);

5. Mean MSQ, timepoints: every week (6 weeks in total);

6. Occurence of side effects, timepoints: week 1, week 2, week 4, week 6;

7. Satisfaction with oral glycopyrroniumbromide, timepoints: week 2, week 4, week 6.

Intervention

Alternating treatment with 1 mg glycopyrroniumbromide oral solution or placebo oral solution for 1 week interrupted by 1 week wash-out.

Patients who have no problems enduring the treatment with 1 mg glycopyrroniumbromide will be treated with 2 mg
glycopyrroniumbromide oral solution in the extended open label phase.

Intervention medicine: Glycopyrroniumbromide oral solution 0,2 mg/ml (ATC-code: A03AB02).

Dose during double-blind phase: 1 mg (5 ml).

Dose during open-label phase (if applicable): 2 mg (1 ml).

Control intervention: Placebo oral solution, 5 ml during double-blind phase.

Other interventions: Short questionnaires.

Contacts

Public
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Eligibility criteria

Inclusion criteria

1. Patients using clozapine who are diagnosed with schizophrenia, a schizoaffective disorder or other psychiatric condition meeting DSM-IV criteria;

2. A clozapine dosage that remained unchanged for three months prior to inclusion;

3. Age between 18 and 65 years;

4. Nocturnal sialorrhea defined as a score > 2 on the PGI-S (Patient Global Impression of Severity Questionnaire);

5. No change in dosages of specific comedication (clonidine, sulpride, moclobemide) that potentially reduces salivary flow for 1 month prior to inclusion;

6. The patient is able to answer questionnaires during a weekly consultation (by telephone) with the researcher;

7. The patient is willing to give informed consent for participating in the study;

8. The patient is, according to the treating psychiatrist, competent and able to give informed consent for participating in the study.

Exclusion criteria

1. Known hypersensitivity to glycopyroniumbromide, sorbic acid or saccharine sodium;

2. A comorbidity associated with sialorrhea (Parkinsons disease, cerebral palsy);

3. One of the following comorbidities: Inadequately treated constipation, urine retention,

bladder obstruction;

4. Concurrent use of anticholinergic agents: Tricyclic antidepressants or anticholinergics (atropine, ipratropiumbromide, trihexyfenidyl, biperiden, scopolamine, oxybutinine);

5. Concurrent use of medications that potentially interact with glycopyrroniumbromide (potassium chloride retard tablets, digoxine, corticosteroids);

6. Pregnancy or lactation;

7. A history of myasthenia gravis, cardiac arrhythmia, symptomatic coronary insufficiency, glaucoma, pyloris stenosis, paralytic ileus, prostate hypertrophy, renal failure;

8. Unable to autonomic medication intake.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-02-2013
Enrollment:	33
Type:	Actual

Ethics review

Positive opinion

Date:	06-11-2012
Application type:	First submission

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	NL3539
NTR-old	NTR3694
Other	EUDRACT : 2012-002299-15
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A