Ergebnisbericht über eine klinische Prüfung nach § 42b AMG

Study:

Effects of intranasal application of oxytocin on empathy and mentalising in patients with psychotic disorders and severe personality disorders

EudraCT-No.: 2007-006561-32

Study Code: OxyCog-01

1) Name of Sponsor/Company

LWL University Hospital Bochum
Department of Psychiatry and Psychotherapy
Ruhr-University Bochum
Alexandrinenstraße 1
44791 Bochum
Germany

2) Name of Finished Product

Syntocinon (oxytocin spray for intranasal use, commercially available, Defiante Farmaceutica, Funchal, Portugal)

3) Name of Active Substance

Oxytocin

4) Individual Study Table: Referring to Part of the Dossier (Volume, Page)

n/a (as this is only required in combination with the submission of a Common Technical Document)

5) Title of Study

Effects of intranasal application of oxytocin on empathy and mentalising in patients with psychotic disorders and severe personality disorders

EudraCT-No.: 2007-006561-32

Study Code: OxyCog-01

Version: 1.2 (Substantial amendment, date: February 9, 2011)

6) Investigators

Principal Investigator:

Name: Prof. Dr. med. Martin Brüne
Title: Head of Research Division

Co-Investigator:

Name: Dr. med. Patrik Roser
Title: Research Assistant

Co-Investigator:

Name: Dr. med. Andreas Ebert
Title: Research Assistant

Co-Investigator:

Name: Dr. med. Jörg Heller
Title: Research Assistant

7) Study centre

LWL University Hospital Bochum
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8) Publication (reference)

Brüne M, Kolb M, Ebert A, Roser P, Edel MA. Nonverbal Communication of Patients with Borderline Personality Disorder during Clinical Interviews: A Double-Blind Placebo-Controlled Study Using Intranasal Oxytocin. J Nerv Ment Dis. 2015. *In press*

Brüne M, Ebert A, Kolb M, Tas C, Edel MA, Roser P. Oxytocin influences avoidant reactions to social threat in adults with borderline personality disorder. Hum Psychopharmacol. 2013;28(6):552-61.

Ebert A, Kolb M, Heller J, Edel MA, Roser P, Brüne M. Modulation of interpersonal trust in borderline personality disorder by intranasal oxytocin and childhood trauma. Soc Neurosci. 2013;8(4):305-13.

9) Studied period (years): date of first enrolment, date of last completed

The study (2011-2014) started with the first enrolment on 03/03/2011, last completed enrolment was on 06/12/2013.

10) Phase of development

Because of the increasing evidence and scientific interest in the significance of the neuropeptide oxytocin on the perception and interpretation of emotional stimuli, our university hospital started to plan a study with intranasally administered oxytocin in psychiatric patients. An application to the BfArM (German Federal Institute for Drugs and Medical Devices) was submitted. Due to a rapidly growing body of evidence and data on this topic, a substantial amendment of the protocol was submitted in January 2011. We focused on patients with Borderline Personality Disorder as recent studies (e.g. Bartz et al., 2011) hinted towards complex and partially paradoxical effects in this group.

11)Objectives

- Changes in the perception and interpretation of emotional stimuli and in behaviour with regard to the perception of unfairness
- Changes in mental perspective-taking

<u>Safety Objectives:</u>

- 12-lead ECG

- Vital signs
- Clinical laboratory testing
- Physical and neurological examination
- Pregnancy test (females only)

12) Methodology

Measurement of the effects of a single dose of oxytocin on the perception and interpretation of social stimuli, including emotion recognition and the ability to infer the mental states of others.
Subjects received a single dose of 24 IU of oxytocin or placebo intranasally before testing. Oxytocin and placebo challenges took place one week apart. Participants then performed emotion recognition and mentalising tasks.

13) Number of patients (planned and analysed)

30 patients (and healthy controls) per diagnosis planned; analysed 15 patients (Borderline Personality Disorder) and 15 controls

14) Diagnosis and main criteria for inclusion

- male or female patients, 18 to 45 years of age
- diagnosis of personality disorder, as defined using research diagnostic criteria according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)
- healthy male and female controls, age 18 to 45 years
- participants must be considered reliable, have a level of understanding sufficient to perform all tests and examinations required by the protocol
- participants must be able to understand the nature of the study and give written informed consent

15) Test product, dose and mode of administration, batch number

Oxytocin, 24 IU, intranasal; commercially available Syntocinon nasal spray (Defiante Farmaceutica, Funchal, Portugal -> relabelled for blinding by our hospital pharmacy)

16) Duration of treatment

2 experimental sessions per subject, once with verum (oxytocin), once with placebo with one week in between

17) Reference therapy, dose and mode of administration, batch number

n/a

18) Criteria for evaluation: Efficacy, Safety

Efficacy:

Observed changes of the perception and interpretation of emotional stimuli after the administration of oxytocin, assessed via psychiatric tests (e.g. a dot-probe-task and a trust game)

Safety:

12-lead ECGs at screening and as well as after administration of either oxytocin or placebo.

Blood pressure (BP [mmHg]) and heart rate (bpm) were measured at baseline and before and after the experimental sessions.

Clinical Laboratory Testing:

The following parameters were measured (baseline, and after experimental sessions):

Hematology:	Hemoglobin, hematocrit, erythrocyte count, leukocyte count, platelet count, differential cell count, MCV, MCHC
Clinical Chemistry:	Sodium, potassium, urea, creatinine, glucose, prolactin
Screening Tests:	Urine pregnancy test, urine drug screening [amphetamines, cocaine, opiates, cannabinoids]

Physical and neurological examination were performed at screening and at the end of the study

19)Statistical methods

All parameters were analyzed using descriptive methods.

Formal statistical hypothesis testing with pairwise comparisons was performed using adequate parametric or nonparametric statistical tests and methods (e.g., ANOVA, Student's t-test). The significance level was set to 5% for all tests.

20) Summary – Conclusions: Efficacy Results, Safety Results, Conclusion

As the study was intended to primarily assess putative effects of oxytocin on the perception and interpretation of emotional stimuli in subjects, "efficacy" in the traditional meaning cannot be clearly evaluated. Nonetheless, the study provided interesting new data about those effects as well in patients with personality disorders and control subjects. For instance, patients with Borderline Personality Disorder exhibited an altered reaction when presented with stimuli which indicated social threat after administration of oxytocin. A paradoxical effect on trust in patients compared to controls was also shown; this effect seems to be influenced by the perceived attractiveness of the counterpart. Additionally, differences in affiliative and flight behaviours were also shown regarding nonverbal behaviour of patients under the influence of oxytocin. In other domains, like insight and the interpretation of observed nonverbal behaviour by the subjects, no significant differences could be shown compared to the placebo group.
No side effects of oxytocin were observed.

In a nutshell, data from the study supports the view that oxytocin exerts differential and complex effects depending on the diagnosis and early childhood traumatization thus providing further knowledge of the effects of oxytocin on social cognition which might be important concerning the development of new therapy approaches in the future.

21) Date of report

January 27, 2015