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S47. Add-on spironolactone for the treatment of schizophrenia (spiro treat)

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Angaben zur Veröffentlichung / Publication details:

Röh, Astrid, Stefan Leucht, Peter Falkai, Berthold Langguth, Irina Papazova, and Alkomiet Hasan. 2018. "S47. Add-on spironolactone for the treatment of schizophrenia (spiro treat)." *Schizophrenia Bulletin* 44 (suppl_1): S342–42. https://doi.org/10.1093/schbul/sby018.834.

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Background: A six-item version (PANSS-6: P1=Delusions, P2=Conceptual disorganization, P3=Hallucinations, N1=Blunted Affect, N4=Social withdrawal, N6=Lack of spontaneity/flow of conversation) of the 30-item Positive and Negative Syndrome Scale (PANSS-30) has shown promise in the measurement of symptom severity in acutely exacerbated- and chronic schizophrenia, but its validity in treatment-resistant schizophrenia remains unknown. Therefore, we tested the validity and sensitivity of PANSS-6 based on data from the clozapine phase of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study.
Methods: I) The scalability of PANSS-6 and PANSS-30 (i.e., whether all items provide unique information regarding syndrome severity) was tested by means of item response theory analysis ad modum Rasch; II) The correlation between PANSS-6 and PANSS-30 total scores was investigated by means of Spearman correlation analysis; III) The accuracy of PANSS-6 in identifying symptom remission was tested by comparing remission on PANSS-6 (score of ≤3 on each of the six PANSS-6 items) with remission according to the Andreasen criteria (score of ≤3 on the 8 PANSS items considered in the Andreasen criteria); and IV) The antipsychotic effect of clozapine was compared to that of olanzapine, risperidone and quetiapine using the "speed of change" on PANSS-6 and PANSS-30 (change in total score per day) as outcomes.
Results: We found that I) only PANSS-6 and not PANSS-30 was scalable; II) The correlation between PANSS-6 and PANSS-30 total scores was high (Spearman coefficient: 0.85), III) PANSS-6 did accurately classify syndrome remission as defined by the Andreasen criteria, and IV) The only antipsychotic that resulted in improvement (speed of change significantly lower than 0 during the first three months of treatment) was clozapine, both when using PANSS-6 (speed of change: -0.072 points/day; 95%CI: -0.121, -0.024) and when using PANSS-30 (speed of change: -0.201 points/day; 95%CI: -0.400, -0.002) as outcome measures.
Discussion: These findings suggest that PANSS-6 validly measures severity, remission and antipsychotic efficacy in treatment-resistant schizophrenia.

S47. ADD-ON SPIRONOLACTONE FOR THE TREATMENT OF SCHIZOPHRENIA (SPIRO TREAT)

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Background: Patients with schizophrenia often display three main types of symptoms: positive symptoms (e.g. auditory hallucinations or delusions), negative symptoms (e.g. blunted affect, lack or decline in speech, social withdrawal) and cognitive symptoms (e.g. impairment of working memory and declarative memory). Treatment of positive symptoms with available antipsychotics is well established, while therapy options for cognitive and negative symptoms are lacking. Neurobiological studies identified an enhanced NRG1-ERBB4 signaling as a risk pathway in schizophrenia. Spironolactone was found to function as an inhibitor of the ERBB4 receptor. In Nrg1 type III transgenic mice, spironolactone treatment led to an improvement of schizophrenia-like symptoms (Wehr et al. 2017). This is the first study to investigate an add-on spironolactone treatment in schizophrenia patients for the treatment of cognitive deficits.
Methods: This is a multicenter, randomized, double-blind, parallel (3-groups), longitudinal pilot study including 3 x 27 (81) patients with a clinically stable schizophrenia. Patients are randomized in three groups: one group receives add-on spironolactone 100 mg for three weeks (intervention I), one group receives add-on spironolactone 200 mg for three weeks (intervention II) and one group receives add-on placebo for three weeks (control group). The primary endpoint is the modification of the working memory in dependence to the intervention as investigated with the n-back task (0-, 1- and 2-back). Secondary endpoints include: modification of other cognitive functions (e.g. declarative memory and attention), psychopathology (e.g. PANSS and CDSS), overall level of functioning via GAF and severity of disease via CGI, changes in the number of patients in remission using the Andreasen Criteria, modifications of the inhibitory cortical function in the context of the prepuls paradigm with TMS, evaluating possible dose-differences, spironolactone effects on mRNA levels in peripheral blood lymphocytes (PBMC measures). Statistical analysis of the primary endpoint will be based on the intention-to-treat (ITT) population including all randomised patients using a mixed model ANOVA.
Results: The first patient was recruited in July 2015. Currently 45 patients are included in the trial. The overall tolerance of the medication was satisfactory with 48 reported AE (adverse events). In 3 cases, the causality of the medication was definite, in 4 cases probable and in 5 cases possible. The other cases were probably or definitely not related to the study medication. SAE (serious adverse events) were not reported. The current state of research will be discussed on the conference.
Discussion: This is the first study to describe the effects of an add-on treatment of spironolactone in patients with a clinically stable schizophrenia. Also, it is the first study with a direct target of a biochemically disturbed signaling pathway in schizophrenia patients with a possibly new treatment option in this severe disease.
Funded by Stanley Foundation: (13T-004). EUDRACT: 2014-001968-35, WHO-Clinical-Trials: http://apps.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2014-001968-35-DE
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S48. INTER-RATER RELIABILITY OF PANSS-6 SCHIZOPHRENIA SEVERITY RATINGS OBTAINED USING THE SIMPLIFIED NEGATIVE AND POSITIVE SYMPTOMS INTERVIEW (SNAPSI)

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Background: Schizophrenia is a severe mental disorder requiring multimodal treatment. Monitoring the severity of schizophrenia during treatment is essential to a successful outcome. The most widely used measure of the severity of schizophrenia is the 30-item Positive And Negative Syndrome Scale (PANSS-30) obtained by the Structured Clinical Interview, SCI-PANSS, which takes approximately an hour to administer. This is too long for routine clinical use. Recently, our group extracted a 6-item scale (PANSS-6), which has shown promising psychometric properties. The scale consists of the following items: P1 - Delusions, P2 - Conceptual disorganization, P3 - Hallucinatory behavior, N1 - Blunted Affect, N4 - Passive/apathetic social withdrawal and N6 - Lack of spontaneity & flow of conversation. For now, it remains unknown whether it is possible to obtain sufficient information for PANSS-6 rating via a short and focused interview. Recently, our group developed an interview, the Simplified Negative and Positive Symptoms Interview (SNAPSI), which enables PANSS-6 rating. Field-testing at hospitals in the United States and Denmark has shown that the patient section of SNAPSI can be completed in approximately 15–25 minutes by raters who are unfamiliar with the interview and involving patients hearing the

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