EPP0461

Relapse prevention with cariprazine in patients with early-stage schizophrenia

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Introduction: Relapse is defined as the return of psychotic symptoms after a period of improvement/stability. Relapse is often associated with the disruptive re-hospitalization of patients. Importantly, relapse history is a strong predictor of subsequent relapses and poorer outcomes. Therefore, relapse prevention in the beginning of the disorder is especially important. Cariprazine, a novel D_3-D_2 partial agonist, has been effective in preventing relapse compared to placebo in stabilized patients with schizophrenia.

Objectives: To present the efficacy of cariprazine in preventing relapse in patients with early-stage schizophrenia.

Methods: Post-hoc analysis of data from a ~96 weeks, multicentre, randomized, double-blind, placebo-controlled, parallel-group study in adults with schizophrenia. The study was composed of two parts: a 20-week open-label treatment phase and a double-blind treatment phase up to 72 weeks. During the open-label phase, patients were stabilized with cariprazine 3.0-9.0 mg/day. Then, they were randomized to continue cariprazine (fixed dosing: 3.0, 6.0, or 9.0 mg/day) or receive placebo. Relapse was defined as a deterioration of symptom scores as measured by the Positive Negative Syndrome Scale (PANSS), admission to a psychiatric hospital, exhibiting aggressive behaviour, or risk of suicide. In the present analysis, patients with a schizophrenia diagnosis history of 0-5 years were defined as early-stage patients. Baseline characteristics, and risk ratios (after the double-blind phase) with number-needed-to-treat (NNT) were calculated.

Results: Of 200 patients, 71 (35.5%) met the early-stage criteria: 32 patients in the cariprazine (CAR) and 39 in the placebo (PBO) arm. The mean age was 31.6 years in both groups with an average illness duration of 2.51+/-1.03 years in the CAR and 2.75+/-1.24 years in the PBO arm. 47% of patients in the CAR arm and 77% in the PBO arm were men. The average number of previous hospitalisations was comparable in the two groups (CAR: 2.3; PBO: 2.6), as was the severity of illness: mean PANSS Total score: 89.2 (CAR), 90.4 (PBO). Patients in both groups were highly compliant (pill-count: CAR: 98.2%; PBO: 99.5%). The main reported adverse effects were headache (CAR: 11.3%, PBO: 7.0%), insomnia (CAR: 5.6%, PBO: 4.2%), and increased triglycerides (CAR: 5.6%, PBO: 1.4%), discontinuation due to adverse event was 3.1% in the CAR and 2.6% in the PBO group. Altogether, 9.4% of patients relapsed in the cariprazine group compared to 48.7% on placebo (risk ratio=0.19 (95% confidence interval (CI): 6.3-59.2%, p=0.0041; NNT: 2.5 (95%CI: 1.7-5.1).

Conclusions: In this post-hoc analysis of patients within the first five years of schizophrenia, the relative risk of relapse was 81% reduced with cariprazine with prevention of one additional relapse after each third patient exposed to cariprazine vs placebo. Cariprazine seems to be a good treatment option for early-stage patients for preventing relapse.

EPP0462

"Neighbohod Vulnerability and Disability in First Episode of Psychosis".

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Introduction: Neighborhood socioeconomic status seems to be related to functioning in patients with first episode of psychosis (FEP).

Objectives: The present study aimed to assess if neighborhood vulnerability and risk of social exclusion could predict functional outcomes in people with FEP after controlling for other key variables identified in previous literature.

Methods: A total of 137 patients with FEP (DSM-IV-TR criteria) and 90 controls comprised the study sample from February 2013 to May 2019. Functioning was assessed with the WHO Disability Assessment Schedule. Neighborhood vulnerability was measured using a multidimensional socioeconomic deprivation index; data for the index were collected by the Madrid City Council and based on the participant's home address. Multilevel mixed-effects regression analyses were conducted to estimate the effects of neighborhood vulnerability on functioning.

Results: Our results show that FEP patients could be more vulnerable to the effects of neighborhood-level characteristics than healthy controls (B = 1,570.173; z = 3.91; Pc .001). In addition, our findings suggest that higher neighborhood vulnerability is related to greater functional disability in people with FEP, after controlling for other relevant confounders (B = 1,230.332; 2=2.59; P=.010). based on the participant's home address. Multilevel mixed-effects regression analyses were conducted to estimate the effects of neighborhood vulnerability on functioning.

Results: Our results show that FEP patients could be more vulnerable to the effects of neighborhood-level characteristics than healthy controls (B = 1,570.173; z = 3.91; Pc 001). In addition, our findings suggest that higher neighborhood vulnerability is related to greater functional disability in people with FEP, after controlling for other relevant confounders (B = 1,280.332; z=2.59; P= 010).

Conclusions: These results highlight the importance of incorporating contextual factors into assessment of patients with FEP, since psychosocial difficulties observed In these patients could be

partially related to the quality of neighborhood social-related resources.

EPP0463

Direct adjusted comparison of expressed emotion towards patients with schizophrenia between halfway houses and family settings

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Introduction: Rates of high expressed emotion (EE) towards patients with schizophrenia have only indirectly been compared between families and community residential facilities, since studies including patients in both settings are unfortunately lacking. High EE rates in staff-patient studies are typically lower than in families, with negligible rates of high emotional overinvolvement (EOI). However, indirect comparisons can suffer from many biases.

Objectives: This study directly compared patients with schizophrenia living in halfway houses or with their families on the EE of their caregivers, adjusting for patient- and caregiver-related confounders.

Methods: We included 40 inpatients with schizophrenia living in halfway houses and 40 outpatients living with their families and recorded the EE of the caring staff (N=22 nurses) or parents (N=56), respectively, through Five Minutes Speech Sample interviews. Each nurse rated 1-12 inpatients and each inpatient was rated by 2-5 nurses, totaling 155 nurse ratings. Each outpatient was rated by one or both parents. Due to the multilevel structure of EE ratings, generalized linear mixed models were fitted. We first adjusted only for differences in patient-related confounders between groups and then added basic caregiver-related demographics.

Results: Compared to outpatients, inpatients were older (p=0.001), less well educated (p=0.002), had a longer disease duration (p=0.047), more hospitalizations (p=0.012), lower severity of psychotic (p=0.027) and, specifically, negative symptoms (p=0.015), and lower perceived criticism (p=0.001). Nurses were younger (p<0.001) and better educated (p=0.001) than parents. After adjusting for patient-related confounders only, EOI was significantly higher in parents (p=0.027) while criticism did not significantly differ between groups. However, after also adjusting for caregiver demographics (age, gender and education), criticism was significantly higher in nurses (p=0.027) while differences in EOI became non-significant.

Conclusions: Differences in EE, when directly compared between parents and professional caregivers, may be explained by differences in patient-related characteristics, caregiver demographics as well as other caregiver characteristics to be investigated in future studies.

EPP0466

Relationship between different PANSS cognitive factors and cognition assessed with MCCB in patients with first psychotic episode of schizophrenia

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Introduction: The Positive and Negative Syndrome Scale (PANSS) has been used as a universal instrument for clinical assessment of psychopathology in schizophrenia. Different studies have analyzed the factorial structure of this scale and have suggested a five-factor model: positive, negative, excited, depressive, and cognitive/disorganized factors. Two of the most used models are the Marder´s solution and the Wallwork´s one.

Objectives: The aim of this work was to study the correlations of the two cognitive factors (Marder and Wallwork) with a cognitive assessment performed with a standard cognitive battery, in a sample of patients with first psychotic episode of schizophrenia.

Methods: Seventy four patients with first psychotic episode of schizophrenia (26.9, SD:7.8 years old; 70.3% male) were included. The cognitive assessment was performed with the MATRICS Consensus Cognitive Battery (MCCB). The MCCB present seven cognitive domains: Speed of processing, Working memory, Attention/ Vigilance, Verbal Learning, Visual Learning, Reasoning and Problem Solving, and Social cognition). Pearson correlations were performed between MCCB scores and Marder´s PANSS cognitive factor (P2, N5, G5, G10, G11, G13, G15) and Wallwork´s one (P2, N5, G11).

Results: Correlation between MCCB scores and cognitive factors of Marder and Wallwork can be seen in the table.

	Marder´s cognitive factor	Wallwork´s cognitive factor
Speed of processing	r = -0.461; p<0.001	r = -0.455; p<0.001
Attention/Vigilance	r = -0.414; p<0.001	r = -0.415; p<0.001
Working memory	r = -0.449; p<0.001	r = -0.468; p<0.001
Verbal Learning	r = -0.511; p<0.001	r = -0.405; p<0.001
Visual Learning	r = -0.252; p=0.024	r = -0.254; p=0.029
Reasoning and Problem Solving	r = -0.244; p=0.036	r = -0.272; p=0.019
Social cognition	r = -0.268; p=0.024	r = -0.202; p=0.091