Introduction: Predictors consistently associated with psychosis liability and course of illness in schizophrenia (SCZ) spectrum disorders (SSD), including the need for clozapine treatment, are lacking. Longitudinally ascertained medication use may empower studies examining associations between polygenic risk scores (PRSs) and pharmacotherapy choices.
Objectives: To examine associations between PRS-SCZ loading and groups with different liabilities to SSD: individuals with SSD on clozapine, individuals with SSD on other antipsychotics, their parents and siblings, and unrelated healthy controls; and between PRS-SCZ and the likelihood of receiving a prescription of clozapine relative to other antipsychotics.
Methods: Design: Six-year follow-up and cross-sectional observational cohort study.
Setting: Multi-center.
Participants: Individuals diagnosed with SSD using clozapine or other antipsychotics, their parents and siblings, and unrelated healthy controls.
Exposure: PRS-SCZ.
Main Outcomes and Measures: We used multinomial logistic regression to examine possible differences between groups by computing risk ratios (RRs), i.e., ratios of the probability of pertaining to a particular group divided by the probability of healthy control status. We also computed PRS-informed odd ratios (ORs) for clozapine use relative to other antipsychotics.
Results: PRSs-SCZ were generated for 2344 participants (mean age: 36.95 years; 42.4% female) remaining after quality control (557 individuals with SSD on clozapine, 350 individuals with SSD on other antipsychotics during six-year follow-up, 542 parents and 574 siblings of individuals with SSD, and 321 unrelated healthy controls). All RRs were significantly different from 1; RRs were highest for individuals with SSD on clozapine (RR=3.24 [95%CI 2.76-3.81], $p=2.47x10^{-46}$), followed by individuals with SSD on other antipsychotics (RR=2.30 [95%CI 1.95-2.72], $p=3.77x10^{-22}$), parents (RR=1.44 [95%CI 1.25-1.68], $p=1.76x10^{-6}$), and siblings (RR=1.40 [95%CI 1.21-1.63], $p=8.22x10^{-6}$). PRS-SCZ was positively associated with clozapine versus other antipsychotic use (OR=1.41 [95%CI 1.22-1.63], $p=2.98x10^{-6}$), suggesting a higher likelihood of clozapine prescriptions in individuals with higher PRS-SCZ.
Conclusions: PRS-SCZ loading differs between groups of individuals with SSD, their relatives, and unrelated healthy controls, with clozapine users being at the far end of PRS-SCZ loading. Additionally, PRS-SCZ is associated with a higher likelihood of clozapine prescribing. Our findings may inform early intervention and prognostic studies into the value of PRS-SCZ for personalized antipsychotic treatment.

Disclosure of Interest: None Declared

O0054

Combination therapy for bipolar disorder : What to combine and which cautions to take ?

M. Gardabbou*, M. Maalej, R. Feki, I. Gassara, N. Smaoui, L. Zouari, J. Ben Thabet, S. Omri, N. Charfi and M. Maalej

psychiatry C department, Hedi Chaker, Sfax, Tunisia
*Corresponding author.
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Introduction: Bipolar disorder is one of the leading causes of disability among young adults. Given the heterogeneity of the disorder and the complexity of its etiopathogenesis, combination therapy is often considered as part of the treatment regimen.
Objectives: To assess the place of non-pharmacological interventions as a co-adjuvant to pharmacological treatment, to discuss the role of polytherapy in the management of bipolar disorder and to underline the drug to drug interactions to keep in mind.
Methods: We present a critical review of recent international recommendations for the management of bipolar disorder. Two main evidence-based guidelines were included: The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders and The 2018 Canadian Network for Mood and Anxiety Treatment.
Results: According to guidelines, the outcomes in bipolar disorder are improved when medication is combined with evidence-based psychological treatment and lifestyle changes. As to polytherapy, it is often recommended to maximise the treatment efficacy. Studies have shown that combination treatments tend to work faster and more effectively than monotherapy especially in episodes with higher index severity. For the management of agitation, an adjuctive treatment by Haloperidol with midazolam or promethazine can be prescribed. In acute mania, combination therapy with quetiapine, aripiprazole, risperidone or asenapine and lithium or divalproex is recommended as first-line treatment options. Combinations of mood-stabilizing drugs may be more often necessary when rapid cycling is present. In a manic episode with mixed features the use of divalproex with an atypical antipyshcotic is recommended. In bipolar I depression, lurasidone and lamotrigine are often used as adjunctive therapies. When anxious distress is present, the combination of olanzapine and fluoxetine has shown to be effective. In a depression with atypical features, tranylcypromine (IMAO) can be added to lithium, divalproex or a second generation antipsychotic for a better result. Adjunctive treatment of olanzapine with fluoxetine may be necessary in a depression with mixed features. However, in bipolar II depression and for maintenance treatment no adjunctive therapies are recommended. Finally, it is important to consider the adverse effects resulting from polytherapy. Using lithium as an adjunctive medication may increase the risk of tremor and acute dystonic reactions and can be a contributing factor for neuroleptic malignant syndrome, whereas divalproex can be an inducer or an inhibitor of some atypical antipsychotics.
Conclusions: Rational polytherapy allows better and faster control over symptoms of bipolar disorder and should be considered after a detailed discussion of risks and benefits.

Disclosure of Interest: None Declared

O0055

Evaluation of factors that may influence the development of chronic kidney disease in patients with bipolar disorder treated with lithium.

N. Gutiérrez Mora[1]*, J. Torres Cortés[2], I. Esteban Avendaño[2], V. Burguera Vion[3] and J. M. Montes Rodríguez[2]

[1]Hospital Universitario Ramón y Cajal, Madrid, Spain; [2]Psychiatry and [3]Nephrology, Hospital Universitario Ramón y Cajal, Madrid, Spain
*Corresponding author.
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