Psychoneuroimmunology

EPP321

Investigation of cytokine imbalance in schizophrenia, assessment of the possible role of serum cytokine levels in predicting treatment response, prognosis and psychotic relapses

K. Bodnar[1]*, L. Hermán[1], R. Zsigmond[1], J. Réthelyi[1], Á. Dénes[2] and K. Tóth[2]

[1]Department of Psychhiatry and Psychotherapy, Semmelweis University and [2]Laboratory of Neuroimmunology, HUN-REN Institute of Experimental Medicine, Budapest, Hungary
*Corresponding author.
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Introduction: Schizophrenia, a multisystem chronic psychiatric disorder of unknown etiology, is associated with several immune dysfunctions, including abnormal levels of circulating cytokines. Emerging data suggest a potential causative role for cytokines in schizophrenia symptom development. Furthermore, disease duration, symptom severity, aggressive behavior, and cognitive deficits are correlated with levels of inflammatory cytokines. Despite the development of new antipsychotics, the negative and cognitive symptoms of schizophrenia often do not respond adequately to pharmacotherapy.
Objectives: 1. Can there be a cytokine or cytokines among the different cytokine levels detected in schizophrenia that can be used as biomarkers of treatment response? 2. Can changes in cytokine levels indicate the occurrence of psychotic relapse? 3. Can changes in the cytokine level play a role in predicting the prognosis of the disease?
Methods: We investigated cytokine levels in blood samples collected at hospital admission. Plasma levels of established inflammatory cytokines and chemokines have been measured by Cytometric Bead Array. The possible role of abnormal cytokine levels and their association with symptoms severity and their potential clinical implications have been investigated. The severity of the symptoms is monitored with the PANSS
Results: 16 schizophrenic patients who were hospitalized due to a psychotic relapse have been included. Blood samples were collected to measure cytokine levels, and the PANSS scale was recorded during a psychotic relapse. Additionally, we have included 11 age- and gender-matched healthy controls, from whom blood samples were also collected for cytokine measurement.. We found no differences plasma levels of G-CSF, GM-CSF, TNF, INF, VEGF, Il-6 and Il-10 in the patients compared with healthy controls. The levels of MCP-1 were higher in the schizophrenia patients than in the healthy control group.
Conclusions: These data demonstrated elevated plasma levels of MCP-1 in schizophrenia patients. The role of MCP-1 in various CNS disorders that involve inflammation is emerging. Among these, chronic inflammation reportedly contributes to the onset and progression of neurodegenerative disorders such as Parkinson's disease (PD), Alzheimer's disease (AD), and Multiple Sclerosis. Links between circulating MCP-1 levels and the progression of schizophrenia has also been suggested by previous studies and further studies are required understand the underlying mechanisms.
Significant outcomes: Patient with a psychotic relapse showed higher levels of plasma MCP-1 compared with healthy controls.
Limitation: The number of samples is too low to detect a statistically significant differences in blood MCP-1 during a psychotic relapse. Involvement of additional patients is ongoing.

Disclosure of Interest: None Declared

Psychopharmacology and Pharmacoeconomics

EPP322

Clozapine: overview of high-risk drug associations in French psychiatric hospitals. A multicenter survey on a given day

M. Bordes[1]*, R. Klein[1] and E. Queuille[2,3]

[1]Ferrepsy, Toulouse; [2]CH Charles Perrens, Bordeaux and [3]Association du réseau PIC, Armentieres, France
*Corresponding author.
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Introduction: Clozapine is the reference treatment for resistant schizophrenia. Its pharmacokinetic characteristics (metabolism by cytochromes CYP1A2, CYP2C19, and CYP3A4, among others) as well as its pharmacodynamic properties are the source of numerous high-risk drug interactions. According to the French marketing authorization, clozapine is contraindicated with bone marrow depressants, and associations with benzodiazepines, omeprazole, fluvoxamine, and lithium require specific precautions.
Objectives: Collaboration between a national multi-professional network operating in various public or private mental health hospitals (the PIC network) and a regional psychiatric research federation (FERREPSY Occitanie) enabled the implementation of a study describing the prevalence of high-risk drug associations in a large panel of French psychiatric hospitals
Methods: An observational cross-sectional study was conducted in December 2023 across 30 centers that are members of the PIC network and/or FERREPSY.
Results: The medical records of 795 patients were analyzed by hospital pharmacists from the participating centers. Several high-risk associations with clozapine were identified. In 1.5% of cases, clozapine was associated with carbamazepine, in 1.1% of cases with omeprazole, and in 3% of cases with fluvoxamine. More frequently, associations with lithium salts were found in 15.6% of patients and with benzodiazepines in 68.3% of patients.
Conclusions: This study provided an overview of high-risk co-prescriptions with clozapine in French psychiatric institutions. It highlights a high prevalence of certain high-risk associations, which underscore the discrepancy between clinical practices and health agency recommendations.

Disclosure of Interest: None Declared

Psychoneuroimmunology

EPP323

Effects of circulating tryptophan, kynurenine, kynurenic acid, IL-8, IFN-γ and IL-1β on neurocognition in clinically stable schizophrenia patients

M. Marković[1]*, T. Nikolić[2,3], M. Stašević[4], M. Stojković[5], M. Velimirović Bogosavljević[2,6], T. Stojković[2,3], S. Ristić[2], I. Stašević Karličić[4,7,8], S. Totić Poznanović[3] and N. Petronijević[2,3]

[1]Clinic for Psychiatry, University Clinical Centre of Serbia; [2]Institute for medical and clinical biochemistry; [3]Faculty of Medicine, University of Belgrade; [4]Clinic for Mental Disorders "Dr Laza Lazarević", Belgrade; [5]Clinic for neurology, University Clinical Centre of Niš, Niš; [6]University of Belgrade, Belgrade; [7]Faculty of Medicine, University of Priština – Kosovska Mitrovica, Kosovska Mitrovica and [8]Ministry of Health, Belgrade, Serbia
*Corresponding author.
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Introduction: Cognitive impairments represent core features in schizophrenia, impact the functional capacity of patients, and are highly predictive of poor functional outcomes. There is a huge unmet need for improvement of these impairments, and the development of new therapies is conditioned by understanding underlying pathophysiology that is not clear enough. Kynurenic acid (KYNA) is the major matabolite of kynurenine (KYN) pathway (KP) of tryptophan (TRP) degradation, which acts as the inhibitor of NMDA and α7-nicotinic receptors that are crucial for cognitive functioning. Excessive antagonism of these receptors by KYNA is hypothesized to contribute to cognitive deficits while data indicate that proinflammatory cytokyines activate this TRP catabolic cascade.
Objectives: The objective of this study was to assess correlation between blood levels of TRP, KYNA, KYN, KYN/TRP ratio, IL-8, IFN-γ, IL-1β and cognitive functioning in clinically stable schizophrenia patients.
Methods: We measured plasma concentrations of TRP, KYNA, KYN, IL-8, IFN-γ, IL-1β and conducted assessment of cognitive functioning in domains of verbal memory, working memory, attention and processing speed, motor speed, verbal fluency, and executive functions using Brief Assessment of Cognition in Schizophrenia Scale (BACS) in 64 clinically stable schizophrenia (SCZ) patients. Patients were matched by age, sex and body mass index and exclusion criteria included obesity class 2 or higher, any concomitant organic mental or neurological disorder, acute or chronic inflammatory disease, and use of immunomodulatory drugs or psychoactive substances.
Results: A significant positive correlation was observed between BACS verbal fluency subtest score and kynurenine levels ($p<0.05$), along with a significant negative correlation with IL-β levels ($p<0.05$). There were no other significant correlations of blood levels of TRP, KYNA, KYN, KYN/TRP ratio, IL-8, and IFN-γ, and cognitive impairments in domains of verbal memory, working memory, attention and processing speed, motor speed, and executive functions.
Conclusions: While the relationship between KP metabolites and cognitive functioning in schizophrenia in domains of verbal and working memory is more reported, specific correlation between KYN levels and verbal fluency observed in our study is less studied and understood. Furthermore, negative correlation between IL-1β levels and verbal memory performance is a valuable finding and can be further explored in the context of suggested detrimental role of IL-1β on hippocampal neurogenesis. Our findings should be interpreted cautiously and corroborated in larger studies with parallel measurement of preferal and central levels of analyzed parameters since there are data that suggest that peripheral concentrations of TRP, KYNA, KYN, IL-8, IFN-γ, IL-1β do not mirror those in the central nervous system.

Disclosure of Interest: None Declared

Psychopharmacology and Pharmacoeconomics

EPP324

Evaluating the in-hospital initiation of 6-monthly paliperidone palmitate: a retrospective study

J. Mesones[1]*, A. Miller[1], A. Martínez[1] and G. Carretero[1]
[1]Psychiatry, Torrevieja University Hospital, Torrevieja, Spain
*Corresponding author.
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Introduction: Long-acting injectable antipsychotic treatments (LAIA) have marked a significant therapeutic advancement. For certain patients, clinical necessity may dictate that the most suitable treatment option is to initiate a 6-monthly LAIA earlier than standard protocols recommend. This can involve transitioning directly from an oral antipsychotic regimen or accelerating the switch from a monthly LAIA, a process known as alternative initiation.
Objectives: The objective of this study is to describe our experience with alternative initiation protocols for 6-monthly paliperidone palmitate (PP3M) in psychotic patients, as implemented at Torrevieja University Hospital.
Methods: This retrospective descriptive study utilized a sample selected through non-probabilistic consecutive sampling over a 27-month period (n=43). The study included patients who initiated 6-monthly paliperidone palmitate treatment through an alternative approach between May 2022 and August 2024 at Torrevieja University Hospital. All alternative initiations were performed in acute patients, who were decompensated at the time of initiating PP6M treatment, with very low therapeutic adherence. A descriptive analysis was conducted, with mean and standard deviation calculated for quantitative variables, and frequencies (N) and percentages calculated for categorical variables.
Results: Over the 27-month duration of this study, PP6M was administered to 43 patients (n=43). The average age was 41 years (SD ± 14.07). 53.49% (n=23) were male and 46.51% (n=20) female. The mean duration of disease progression was 6.67 years (SD ± 7.16). 20.9 % (n=9) of the patients were using substances with abuse potential. The diagnoses were distributed as follows: schizophrenia (32.56%), unspecified psychosis (30.23%), bipolar disorder (11.63%), delusional disorder (11.63%), borderline personality disorder (9.30%), and schizoaffective disorder (4.65%).
A total of 24 alternative initiations were made from oral antipsychotics, 15 from monthly paliperidone palmitate (PP1M), and 4 from aripiprazole LAIA 400 mg/month. During the 27-month study period, there were 4 hospital admissions and 7 visits to the emergency department. Treatment adherence after the alternative initiation of PP3M was 72 %, with patients completing all administrations on the scheduled dates. 74% of the patients are in outpatient follow-up. One patient experienced extrapyramidal symptoms as a side effect..
Conclusions: The present study indicates that there is a subset of patients who may benefit from an alternative initiation with PP6M, potentially enhancing adherence due to the simplified administration regimen. Initiating PP6M as an alternative, whether transitioning from oral antipsychotics, from PP1M or from another LAIA, could be an effective approach for managing decompensated patients with very low therapeutic adherence, demonstrating excellent tolerability and improved adherence.

Disclosure of Interest: None Declared