FIRST-EPIISODE PSYCHOSIS AND INFLAMMATION

WHAT DO WE KNOW?

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BACKGROUND

There is robust evidence that severe mental disorders, including schizophrenia and bipolar disorder (BD), are characterized by an activation of the immune-inflammatory response system (IRS)¹. However, the usefulness of inflammatory or immunological markers is yet to be established.

OBJECTIVE

To review the evidence on the influence of inflammation in first-episode psychosis, namely in clinical outcomes.

METHODS

A research in Pubmed with the key words “inflammation” and “first-episode psychosis” was conducted and followed by a review of the articles published in the last 5 years. Relevant references cited in papers within the search results were also included.

RESULTS AND DISCUSSION (1)

Several biomarkers have been investigated in patients with first-episode psychosis (FEP), such as interleukines (IL), chemokines, complement factors, highsensitivity C-reactive protein (hsCRP), C-reactive protein, e-selectin and vascular cell-adhesion molecule 1 (VCAM-1)^{1,2,3,4}

Symptoms severity: Keinänen et al found that hsCRP, along with triglycerides and BMI, was associated with negative symptoms severity at baseline and predicted positive, overall symptoms severity and general psychopathology at 1-year follow-up.² Nunes et al concluded in their study that proinflammatory cytokines, such as IL-6 and IL-8, are strongly associated with positive and negative symptoms, excitement, psychosis and mood symptoms.¹

Treatment response: In the same study it was found that FEP patients with lower serum levels of interleukin IL-15, higher serum levels of C-X-C motif chemokine 12 and previous exposure to cytomegalovirus (CMV) present higher odds of being non-remitters.¹

Neuronal functioning and cognition: FEP patients seem to be prone to the detrimental effects of M1, Th-1, Th-17 and Th-2 cells¹, which are known to cause long-lasting abnormalities in brain circuitry, affecting neurotransmitter activity, neuroplasticity, apoptosis, neurogenesis and memory^{5,6}.

RESULTS AND DISCUSSION (2)

Role of metabolic alterations and cardiovascular risk:

Various studies establish the relation between cardiovascular risk, inflammatory biomarkers and FEP. Metabolic abnormalities and peripheral inflammation have been increasingly reported in patients at the onset of psychosis and associated with important physical health disorders and increased mortality.²

Marked increases in weight and waist circumference and hs-CRP were observed in FEP during the 12-month follow-up.³

Weight gain, increased visceral fat and impaired glucose metabolism have been detected also in drug naïve patients⁷. Besides, alterations in cytokine profiles, with elevated levels of IL-1β, sIL-2R, IL-6 and TNF- α were shown in antipsychotic naïve FEP patients.^{1,8,9} This suggests these abnormalities to be partly independent of treatment and rather to be linked to innate mechanisms of psychiatric illness, including a chronic inflammation state. All this evidence supports the relevance of considering a combined metabolic-inflammatory status when looking for biomarkers of clinical outcomes of psychosis.³

CONCLUSION:

The available evidence shows that inflammation may be a predictor of clinical outcomes in FEP, particularly in **severity of symptoms, response to medication** and **cognitive function**. Also, **metabolic alterations** may play a key role as predictors of the clinical course of psychosis, independently of the antipsychotic treatment.

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