Inflammation in Schizophrenia: implications for pathophysiology and treatment

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INTRODUCTION

Schizophrenia is a disease affecting 1% of the world population. Although the knowledge of its pathophysiology is still incomplete, there has been much discussion about the neuroinflammatory hypothesis. Cytokines are substances secreted by immune cells having important functions for cellular communication in the innate and adaptive immune system. These substances are able to overcome the blood-barrier and allow a dialogue between the Central Nervous System and the Immune System to influence maturations synaptic, dopaminergic and gamma-aminobutyric acid (GABA)-ergic differentiation. Several studies have confirmed that there are systemic inflammatory changes in patients with schizophrenia.

OBJECTIVES

The scope of this review is to discuss the findings from literature about the role of inflammation in schizophrenia's pathophysiology and to analyze the possible benefits of anti-inflammatory therapy.

METHODS

Internet databases indexed at MEDLINE were searched up to January 2017 using combinations of the MeSH terms: "schizophrenia", "inflammation", "pathophysiology" and "anti-inflammatory agents" and twenty-six significant articles published on the topic were selected.

REFERENCES


RESULTS

Increased pro-inflammatory and anti-inflammatory activity was found by measuring specific cytokines and inflammatory markers in schizophrenia.

Some of the elevated cytokines, particularly interleukin-1 beta (IL-1B), IL-6 and transforming growth factor beta (TGF-β), were considered to be “status markers” for the disease since they increased during acute episodes and then returned to normal after treatment with antipsychotics [1].

Other cytokines such as IL-32, interferon gamma (IFN-γ) and tumor necrosis factor alpha (TNF-α) remained high even after drug therapy and were dubbed “trait markers” of disease [1].

Interleukin-6 has been identified as a possible biomarker for diagnosing the disease and its elevation was observed particularly in individuals with an earlier onset of the disease and with more positive symptoms [2].

Some cytokines may be linked to the severity of the disease such as IL-2, IL-4, IL-10 and TNF-α [3]. It was found that C-Reactive Protein (CRP) levels are elevated in patients with schizophrenia, supporting the idea of the presence of systemic inflammation [4].

In relation to inflammatory responses, experiments have shown an inhibition of Th1 response in the early stages of schizophrenia followed by an amplification of Th2 response in the later stages [5]. This data appears to be associated with negative symptoms by contributing to the increase of kynurenic acid synthesis by astrocytes [5].

Prenatal infections are also related to genetic and behavioural changes in offspring, with a consequent increased risk of developing the disease [6] [7].

The therapeutic effects of nonsteroidal anti-inflammatory drugs, COX-2 inhibitors and other classes of drugs added to antipsychotics have been tested, with beneficial results in terms of symptomatology [8].

CONCLUSIONS

A pro-inflammatory state coexists with schizophrenia, as well as with other mental illnesses, such as depression and bipolar disease. Clinically, and with the help of further research, it may be possible to use some cytokines as biomarkers that reflect the clinical situation in schizophrenia. Although with some limitations, there are promising results for the efficacy of anti-inflammatory therapy, which appears to be more effective during the early stages of the disease with fewer beneficial effects during the later stages [8]. Therefore the two groups of patients should be analyzed separately. Due to the small number of studies and patients analyzed, it is difficult to extract solid conclusions to clinical practice.

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