RESEARCH

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CRP elevations in patients with schizophrenia

Shashi K. Agarwal☼

Medical Director, Agarwal Health Center, 52 Richard Road, Edison, NJ 08820 USA

☼Correspondence to:
Medical Director, Agarwal Health Center, 52 Richard Road, Edison, NJ 08820 USA, E-mail: usacardiologist@gmail.com, 732-895-3200

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ABSTRACT

There is a compelling body of evidence relating subclinical chronic inflammation and schizophrenia in adults. Prenatal infections during pregnancy have been shown to be associated with an increased risk of schizophrenia in the offspring during adulthood. Inflammation in these patients may also be contributing to the high burden of metabolic and cardiovascular diseases experienced by these patients. CRP is a sensitive, inexpensive and easy biomarker for diagnosing chronic low grade inflammation. This study reveals that one half of our adult patients with schizophrenia suffer from chronic low grade inflammation as evidenced by elevated CRP levels. These findings may have therapeutic and prognostic implications.

Keywords: schizophrenia, inflammation, CRP

Abbreviations: ESR: Erythrocyte sedimentation rate; IL-6: Interleukin-6; IL-18 Interleukin-18; TNF-α: Tumor necrosis factor-alpha; CRP: C-reactive protein

1. INTRODUCTION

1.1. Epidemiology

Schizophrenia is a worldwide disease, with a prevalence of approximately 1% (Bhugra 2005). It is the third leading cause of global disability in persons aged 15-44 years. It is responsible for 2.8 percent of the global burden of disability (Health Organization, 2001). The clinical features and management of schizophrenia has been well studied (APA, 2000; Sullivan et al, 2003; Woo et al, 2004). Patients with schizophrenia have a two to three fold higher mortality rate compared to the general population (Laursen et al, 2007; Saha et al, 2007; Brown et al, 2010). They also have a higher rate of suicide and accidents (Palmer et al, 2005). They usually pursue unhealthy lifestyles. These include poor diet, lack of exercise and excessive smoking and increased alcohol intake (Wildgust et al, 2010). They commonly partake in substance abuse (Foti et al, 2010). Schizophrenic patients also are more likely to be homeless or incarcerated, due to crimes, and this further contributes to a suboptimal lifestyle (Fazel et al, 2009). Anti-psychotics also appear to contribute to an excess mortality due to adverse effects (De et al, 2010). And finally, these patients appear to receive sub-optimal medical care (Mitchell et al, 2010). As a result of all these factors, patients with schizophrenia suffer from a 10-25 year reduction in life expectancy. They also account for approximately ten percent of America's totally and permanently disabled population (Rupp et al, 1993).

1.2. Etiology

The etiology of schizophrenia is not known. However, genetic, perinatal and socio-environmental factors appear to play a role in its causation. In biologic relatives, the risk of developing schizophrenia is elevated. The risk is as high as 40% developing in a child if both parents have schizophrenia (Kety et al, 1994). Perinatal factors include malnutrition (Brown et al, 2010), obstetric complications (Geddes et al, 1995) and viral illnesses (Brown et al, 2004) in the mother during pregnancy. Schizophrenia is also more common in children born in the winter months (Torrey et al, 1993). Increasing evidence is linking sub-clinical inflammation as an etiological factor in the patho-physiology of schizophrenia.

2. METHODS

We retrospectively reviewed the laboratory results of all schizophrenia patients seen in our office during a period of one year. These visits were for routine yearly physical. None of the patients had any acute illness or infection. All patients were diagnosed to be suffering from schizophrenia by psychiatrists according to the criteria established by the revised fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). All patients met the three diagnostic criteria: A. Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated): (1) delusions (2) hallucinations (3) disorganized speech (e.g., frequent derailment or incoherence) (4) grossly disorganized or catatonic behavior (5) negative symptoms, i.e., affective flattening, alogia, or avolition. B. Social/occupational dysfunction: For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement). C. Duration: Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences) (DSM-IV, 2000). All patients were regularly seen by their psychiatrists and were stable on anti-psychotic medications. Presence of inflammation was confirmed by measuring Hs CRP and ESR. CRP is an acute phase reactant produced in the liver by the hepatocytes. Low grade inflammation produces minor elevations of CRP in the 1- to 10 mg/L range. C-reactive protein levels above 10 mg/L usually suggest the presence of active infectious or inflammatory disease (Pepys et al, 2003). The erythrocyte sedimentation rate (ESR) also helps detect conditions associated with acute and chronic inflammation, including infections, cancers, and autoimmune diseases. Unlike CRP, it is more non-specific and less rapid in its rise and fall (Westergren, 1957). High sensitive C-reactive protein and ESR were done as part of a yearly blood screening and sent to a commercial laboratory for testing and results.

3. RESULTS

We reviewed the charts of all patients with schizophrenia seen in our office during a period of one year. We found 60 patients who had CRP measured during this period. Of these, 52 patients also had their ESR levels measured. There were 47 men and 13 women.

Their ages ranged from 22 to 54 years. CRP was considered indicative of low grade and chronic inflammation if it measured between 1 and 10. CRP was more than 1mg/L and less than 10mg/L in 30 (50%) of 60 patients. (Fig.1) Of the 47 men, CRP was in this range in 22 (47%) and out of the 13 females, CRP was in this range in 8 (61%). ESR was considered abnormal if it was more than 20. ESR elevated in 21(40%) out of 52 patients. Out the 41 men 15 (37%) had elevated ESR while out of the 11females 6 (55%) had elevated ESR.

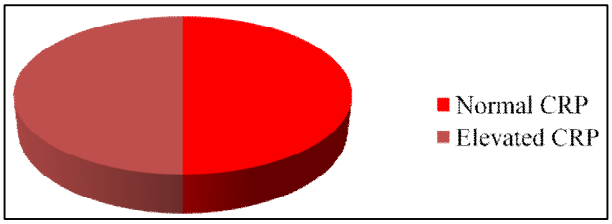

Figure 1
CRP level

4. DISCUSSION

There is a growing body of evidence to suggest that neuro-inflammation may play a role in the pathogenesis of many psychiatric conditions such as depression (Ford et al, 2004; Lesperance et al, 2004) and cognitive impairment (Yaggffe et al, 2003; Weuve et al, 2006). Neuro-inflammation also plays a role in several neurodegenerative diseases such as multiple sclerosis, Parkinson disease, and Alzheimer disease (Doorduin et al, 2008). An association of inflammation has also been shown in adults suffering from schizophrenia (Eric et al, 2009; Muller et al, 2008). There are several markers of acute and chronic inflammation in the body. These include: ESR, IL-6 , IL-8, IL-18, TNF-α, CRP, insulin and leptin. CRP is a sensitive, reliable and easy test to perform and can be used to document the presence of subclinical inflammation in patients. Our data suggests that almost one half of the patients with schizophrenia have evidence of chronic inflammation as evidenced by an elevated CRP. This may have therapeutic and prognostic implications. Schizophrenic patients with increased levels of CRP are more likely to have acute manic phases (Huang et al, 2007; Cunha et al, 2008; Wadee et al, 2002) and the level of CRP elevation has been linked to the intensity of manic symptoms (Dickerson et al, 2007). Another study has shown that cognitive function impairment also mirrors the increased levels of CRP in these patients (Faith Dickerson et al, 2007). People with schizophrenia also suffer from high rates of physical co-morbidity (Jeste et al, 1996). These include pulmonary, cardiovascular and endocrine diseases (Casey et al, 2011; Goff et al, 2005; Copeland et al, 2007). Chronic inflammation may play a major role in the development and progression of these co-morbidities. Elevated CRP has been implicated in the development and progress of diabetes mellitus (Fan et al, 2007) and cardiovascular events in this population (Sicras-Marinar et al, 2011).

5. CONCLUSIONS

Patients with schizophrenia have a two to three fold higher mortality rate compared to the general population (Laursen et al, 2007; Saha et al, 2007; Brown et al, 2010). Overall, patients with schizophrenia suffer from a 10-25 year reduction in life expectancy. They also account for approximately ten percent of America's totally and permanently disabled population (Rupp et al, 1993). Identification of chronic inflammation and techniques to reduce inflammation in these patients via monitoring of CRP may have a therapeutic value. It may help reduce some of the excessive morbidity and mortality burden experienced by these patients. The prophylactic use of aspirin, statins and metformin in selected patients with or without elevated CRP needs to be further studied in this population.

SUMMARY OF RESEARCH

Considerable experimental, epidemiological and clinical evidence has documented an inflammatory role in the etiology and course of schizophrenia. Our research shows that elevated CRP levels indicating low grade chronic inflammation are present in one half this population. This may also contribute to the metabolic disturbances seen in these patients. It is logical to postulate that focused therapeutics to curb inflammation may help treat both the psychopathology of schizophrenia as well as the devastating co-morbid conditions seen in these patients.

DISCLOSURE STATEMENT

The author has no conflicts of interest to disclose.

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