Effect of SSRI on C-Reactive Protein in Case of Depression

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Introduction: Depression can present with several symptoms, such as loss of pleasure, feelings of guilt, low self esteem, and disturbed sleep or appetite. In recent socio-economic scenario incidence & prevalence of depression is on increasing trend. SSRIs are the mainstay of treatment of depression.

Objective: the anti-inflammatory role of escitalopram in freshly diagnosed depression case and also to find any correlation between depression & inflammation.

Material & Methods: It was a cross-sectional analytical study conducted at College of Medicine and Sagore Dutta Hospital by Department of Psychiatry in collaboration with Department of Biochemistry. 71 Patients attending psychiatric OPD who are newly diagnosed as Major depressive disorder (MDD) were selected. 73 Age and sex matched healthy family members of the patients were taken as controls. Before starting treatment C reactive protein (CPR) & Hamilton depression rating scale (HAMD) was assessed. After 12 weeks of treatment same parameters were assessed again.

Results: after 12 weeks of treatment mean CPR & HAMD score is significantly reduced in case group as compared to the baseline values respectively. The reduction of HAMD score is negatively correlated with the baseline CPR.

Conclusion: Escitalopram significantly reduce the CPR value which may have a role in improvement of HAMD score.

Keywords: Major Depression, CPR, HAMD, SSRI

Introduction

Depression is a serious psychiatric disorder that can lead to emotional and physical problems, including loss of interest or pleasure, feelings of guilt or low self-worth, and disturbed sleep or appetite. Recently it is emerging as a major public health problem affecting large number to human populations worldwide irrespective of age. Women are significantly more prone to develop depression...
than males and often have a more chronic course\(^2\). Furthermore, the lifetime risk of developing depression increases to as high as 40% when comorbid chronic medical illnesses such as diabetes and cardiovascular disease (CVD) are present\(^3\). The immune system, particularly the inflammatory response, plays an important role in depression and its pharmacological treatment. Recently several studies have been conducted to find the role of inflammation in psychiatric illnesses like depression\(^4-5\). Some studies have shown that inflammatory markers are elevated in central nervous system tissues collected from individuals with depression than compared to healthy controls, including increased concentrations of pro-inflammatory cytokines and immune mediators in cerebrospinal fluid\(^6-7\). CVD is the leading cause of morbidity and mortality worldwide, which is further influenced by an abundance of modifiable risk factors. CRP is one among them These factors also appear to be involved in the pathophysiology of depression, and may account for the higher cardiovascular risk observed in this disorder\(^8\).

A combination of psychological and pharmacological therapies is the predominant treatment modalities for depression. Antidepressants are the mainstay of pharmacological intervention for moderate to severe depression which is used to alleviate mood and behavioral symptoms. Most of the widely prescribed classes of antidepressants are selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, paroxetine, escitalopram and sertraline. Other drugs like serotonin-norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine, desvenlafaxine, and duloxetine\(^9-11\), and tricyclic antidepressants (TCAs) such as imipramine, clomipramine, and desipramine\(^12-14\) are also used.

### Aims & Objectives:
To assess the anti-inflammatory role of escitalopram in freshly diagnosed depression case and also to find any correlation between depression & inflammation

### Materials & Methods

#### Ethical Clearance:
Valid ethical permission was taken from institutional ethics committee of College of Medicine & Sagore Dutta Hospital. The original work was from here only after the permission of ethical committee.

#### Study type and design:
A cross-sectional analytical study

#### Study setting:
It was conducted at College of Medicine and Sagore Dutta Hospital by Department of Biochemistry in collaboration with Department of Psychiatry.

#### Study population:
Patients attending psychiatric OPD who are newly diagnosed as Major depressive disorder (MDD).

#### Inclusion criteria of cases:
Patients, aged between 18-55 years newly diagnosed to have MDD (fulfilling DSM V criteria) or RDD (unipolar)

#### Inclusion criteria for controls:
Age and sex matched healthy family members (brothers, sisters) of the patients

#### Exclusion criteria:
Patients with other acute or chronic disorder e.g Diabetes mellitus, Hypertension, Hypo or hyperthyroid, Seasonal Affective Disorder, other psychiatric disorder, dyslipidemia, malabsorption disorders, malignancy, liver cirrhosis or previous treatment with other anticonvulsants, patients having bipolar depression.

#### Sample size:
71 cases & 73 control

#### Study duration with time scheduling:
December 2021 to May 2022

#### Tools and techniques:
Every individual in both case & control group were asked to be give written consent after explaining the whole process in language which is understandable to them. The confidentiality of the statement and reports were maintained with utmost priority.

5ml overnight fasting blood sample was collected along with the detailed history and fulfilling the exclusion criteria. Serum was separated & collected after centrifugation.

Blood samples were analyzed for serum C-reactive protein by following manufacturer’s instruction with ERBA EM360/640 Autoanalyzer.

Data was collected and analyzed by using statistical software.
Control and cases were grouped. At the beginning of starting treatment the biochemical parameters were measured and clinically assessed for psychiatric function using HAM-D criteria. After 12 weeks of treatment with escitalopram 20 mg daily, again the patients were reviewed and assessed by the same criteria to know the effect. Exposure variable and descriptive analysis were done. Mean, median, standard deviation and distribution of data was assessed. Depending on the distribution of data statistical tools were used to find further significant analysis.

**Results**

**Table 1: Descriptive epidemiology & Comparison of CRP in case & control**

<table>
<thead>
<tr>
<th></th>
<th>Case (n=71)</th>
<th>Control (n=73)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP Mean ±SD</td>
<td>3.10±0.89</td>
<td>1.17±0.67</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

P <0.05 * significant

**Table 2: Comparing CRP & HAMD values in case group before & after 12 weeks of starting treatment**

<table>
<thead>
<tr>
<th></th>
<th>Case before starting treatment</th>
<th>Case after 12 weeks of treatment</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP Mean ±SD</td>
<td>3.10±0.89</td>
<td>1.41±0.29</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>HAMD ±SD</td>
<td>23.23±2.87</td>
<td>9.38±2.30</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

P <0.05 * significant

**Table 3: Association between baseline CRP & HAMD along with treatment response**

<table>
<thead>
<tr>
<th>Baseline CRP</th>
<th>Baseline HAMD</th>
<th>Pearson correction coefficient</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.10±0.89</td>
<td>23.23±2.87</td>
<td>0.59</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Treatment response

<table>
<thead>
<tr>
<th>CRP after 12 Weeks</th>
<th>HAMD after 12 weeks</th>
<th>Pearson correction coefficient</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.41±0.29</td>
<td>9.38±2.30</td>
<td>0.1389</td>
<td>0.04</td>
</tr>
</tbody>
</table>

P <0.05 * significant

**Table 4: CRP baseline & reduction in HAMD**

<table>
<thead>
<tr>
<th>Baseline CRP</th>
<th>Reduction in HAMD</th>
<th>Pearson correction coefficient</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.10±0.89</td>
<td>3.10±0.89±3.91</td>
<td>-0.6566</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

P <0.05 * significant

**Discussion**

In our study we found that CRP is significantly high in the case group when compared to the control. Moreover it was being correlated with the HAM-D scoring at the point of diagnosis before starting any treatment. whereas after 12 weeks of treatment with escitalopram the decrease in HAM-D score is negatively correlated with the baseline CRP level.

CRP is an inflammatory biomarker of that can serve as a prognostic indicator of MDD patients. Patients with MDD showed characteristically elevated CRP levels. Smith et al., 2018 along with several other studies also found that CRP predicted depressive symptoms at follow-up assessments in adjusted models, similar to our findings. On the contrary, several other studies did not show any causal association between genetically increased CRP and the development of depression.

The decrease in CRP following initiation of SSRI treatment indicates the role of this acute phase inflammatory reaction protein as a definite marker of depression. Since antidepressant therapy
significantly decreased CRP concentration, it also proves that antidepressants inhibit this pro-inflammatory protein.

The mechanism of reduction of CRP by SSRIs is due to the fact that there are some pathways through which inflammatory cytokines can lead to reduced synaptic availability of the monoamines. These are by decreasing tetrahydrobiopterin, by stimulating glutamate release, by activating the enzyme indoleamine 2, 3-dioxygenase, or by decreasing Brain Derived Neutrotrophic Factor. SSRIs block these pathways of proinflammatory cytokines leading to reduction of CRP. Another possible mechanism involves serotonergic pathways. Low concentration of extracellular serotonin is necessary for optimal production of cytokines and normal immune functions, whereas higher concentrations of serotonin are immunosuppressive and inhibits cytokine production. SSRIs inhibit the reuptake of serotonin resulting in high extracellular serotonin concentrations and the subsequent inhibition of cytokine production. This is the explanation why in our study, we have got similar results using escitalopram, an SSRi.

**Conclusion**

Baseline evaluation of pro-inflammatory marker like CRP can predict the prognosis and progression of disease. Evaluating the pro-inflammatory stage treatment modality can be planned or modified.

**Limitations:** Small sample size along with lack of prolonged follow-up.

**Conflict of interest:** The authors declare that there is no conflict of interest in the study.

**Source of Funding:** Self

**References**

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