INTRODUCTION

In January 1988, the first selective serotonin reuptake inhibitors (SSRI), fluoxetine was introduced in the United States. The adverse effect profile of fluoxetine was far superior to that of any other available antidepressant because of its selectivity for serotonin receptors. Other SSRIs were soon introduced in the United States and elsewhere. Although the efficacy of the SSRIs is comparable to that of the tricyclic antidepressants (TCA), the SSRIs have significantly fewer side-effects. Compared with the TCAs, SSRIs were initially considered almost free of side effects. However, questions about the safety and tolerability of SSRIs have emerged with their continued use.

Soon after the introduction of the first SSRI, fluoxetine (Prozac) into the United States marketplace in January 1988, reports began to appear describing fluoxetine-induced violence against self and others. In May 1990, the U.S. Food and Drug Administration required the manufacturer of Prozac, Eli Lilly and Company, to add “suicidal ideation” and “violent behaviors” to the post introduction reports section of its label.

Suicide is among the three leading causes of death among those aged 15-44 years in some countries, and the second leading cause of death in the 10-24 years age group; these figures do not include suicide attempts, which can be many times more frequent than suicide. Every year, more than 800,000 people die from suicide; this roughly corresponds to one death every 40 secs. Suicide prevention requires intervention also from outside the health sector and calls for an innovative, comprehensive multi-sectoral approach, including both health and non-health sectors. The present paper highlights a case of intense suicidal ideation presented after the use of SSRI.

ABSTRACT

This report describes a patient suffering from somatoform disorder that developed suicidal ideation specifically due to the treatment with sertraline. After 6-7 months on the regimen, she presented slight suicidal ideations. However, with gradual progress of time and continuation of the therapy, the ideation became intense. She complained of intense restlessness and anxiety. She presented with fresh cuts and bruises on her left arm and neck. On reporting the problem, the drug was withdrawn. Patient experienced gradual improvement in her state. The case report underlines the importance of onset of suicide risk in panic disorders due to specific antidepressants, selective serotonin reuptake inhibitors (SSRIs). The exact neurobiological basis of depression though being uncertain, the role of serotonin has been mostly implicated. Hypothetically, biological alterations in the serotonergic system might have contributed to the suicidal ideation/attempt in the presence of an SSRI. The present case attempts to highlight an incidence of development of suicidal ideation in a patient who is on chronic SSRI therapy.

Keywords: Selective serotonin reuptake inhibitors, Sertraline, Suicidal ideation

Case Report

Selective serotonin reuptake inhibitor associated suicidal ideation: a case report

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CASE REPORT

A 32-year-old married female and mother of three children, reported in the outdoor patient unit, Department of Psychiatry, Medical College Kolkata; with the complaints of increased insomnia, nervousness, agitation, and aggressive behavior. According to the International Classification of Disease: Clinical Descriptions and Diagnostic Guidelines (ICD-10); she was diagnosed a case of F45 somatoform disorder. She had been following a regimen sertraline 50 mg/day for last 22 months, under the supervision of practicing physician. Other concomitant medications prescribed, were sodium valproate 500 mg/day and diazepam 5 mg/day. The laboratory investigations for routine hematology, blood sugar, liver function test, thyroid function test, lithium test, and electrocardiogram were found to be normal. The main precipitating stressor in this case was marital discord. Her family reported that she had violent outbursts for last 4 months and she had even attempted many self-harm/injury, which were quite identifiable during conversation with her. Her family reported that there were no such suicidal ideations during the initial stages of the therapy. After 6-7 months on the regimen; she presented slight suicidal ideations. However, with gradual progress of time and continuation of the therapy, the ideation became intense. She complained of intense restlessness and anxiety. She presented with fresh cuts and bruises on her left arm and neck. She complained that she could not help the situation though at times she is quite aware that she is harming herself. She was found to be completely preoccupied with thoughts and anxiety about her children whom she thinks will be at mess after she dies. She describes in her own words “I wish my children were big enough to take care of themselves, as I will die soon.”

On reporting the problem, the drug was withdrawn. Patient experienced gradual improvement in her state. Incidence of self-harm, intense restlessness resolved with time. No rechallenge was attempted by the practicing physician. Complete withdrawal of the drug eventually helped the patient to return to normal lifestyle. The diagnosis of SSRI induced suicidal ideation was thus made.

DISCUSSION

The class of SSRIs, including fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram and most recently escitalopram, through different mechanisms, increase serotonin levels in the synapse by preventing presynaptic reuptake of this neurotransmitter. Although acute treatment with SSRIs can elicit a rapid change in serotonin levels, this does not correlate well with changes in affect; typically, mood improves after chronic treatment (14-30 days).3

Various studies support the idea that disrupted production or release of serotonin and other neurotransmitters contributes to the neurobiological basis of this disorder. Evidence from various studies supports the involvement of the serotonergic system in the pathophysiology of depression. Cerebrospinal fluid (CSF) studies have noted reduced CSF 5-hydroxyindoleacetic acid, a serotonin metabolite, in both suicidal and impulsive/aggressive patients, regardless of whether they were diagnosed with major depressive disorder (MDD) or bipolar disorder; furthermore, depressed patients were found to have significantly lower maximal velocity of serotonin uptake in the CSF compared with matched controls. Other studies have revealed that individuals with MDD have a blunted physiological response to serotonin receptor 5-hydroxytryptamine (5-HT1A) agonists in vivo and abnormal 5-HT1A receptor binding postmortem. Similarly, recent positron emission tomography studies have yielded in vivo evidence of reduced pre-and postsynaptic 5-HT1A receptor binding in individuals with MDD. Several studies also reported an increased number of postsynaptic 5HT2 receptors in the brains of depressed patients as well as suicide victims.4

Chronic antidepressants generally reduce serotonin turnover in patients, even agents whose primary biochemical target is not the serotonergic system. Chronic treatment with SSRIs reduces cell body 5-HT1A density, thereby increasing serotonergic neuron firing; indeed, antidepressants generally decrease 5-HT2 density in rat prefrontal cortex. Thus, data from a variety of studies suggest that abnormalities of the serotonergic system are present in MDD.

Animal studies have revealed that chronic antidepressant treatment alters critical regulators of neuroplastic function, including the mitogen-activated protein kinase pathway, brain-derived neurotrophic factor, vascular endothelial growth factor, and cyclic adenosine monophosphate response binding (CREB) element.5 Post-mortem findings also support SSRI-mediated increases in CREB activity less abundantly expressed in the temporal cortex of severely depressed individuals.6

Suicide is a complication of all existing psychiatric disorders. The probability of suicidal behavior depends in part on a diathesis that includes more hopelessness and more impulsivity, which are partly related to impaired serotonergic input into the ventromedial prefrontal cortex.7 Future insight into the genetic and neurochemical studies in suicide research may further facilitate suicide prevention.

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