Case Report

Intense Suicidal Thoughts and Self-Harm Following Escitalopram Treatment

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ABSTRACT

In a minority of depressed patients, treatment with an antidepressant drug appears to initiate intense suicidal thoughts and actions. We describe this phenomenon in a 52-year-old woman treated with escitalopram. She did not experience this when treated with six other antidepressants, which were not Selective Serotonin Reuptake Inhibitors. Clinicians need to warn patients and their relatives of the risk that intense suicidal thoughts may develop after an antidepressant drug is started and encourage them to seek help immediately should this occur.

Key words: Antidepressant, suicidal thoughts, selective serotonin reuptake inhibitors

INTRODUCTION

Antidepressant drugs may be prescribed to alleviate suicidal thoughts and prevent suicidal acts, yet in the past decade these have been linked with the initiation of such suicidal thoughts and acts.

Three recent meta-analyses have evaluated the risks of antidepressant drugs initiating non-fatal suicide attempts and completed suicide. When patients receiving Selective Serotonin Reuptake Inhibitors (SSRIs) were compared with those given placebo,[1] a significant increase was noted in the combined risk of non-fatal and fatal suicide acts in the SSRI group [odds ratio (OR): 2.28, 95% confidence interval (CI): 1.14-2.45]. This meta-analysis of Medline reported randomized controlled trials of SSRIs conducted between 1967 and June 2003 also found an increase in the odds ratio of combined fatal and non-fatal suicide acts comparing SSRIs with active therapeutic interventions other than tricyclic antidepressants. No difference was found between SSRIs and tricyclics. In another meta-analysis evaluating placebo-controlled trials of SSRIs derived from the Medicine and Healthcare Products Regulatory Agency,[2] the smaller increase in risk of non-fatal self-harm (OR: 1.57, 95% CI: 0.99-2.55) was not statistically significant; also, there was no evidence that SSRIs increased the risk of suicide as compared to placebo. There was again no difference in the odds ratio of suicide attempts when comparing SSRIs with tricyclic antidepressants. This was also the finding of a meta-analysis utilizing the General Practice Research Database,[3] whose reports from community practice did not have a placebo comparison. However, this study found that for patients aged 18 years or younger there was a higher risk of non-fatal self-harm for SSRIs as compared to tricyclics (OR: 1.59, 95% CI: 1.01-2.50). According to the UK’s National Institute of Clinical Excellence, adolescents are regarded as a high-risk group for the development of non-fatal self-harm.
of suicidality if given an SSRI. The Food and Drug Administration (FDA) in the US had reported on 24 trials of 4,582 children and adolescents and found that the risk of suicidal thinking and behavior for those given an SSRI was 4%, whereas for placebo the risk was 2%. Put differently, of 100 treated patients, one to three might have an increase in suicidality beyond the risk that occurs with depression and arise from short-term treatment with an antidepressant drug. There were no completed suicides in the trials reported by the FDA.[4]

The mechanism by which antidepressant drugs might increase suicidal thinking, suicidal behavior, and suicide is not yet established. One mechanism proposed is that emergent anxiety and akathisia on starting treatment are the risk factors for such activation, leading to the commission of suicidal acts, which otherwise would not have occurred. A second proposed mechanism is that SSRIs promote suicidal thoughts per se, and that patients develop a painful round of pervasive suicidal thoughts. This was described in a few cases shortly after fluoxetine was introduced.[5] These two mechanisms would be in keeping with the finding[6] that the risk for non-fatal suicidal behavior for the first nine days of a new antidepressant prescription was raised fourfold (OR: 4.1, 95% CI: 2.9-5.7) in comparison with the risk for 90 days and beyond. A third mechanism has been proposed related to poor treatment adherence, which often occurs in adolescence and is well documented in teenagers' medical disorders such as asthma and diabetes. This argument is that inconsistent antidepressant drug compliance may result in the frequent occurrence of acute discontinuation symptoms to which adolescents may respond impulsively by self-harm. FDA data[3] have showed a significant negative correlation (Spearman’s rho –0.93, P<0.01) between plasma half-life and suicide risk, the antidepressants with a short half-life having a higher propensity to cause discontinuation symptoms.

We believe our case report is of interest because it illustrates one of the described mechanisms.

**CASE REPORT**

A 52-year-old married woman was suffering from recurrent depressive disorder as described in the International Classification of Diseases (ICD)-10. There is significant family history of mood disorder as the patient’s mother had been hospitalized thrice for depression which affected her during her childhood and teens. The patient is the eldest of three sisters. Her younger sister was suffering from dysthymia and her youngest sister who has a learning disability had undergone treatment for depression.

Her first depressive episode occurred at age 40. She had previously been well and in particular did not have dysthymia or any abnormal personality traits. She was treated with dosulepin (previously called dothiepine) and she recovered with a dose of 150 mg daily, but developed sweating as a side effect. She had migraine and was treated with methysergide. A neurologist thought her migraine might respond to amitriptyline, but she complained of a racing heart while taking it. She did not persist with subsequent treatment with venlafaxine XL 75 mg nocte. Minor side effects explain the diversity of antidepressant drugs she has been prescribed.

After a period of being well, she was referred back to psychiatric services at age 49. Her general practitioner wrote in her referral letter that he had started her again on dosulepin 150 mg nocte six weeks ago. By the time she saw the psychiatrist in October 2001 she was well. She did not persist with dosulepin and in August 2003 had morbid thoughts and suicidal ideas. She was started on mirtazapine and the dose was increased from 15 to 45 mg nocte. By March 2004, she was well, but had stopped taking antidepressant drugs. She was referred again in October 2004 when her general practitioner had started her on lofepramine 140 mg nocte. By December 2004, she was again well, but once more stopped taking the antidepressant.

She was referred again in July 2005 when she reported no point in living. She was started on escitalopram 10 mg nocte. While when previously started on the antidepressant drug treatment she experienced transient suicidal thoughts occasionally, this time her thoughts were considerably more intense, intrusive, and compelling. The thoughts were continuous and persistent. She kept thinking “I can’t go on. I’d be better off dead”. Her impression was that her suicidal thoughts were qualitatively different from any she had previously experienced. She was slightly agitated. Six days after starting on escitalopram she took a large overdose; this was the first time in her life that she had harmed herself. She reported no preceding adverse events or changes. Her husband had continued to be supportive as had been the case in the past. Subsequently, her depression was successfully treated with trazodone, after which she did not experience suicidal thoughts.

**DISCUSSION**

Our patient attributed her qualitatively different experience of suicidal thoughts to the medication she had taken prior to their onset, but alternative explanations are a rapid deterioration of her depressive episode in a trajectory she had not previously experienced or the occurrence of life events of which we remain unaware. If one accepts her perspective in light of the meta-analyses quoted above, then of the
seven antidepressant drugs she had been prescribed, only escitalopram appears to have been associated with intense, compelling, and persistent suicidal thoughts upon which she acted. Escitalopram and citalopram are the most serotonergic of all antidepressants, though the meta-analyses quoted in the introduction reported no greater risks for SSRIs compared to tricyclics, except for those aged under 18. However, the time course of SSRIs’ pharmacodynamic mechanism of action may be relevant. Initially, the action of inhibition of reuptake of neurotransmitters from the cell body’s synapses with resultant increase in synaptic neurotransmitter activates the cell body’s inhibitory 5 Hydroxytryptamine (5HT)1A autoreceptors. This results in reduced cell body firing, with resultant reduced release of serotonin by the axon terminal. Chronic administration of the SSRIs results in downregulation of the cell body’s 5HT1A autoreceptors, which restores cell body firing as well as serotonin release by the axonal terminal. Given the 5HT pump reuptake blockade at the axon terminal synapse, the restoration of serotonin release results in increased serotonin concentration in the axonal synapses. The time course of downregulation of receptors, which occurs over weeks, fits better with the time taken to respond to an antidepressant, whereas serotonin reuptake blockade occurs within a few hours of ingestion of an SSRI. One may speculate about an association of the initial reduction of serotonin release and the onset at the start of treatment of suicidal thoughts and actions.

The early phase of treatment of depression with Tricyclic Antidepressants (TCAs), Electroconvulsive Therapy (ECT), and even light therapy has been considered a risk period for initiation of suicidal thoughts and actions. It was postulated that as patients’ energy returned, they became more active, and hence more able to act on suicidal thoughts. Our case in contrast illustrates the occurrence of intense suicidal thoughts and self-harm in a setting of slight agitation and resembles those described in one of the earliest reports of this phenomenon.[5] These authors and others at the time used the word “violent” to describe the suicidal thoughts, an indication of severity.

Given the serious implications, patients and their relatives should be warned of the phenomenon’s existence so that they may initiate urgent contact with psychiatric services should it occur.

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