Antidepressants triggering suicidal ideation: An area of concern

Himali Rajgadhi, Sapna Gupta¹, Supriya Deepak Malhotra, Advait Thakor¹, Pankaj Patel²

Abstract:
This is a report of four cases of possible suicidal ideation with the use of antidepressants in Indian population. The patients presented to emergency department of a tertiary care hospital with attempted suicide. All of them were prescribed at least one antidepressant. The association of increased suicidal attempts/ideation with antidepressant drugs themselves has been reported in the West, but data in the Indian population are lacking. Antidepressants are widely used not only for treatment of depression but also many other psychiatric illnesses; it is yet unclear whether suicidal ideation is because of these drugs or the progression of the disease. Hence, careful prescribing of these medicines is warranted.

Key words:
Antidepressant drugs, emergency department, treatment-emergent suicidal ideation/thought

Depression is a common disorder with an average national deficit of 77% for psychiatrists in India; depression comes in the 20 leading causes of disability according to WHO.¹ Unipolar depression makes a large contribution to the burden of disease, being at third place worldwide and eighth place in low-income countries.² The risk of suicidal ideation has been frequently reported among children and adults alike. There are various classes of antidepressants such as tricyclic antidepressant, selective serotonin reuptake inhibitors (SSRIs), and atypical serotonin-norepinephrine reuptake inhibitors (SNRIs). All the suicides/suicidal ideation reported with depression may be in part due to progression of depression per se or could be due to drugs used in depression improving the symptoms of depressive illness. The risk of suicidal ideation is more reported with SSRIs in comparison to other antidepressants in a study done in the UK in 2003. It concluded that paroxetine, citalopram, and other SSRIs were contraindicated in youths because of an increased risk of treatment-emergent suicidal ideation.

Case Reports

Case-1 (PVPI ID: 2015-36299)
A 19-year-old female patient was admitted with alleged history of ingestion of 10–15 tablets of venlafaxine, tablet escitalopram, and tablet clonazepam before approximately 6–7 h of admission. She had headache and giddiness on admission. Her vital parameters were heart rate (HR) - 82/min, respiratory rate (RR) - 24/min, blood pressure (BP) - 100/60 mmHg, and SpO₂ - 99% without oxygen support. Her random blood sugar was 68 mg% on admission. The patient was admitted to emergency department and treated with gastric lavage with normal saline, followed by charcoal powder, and supportive therapies were given. Fifty percent dextrose was given to treat hypoglycemia on the 1st day of admission. She had one more episode of hypoglycemia which was treated promptly. Detailed history taken from relatives revealed that she isolated herself from family members. For the last 2–3 days, she was not eating properly and not talking to anyone. She was recently diagnosed to have depressive disorder for 1 month and was on tablet venlafaxine sustained-release (37.5 mg) OD, tablet escitalopram OD, and tablet clonazepam OD. She recovered gradually without any uneventful outcome. Causality assessment as per the WHO-UMC scale suggested a possible association between the suspect drug and the adverse drug reaction.

Case-2 (PVPI ID: 2015-36298)
A 22-year-old female patient presented with alleged history of ingestion of unknown amount...
of amitriptyline 1 h before. She was admitted with chief complaints of giddiness and drowsiness. Her vitals were pulse - 122/min, RR - 34/min, and BP - 110/70 mmHg. Her arterial blood gas (ABG) was showing metabolic alkalosis (P - 7.483, pCO₂-19.4, pO₂-63, and SpO₂-99.3%). On examination, she was drowsy and not following verbal commands. She was intubated immediately to secure the airway, and general treatment started with gastric lavage, followed by charcoal powder instillation and forced alkaline diuresis. She regained consciousness in 1 day and was extubated on the 2nd day of admission. Her HR and ABG parameters normalized within 24 h. She was kept in the Intensive Care Unit for 3 days and then discharged having uneventful hospital course afterward. On detailed history, she told that she took ten tablets of amitriptyline for the purpose of getting sleep. She had history of multiple suicidal attempts 2–3 times in the last 1 year. She was on treatment for depression for the last 4–5 months and she was taking tablet paroxetine and amitriptyline since 4 months. During the hospital stay, her psychological evaluation was done. Causality assessment as per the WHO-UMC scale suggested a possible association between the suspect drug and the adverse drug reaction.

**Case-3 (PVPI ID: 2016-32991)**

A 19-year-old medical student presented with diaphoresis and palpitation after taking heavy dose of duloxetine (15 tablets each of 20 mg) prescribe for examination related anxiety and depression from private side. On admission, he was unstable, with HR - 110/min, RR - 38/min, BP - 110/70 mmHg, and SpO₂-85% on air. He was frothing from mouth and was immediately comatose. The patient was immediately intubated to secure the airway. Ryle’s tube insertion and gastric lavage were done. He became fully conscious in 2 days and was extubated. His hospital day of 6 days was uneventful. On detailed history, he was a known case of psychiatric illness and was admitted to private hospital for major depression recently. He had a history of suicidal attempts 2–3 times before he was on this antidepressant medication since 5 years. Causality assessment as per the WHO-UMC scale suggested a possible association between the suspect drug and the adverse drug reaction.

**Case-4 (PVPI ID: 2016-33006)**

A 21-year-old male patient presented to with alleged history of ingestion of some tablets of clomipramine. On admission, he was unstable, with HR - 110/min, RR - 38/min, BP - 110/70 mmHg, and SpO₂-85% on air. He was frothing from mouth and was immediately comatose. The patient was immediately intubated to secure the airway. Ryle’s tube insertion and gastric lavage were done. He became fully conscious in 2 days and was extubated. Her arterial blood gas (ABG) was showing metabolic acidosis with HR - 120/min, RR - 38/min, BP - 110/70 mmHg, pupils were dilated, temperature was 104°F, and electrocardiogram showed sinus tachycardia with QT prolongation. Patient was admitted, Ryle’s tube inserted, activated charcoal administered, and blood samples were drawn. Cold tepid sponging was carried out for hyperthermia. During this, the patient had an episode of generalized tonic-clonic seizures which was terminated by lorazepam. No antiepileptic was started. All other blood reports were normal except nonsignificant hyponatremia 126 mEq/L and creatine phosphokinase total being high. The patient showed dramatic improvement the next day, HR - 90 per min, BP - 128/90 mmHg, and was discharged thereafter, without further significant events. Causality assessment as per the WHO-UMC scale suggested a possible association between the suspect drug and the adverse drug reaction.

All four cases recovered and were stable vitally in 3–4 days of hospital courses they all were treated as general toxicology protocol and supportive therapy. All routine laboratory parameters were found to be within normal limits in all the four cases. As per protocol, urine of all patients for toxicological screen was sent, which was negative.

**Discussion**

Suicidal ideation is an uncommon symptom than can emerge during antidepressant treatment. In 2003, the UK Medicines and Healthcare Products Regulatory Agency concluded that paroxetine, citalopram, and other SSRIs were contraindicated in youths because of an increased risk of treatment-emergent suicidal ideation.[3] Treatment-emergent suicidal ideation and behavior are infrequent; the average incidence is 4% for antidepressants and 2% for placebo. The highest risk seems to be within a few weeks after initiation of treatment overdose adjustment.[4]

It is not clear whether treatment-emergent suicidal ideation leads to actual suicidal behavior in children or adults. Of the 4400 pediatric patients who participated in the clinical trials of SSRI analyzed by the Food and Drug Administration (FDA), no completed suicides were reported.[5]

The biological basis of treatment-emergent suicidal ideation is unknown. Genetic markers may shed light on the causes of treatment-emergent suicidal ideation and help identify individuals at high risk who may benefit from closer monitoring, alternative treatments, or specialty care.[6]

This case series points to the fact that there is a suicide risk during antidepressant treatment. This can be substantiated by the fact that in March 2004, the US FDA warned physician and patient regarding increase risk of suicide with ten newer antidepressants (bupropion, citalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone, paroxetine, sertraline, escitalopram, and venlafaxine), especially in pediatrics, adolescents, and adults.[7]

In our case series, suicidal ideation/suicidal attempt was observed with escitalopram and venlafaxine; suicide risk is higher in the initial days of starting treatment. In our case series, two patients developed this risk in the 1st week of therapy and two developed subsequently. Another literature pointing toward the association between SSRI antidepressant and suicide points out the facts that during initial therapy that risk of suicide may increase as some aspects of depression resolved (psychomotor retardation), thereby energizing the patient to suicide.[8] One of the plausible mechanisms with the SSRI (paroxetine) was associated with increased risk of treatment-emergent mania or hypomania which could be related to risk of suicidality.[9] A study identified markers which reside within the gene GRIA3 and GRAIK2 both of which encode ion tropic glutamic receptor and involved in glutamate signaling pathway.[10] These findings are preliminary and require several thousand patients who may need to be studied before conclusive findings are obtained.

In the past decade, there has been increase in the use of drugs in the class of SNRIs and SSRIs.
There are not only indicated for depression but also a variety of others psychiatric disorders (anxiety disorders, obsessive-compulsive disorder). They are also now used off-label in chronic fatigue syndrome, attention deficit hyperactivity disorder, and autism. This would necessitate more care full prescribing by the physicians as these drugs are strongly associated with suicide.

The association of antidepressant use with suicide is circumstantial since no rigorous clinical trials have been performed on depressed patient to confirm the association. Moreover, it is difficult to study suicide attempts suicidal ideation or suicide completion even in well-planned, randomized controlled trials. To the best of our knowledge, no such case reports or case series have been reported for Indian population. Hence, this case report points to the occurrence of treatment-emergent suicide attempt/suicide with antidepressants.

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Conflicts of Interest
There are no conflicts of interest.

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