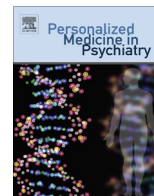




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Withdrawal symptoms after discontinuation of a noradrenergic and specific serotonergic antidepressant: A case report and review of the literature

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ABSTRACT

Although the phenomenon of withdrawal symptoms is well known for some psychotropic drugs, including serotonin selective reuptake inhibitors and serotonin-noradrenaline reuptake inhibitors, reports of withdrawal symptoms following the discontinuation of a noradrenergic and specific serotonergic antidepressant are limited. A case of a female patient who experienced rebound withdrawal after tapering and discontinuing (30 mg) mirtazapine is herein described. The present clinical case supports a growing literature suggesting that withdrawal symptoms might occur after the discontinuation of antidepressants. It highlights the importance of diagnosing withdrawal due to the discontinuation of a noradrenergic and specific serotonergic antidepressant and suggests that such a withdrawal might be treated with a different strategy than reintroducing the drug previously discontinued.

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Introduction

The phenomenon of withdrawal symptoms is well known for some CNS drugs, including serotonin selective reuptake inhibitors (SSRIs) and serotonin-noradrenaline reuptake inhibitors (SNRIs) [1] and a new classification of SSRI withdrawal has been formulated [2]. Withdrawal from CNS drugs produces psychiatric symptoms that can be confounded with relapses or recurrences of the original illness [1]. Thus, when withdrawal occurs, it must be identified to avoid prolonging treatments or giving unnecessary high pharmacological doses [3].

Only few papers (only case reports) referred to withdrawal symptoms induced by the discontinuation of antidepressants different from SSRIs and SNRIs. In 1989, withdrawal symptoms that occurred after the discontinuation of a noradrenergic and specific serotonergic antidepressant (NaSSA) were for the first time documented after abrupt discontinuation of mianserin [4]. Later on, 5 case reports described withdrawal symptoms after abrupt discontinuation of mirtazapine [5–9] and 1 case report referred to withdrawal after tapering and discontinuing mirtazapine [10].

A case is presented herein of a patient who experienced rebound withdrawal after tapering and discontinuing (30 mg) mirtazapine.

Case report

X is a 32-year-old married woman who reported no family history for psychiatric disorders and a past personal history of separation anxiety. At 23 years of age, she had a major depressive episode treated with sertraline and recovered in about 8 months, sertraline was discontinued but no information was available on withdrawal symptoms. At 30 years of age, she had a novel major depressive episode treated with a psychodynamic intervention with no pharmacological intervention. After 6 months of therapy, X. withdrew feeling worse due to the occurrence of panic attacks and avoidance. The patient asked for a pharmacological help and in 2 years followed several pharmacotherapies (i.e., alprazolam, haloperidol, quetiapine, venlafaxine, fluvoxamine, citalopram, escitalopram, mirtazapine, valproic acid) without benefits. At first visit, X. was under valproic acid (1000 mg/day), sertraline (75 mg/day), mirtazapine, (30 mg/day), lorazepam (1 mg/day) from 6 months. The patient mainly complained about diurnal panic attacks; nightmares (mean: 1 per week); depressed mood; muscular stiffening, numbness, leg burn. She also was really disappointed to have

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Table 1
Review of reported cases of withdrawal symptoms following the discontinuation of a noradrenergic and specific serotonergic antidepressant.

Authors/year	Age/gender	Medication/daily dose	Diagnosis	Duration of treatment with NaSSA	Tapering (yes/no)	Event	Time to event	Management (medication/daily dose)	Time to resolution	Personal history of psychiatric disorders	Family history of psychiatric disorders
Kuniyoshi et al. [4]	41-year-old woman	Mianserin 30 mg, etizolam 1 mg, flunitrazepam 1 mg	Depression	Not specified	No	Panic anxiety	Not specified	Mianserin 30 mg	Not specified	Depression	Not specified
Benazzi [5]	28-year-old man	Mirtazapine 60 mg, clomipramine 150 mg, nortriptyline 100 mg, and alprazolam 0.25 mg	Chronic major depressive disorder	4 weeks	No	Dizziness, nausea, anxiety, insomnia, paresthesia	24 h	Mirtazapine 60 mg	24 h	Not specified	Not specified
MacCall and Callender [6]	75-year-old woman	Mirtazapine 30 mg	Depressed mood, suicidal ideation, disrupted sleep pattern, poor concentration, anhedonia, lack of motivation	5 weeks	No	Hypomania	48 h	No therapy	6 weeks	Recurrent anxiety and depressive episodes, 1 hypomanic episode	Not specified
Klesmer, Sarcevic, Fomari [7]	51-year-old man	Mirtazapine 15 mg	Depression	Several years	No	Panic attacks	4 days	Mirtazapine 15 mg	24 h	Dysthymia, substance abuse	Not specified
Berigan [8]	25-year-old woman	Mirtazapine 60 mg, clonazepam 1 mg	Major depressive episode, panic disorder without agoraphobia	Not specified	No	Anxiety, restlessness, irritability, nausea, vomiting, insomnia	48 h	Mirtazapine 60 mg	24 h	Not specified	Not specified
Fauchère [9]	53-year-old woman	Mirtazapine 30 mg	Adjustment disorder with depressive reaction	10 weeks	No	Panic attacks	48 h	Mirtazapine 30 mg	Not specified	Not specified	Not specified
Verma and Mohapatra [10]	54-year-old man	Mirtazapine 15 mg, lithium carbonate 800 mg	Bipolar disorder	24 weeks	Yes	Over talkativeness, grandiose talks, irritability, poor boundaries, decreased sleep, increased physical activity	7 days	Olanzapine 10 mg		5 manic episodes, 3 depressive episodes	Negative history

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