ELSEVIER

Journal of Affective Disorders 86 (2005) 277–280

JOURNAL OF AFFECTIVE DISORDERS

www.elsevier.com/locate/jad

Brief report

Agitated dysphoria after late-onset loss of response to antidepressants: A case report

James R. Phelps,*[,1]

Received 3 November 2004; accepted 11 February 2005

Abstract

Background: Antidepressants can sometimes cause agitation, particularly in patients with bipolar disorder, but concern about such effects is generally limited to the first weeks and months of treatment.
Method: Demonstration of the occurrence of agitated dysphoria after loss of response to an antidepressant following continuous administration through 7 years of euthymia; with a worsening on dose increase; and recurrence of agitation on re-exposure 1 year later; in a patient whose previous dysthymia and recurrent depressions had no recognizable manic or hypomanic features.
Results: Only when the antidepressant was removed, twice, was treatment an atypical antipsychotic and lithium effective.
Conclusion: An antidepressant which has been effective for as long as 7 years may still carry risk of inducing agitated dysphoria, even in apparently unipolar depression. In some patients, clinical vigilance for antidepressant-induced dysphoria may be warranted for extended periods of time.

Keywords: Antidepressants; Agitation; Loss of response; Unipolar; Bipolar; Suicidal

1. Introduction

Antidepressants are recognized to cause "switching" from depression to hypomanic or manic symptoms, though there is substantial debate about how often this occurs, with recent estimates ranging from 2–4% in a meta-analysis of 3 (sic) randomized trials (Gijsman et al., 2004) to 20–40% in a review of multiple data sources (Goldberg and Truman, 2003).

A separate concern that antidepressants may have a "destabilizing effect" (Ghaemi et al., 2003), including increased cycle rates during antidepressant exposure (Wehr et al., 1988; Ghaemi et al., 2004) implies that antidepressants can worsen the course of bipolar disorder while they are being administered.

Such adverse reactions most commonly appear within days to weeks of initiating antidepressant treatment, in patients with overt or occult bipolar disorder. But how long should one monitor for adverse reactions to antidepressants, particularly in apparently unipolar patients who may be on these medications for

* Samaritan Professional Building, 3517 Samaritan Dr., Corvallis, 97330 OR, United States. Tel.: +1 541 829 9319; fax: +1 541 768 6560.
E-mail address: jp@co-psych.com.
[1] Private Practice of Psychiatry, Co-Psych.com, Corvallis, OR; and PsychEducation.org, Corvallis, OR.

0165-0327/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2005.02.005

extended periods? If lasting adverse effects took years to develop, typical clinical trials would be much too brief for such an effect to appear. The earliest indication would be suggestive patient experiences. The following case may represent such a warning. Note that for years prior to and during antidepressant treatment, there was no evidence of hypomania or mania.

2. Presenting circumstances

A 61-year-old woman was referred in May 2003 for panic attacks. She gave a clear history, corroborated by her daughter, of recurrent severe depressions, during which she would have decreased energy, motivation, and activity; with increased hopelessness and total sleep time. When not in one of these depressions, described as 0–1 on her subjective 0–10 scale, her mood was dysthymic (3 on her scale). No history of mania or hypomania could be found with a detailed search using broad diagnostic criteria (Akiskal, 1996).

Neither the recurrent depressions nor the dysthymia responded to trials of a tricyclic antidepressant (circa 1980), nor to paroxetine or fluoxetine, which were given in 1994. However, a subsequent trial of sertraline produced a gradual but obvious improvement over several weeks. She felt "normal" in mood and energy for the first time in her life, and remained in this mood state for the next 7 years. This response was also corroborated by her daughter, who confirmed the absence of euphoria, pressured speech, poor judgement or any other features to suggest hypomania. No cyclic changes in mood or sleep during this period were recalled.

In 2002 she began having gradual-onset episodes of severe anxiety and dread, lasting for hours. These were not accompanied by shortness of breath or dizziness, increased heart rate or pounding, or other typical panic symptoms. Sertraline was increased to 150 mg by her gynecologist shortly before referral in an attempt to address these symptoms.

3. Initial evaluation

She presented with intense agitation. Her legs were moving constantly through the interview. She denied suicidal ideation, though in the past this had been present periodically. Her affect was blunted and mood was depressed. The remainder of her mental status exam was unremarkable.

A multigenerational family history of mood disturbance was elicited, including a sister who had been treated with ECT and a son who "goes through highs and lows". None had a diagnosis of bipolar disorder.

Past medical history included a diagnosis of benign essential tremor, treated with propranolol; and a history of treatment with equine estrogens without progesterone at age 46 for "hot flashes", with subsequent hysterectomy in 2001 (for fibroid tumor). At the time of referral she was taking transdermal progesterone and soy estrogen for "hot flashes" which started about 1 month prior, as well as 150 mg of Zoloft and 2 mg of clonazepam.

She consumed alcohol only about three times a year and did not have a prior history of alcohol or other drug use. She had been sexually abused by her father for 8 years in her youth, she reported, but had received psychotherapy for this which she found "cleansing" and she did not regard this as an ongoing problem thereafter.

4. Treatment course

Sertraline was tapered over several months while rapid trials of risperidone, valproate, lithium and olanzapine were conducted due to lack of or partial response. She began to have significant suicidal ideation during this time. Only daily monitoring by family avoided hospitalization several times in this process.

Escitalopram and oral estrogen were started and within 8 days she reported "feeling normal again for the first time in months." However, within 2 weeks she began to feel the same agitation with which she had presented. Lamotrigine was added as the antidepressant was tapered, but caused a blister on her face and was stopped. Quietiapine was tolerable and at 400 mg produced a sustained remission of anxiety, 4.5 months after referral.

Two months later she remained stable, though still experiencing some depression. The severity of her previous symptoms had forced her to take early retirement. She was referred to a therapist, as an