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**Literature search results**

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**Search details**

Patients suffering withdrawal symptoms from antidepressants – generally, with SSRIs in particular.

**Resources searched**

NHS Evidence; TRIP Database; Cochrane Library; AMED; BNI; CINAHL; EMBASE; HMIC; Health Business Elite; MEDLINE; PsychINFO; Google Scholar; Google Advanced Search

**Database search terms:**

**Evidence search string(s):**

**Google search string(s):**

**Summary**

The initial search identified a very large number of articles available on withdrawal symptoms and antidepressants – 171 altogether. Reduced to items from 2000 onwards ND IN English reduced the number to 76.

SSRIs and withdrawal symptoms returns 35 items of which these 19 are the more general ones.

TRIP data base list 1419 items when using the search terms “Withdrawal symptoms and antidepressants”. The first 100 items did not bring up anything general – all deal with specific drug or disorder.

**Guidelines and Policy**
Evidence-based reviews

http://onlinelibrary.wiley.com/cochranelibrary/search There are 13 reviews dealing with withdrawal symptoms and specific drugs and/or conditions. There are no generic reviews on withdrawal symptoms for antidepressants.

Published research – Databases

1. Anxiolytics and sedatives.
Citation: Drug abuse and addiction in medical illness: Causes, consequences and treatment., 2012(231-239) (2012)
Author(s): Bond, Alyson; Lader, Malcolm
Abstract: (from the chapter) Benzodiazepines are classified as anxiolytics or hypnotics, but the term "sedative" describes a group of drugs, including barbiturates and tricyclic antidepressants as well as benzodiazepines, which are abused. These drugs have different pharmacokinetic characteristics. Patients prescribed benzodiazepines seldom escalate their doses, and primary benzodiazepine abuse is rare. However, secondary abuse of all sedative drugs is common, and high doses are frequently consumed by patients dependent on opiates or alcohol to enhance the effects and by stimulant users to alleviate offset effects after a binge. Benzodiazepines cause dependence on prescribed doses with a clear withdrawal syndrome lasting a few weeks evident in 20-30% patients. The consumption of high doses can result in more severe withdrawal symptoms. Benzodiazepines should never be withdrawn abruptly because of the risk of fits or paranoid psychosis. A stepped care approach to reduction is recommended. All sedative drugs have characteristic pharmacodynamic effects, causing sedation, psychomotor slowing and memory impairment. They increase the risk of accidents and injuries and contribute to specific drug-related harms in abusers. Tolerance develops to some effects but long-term users are impaired compared with non-users. However, gradually stopping the drugs, even after several years of use, results in improvement in functioning, and there is no evidence of lasting impairment or cognitive decline. Newer anxiolytics and SSRIs appear to cause less impairment and have lower abuse potential. (PsycINFO Database Record (c) 2013 APA, all rights reserved)
Publication Type: Book; Edited Book
Source: PsycINFO

2. Venlafaxine withdrawal syndrome.
Citation: Psychiatry Danubina, 2011, vol./is. 23/1(117-119), 0353-5053 (2011)
Author(s): Sabljic, Vladimir; Ruzic, Klementina; Rakun, Radmir
Abstract: Dual-action antidepressants serotonin-norepinephrine reuptake inhibitors (SRNIs) are widely used to treat depression. Owing its efficiency and safety, venlafaxine holds a prominent place in this group of depressants. Abrupt venlafaxine discontinuation involves a high risk of withdrawal syndrome. Mechanism of its development is similar to that of selective serotonin reuptake inhibitors (SSRIs), but of higher intensity. Venlafaxine withdrawal symptoms may include several somatic symptoms as well as several psychiatric symptoms. In some cases, symptoms may look like a stroke. A treatment option is re-inclusion of venlafaxine or SSRI antidepressant The paper presents the case of a 70-year-old patient who discontinued of her own accord to take venlafaxine, which she had been taking regularly at a daily dose of 225 mg for more than a year. A few hours after taking the last dose, withdrawal syndrome occurred with severe symptoms resembling a stroke. The patient was examined by a neurologist and the CT and laboratory parameters showed no irregularities. Diagnosis was made after psychiatric observation. Venlafaxine, 150 mg per day, was prescribed, the symptoms disappeared relatively quickly, and the patient fully recovered. Withdrawal syndrome is a real risk for each venlafaxine treated patient: The possibility of its occurrence should be always kept
in mind and patients should be timely informed about it. In this way, the risk of venlafaxine withdraw syndrome could be reduced, unnecessary stress to patients prevented and the costs of medical treatment lowered. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

### 3. A qualitative study of patient views on discontinuing long-term selective serotonin reuptake inhibitors.

**Citation:** Family Practice, December 2007, vol./is. 24/6(570-575), 0263-2136;1460-2229 (Dec 2007)  
**Author(s):** Leydon, Geraldine M; Rodgers, Lynne; Kendrick, Tony  
**Abstract:** Background: There is concern that patients may be remaining on selective serotonin reuptake inhibitors (SSRIs) longer than is clinically indicated. Previous research has explored patients' experiences of taking SSRIs and decisions about starting medication. There has been less research into patients' reasons for long-term use and their views and experiences of discontinuation. Aim: To explore patient experiences of and beliefs about their long-standing SSRI use and understand the barriers and facilitators to discontinuation. Design: Face-to-face semi-structured qualitative interview study. Setting: One group general practice in Southampton, UK. Findings: Three overarching themes were identified: (i) patient uncertainty about the benefits of, and continued need for, SSRI medication; (ii) barriers to stopping, including fear of withdrawal symptoms and fear of relapse; and (iii) the importance of the GP's role in facilitating cessation. Uncertainty and fear about withdrawal symptoms and what patients would be like without their medication were key barriers to stopping, even among patients who felt no discernible benefit from taking SSRIs. Patients indicated a need to share the decision to stop with their GP. However, the majority of patients interviewed had received repeat prescriptions of SSRIs without being reviewed by the GP. Conclusions: Patients prescribed SSRI medication need to be reassured that, as with starting medication, thinking about or actually stopping medication is a task that will not be managed in isolation, but with the support of their GP. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

**Full Text:** Available from Highwire Press in Family Practice

### 4. Why does milnacipran produce so few discontinuation syndromes following abrupt withdrawal?

**Citation:** Neuropsychiatric Disease and Treatment, 2007, vol./is. 3/1(181-182), 1176-6328 (2007)  
**Author(s):** Okada, Fumihiko  
**Abstract:** In the author's clinic, a discontinuation syndrome has sometimes been seen when selective serotonin reuptake inhibitors (SSRIs) or serotonin and noradrenaline reuptake inhibitors (SNRIs) are discontinued suddenly, or when doses are missed or forgotten. In a total cohort of 2,675 depressed patients, 124 cases of antidepressant withdrawal syndrome were identified. Sixty-three of the cases resulted from withdrawal from fluvoxamine (from 1,306 treated patients), 124 cases of antidepressant withdrawal syndrome were identified. Sixty-three of the cases resulted from withdrawal from fluvoxamine (from 1,306 treated patients), 55 were withdrawn from paroxetine (from 453 treated patients), while 6 were withdrawn from milnacipran (from 916 treated patients). With paroxetine and fluvoxamine, respectively, the incidence of discontinuation syndrome was 18.4 times greater and 7.3 times greater than that found with milnacipran. These differences were highly significant. Factors noted include the role of pharmacokinetics and the possible effect of milnacipran's dual action. It is possible that the balance between serotonergic and noradrenergic neurotransmission may be essential in determining the nature and extent of withdrawal-related symptoms. Further preclinical and clinical studies are required to test this hypothesis. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

**Full Text:** Available from National Library of Medicine in Neuropsychiatric Disease and Treatment

### 5. Mania in a case of polypsychopharmacology: pharmacodynamic and pharmacokinetic considerations. Do you believe in magic?

**Citation:** Journal of Psychiatric Practice, May 2007, vol./is. 13/3(178-183), 1527-
Abstract: Case Example: This case involved a 17-year-old female whose parents had divorced when she was 3 years old. In the fall of her junior year of high school, she became distressed after breaking up with her first boyfriend. The psychiatrist who first saw the patient immediately hospitalized her and started her on the selective serotonin reuptake inhibitor (SSRI) paroxetine. Nevertheless, the safety and tolerability profile of SSRIs such as paroxetine is such that a significant percentage of clinicians, perhaps even the majority, might agree with the decision to immediately initiate an empirical trial. SSRIs as a class have a flat dose-response curve, meaning that, on average, there is no advantage to raising the dose above the usually effective dose in most, but not all, patients. This patient did not receive an adequate trial of the usually effective dose of paroxetine, 20 mg/day. She was on this dose only 6 days before it was escalated to 30 mg/day. Within 2 weeks of starting this drug, she was on 60 mg/day, which is above the maximum recommended dose in adults. This patient was kept on 60 mg/day for 3 weeks and then the dose was escalated to 80 mg/day. Interpretation of this patient's trial of paroxetine is further complicated by the rapid addition and subsequent periodic dose escalation of buspirone, another serotonin active medication. In this case, the patient almost undoubtedly had substantial serotonin uptake inhibition to which was added the effects of buspirone and 1-PP on both 5-HT1a and alpha-2 adrenergic receptors. Withdrawal can cause a number of symptoms that can mimic a worsening of the patient's psychiatric status. This case illustrates the complex considerations that must be kept in mind when resorting to the use of multiple medications. It also illustrates the long commitment that such a treatment strategy requires. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

Publication Type: Journal; Peer Reviewed Journal

Source: PsycINFO


Citation: International Clinical Psychopharmacology, May 2006, vol./is. 21/3(131-142), 0268-1315;1473-5857 (May 2006)

Author(s): Nardi, Antonio E; Perna, Giampaolo

Abstract: An updated overview over the past decade is provided with respect to the use of clonazepam in a variety of psychiatric disorders. The efficacy of clonazepam monotherapy for the short-term treatment of panic disorder (PD) was fully established in two large pivotal multicentre studies in the late 1990s in a total of >800 patients. Other studies support a role for clonazepam, in association with selective serotonin reuptake inhibitors (SSRIs), to accelerate treatment response in PD. Although some longitudinal data suggest an ability to maintain improvement without tolerance for up to 3 years, long-term controlled studies of clonazepam in PD are lacking. Studies have shown that clonazepam can also block CO2-induced panic and improve certain aspects of quality of life in PD. Clonazepam has shown some efficacy in social phobia; however, because this evidence is based on few studies, further studies are warranted before definitive conclusions can be drawn. Finally, evidence for the use of clonazepam in acute mania and as augmentation therapy with SSRIs to accelerate response in depression is examined. The long half-life and higher potency of clonazepam may allow easier discontinuation with fewer withdrawal symptoms compared to other benzodiazepines and studies using a slow clonazepam taper appear promising. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

Publication Type: Journal; Peer Reviewed Journal

Source: PsycINFO

7. Spontaneous ecchymoses developed on a patient under medication of paroxetine for panic disorder, even though her platelet count and bleeding time were normal.

Citation: Seishin Igaku (Clinical Psychiatry), April 2006, vol./is. 48/4(425-429), 0488-1281 (Apr 2006)

Author(s): Nakashima, Sumihiro

Language: Japanese  I have included this for information in the abstract!

Abstract: A 30-year-old woman diagnosed as panic disorder and who was under medication of paroxetine 30mg/day developed ecchymoses on her four extremities, but the investigations showed that her platelet-count and bleeding time were normal. By decreasing the dose of paroxetine her ecchymoses gradually diminished, but withdrawal symptoms, headache and hypersensitivity developed, which made it difficult to deal with the bleeding event. This is the first Japanese case report of bleeding with normal platelet count and normal bleeding time under medication of paroxetine. The patient had not
noticed the event was due to paroxetine and continued to take it as had other patients described in some of the reports on this phenomenon. Practitioners should give an explanation of the bleeding side-effect of this selective serotonin reuptake inhibitor (SSRI) to patients for whom they prescribe paroxetine. Withdrawal symptoms of SSRI make it difficult to deal with the bleeding. The process of the bleeding events caused by SSRIs may be related to the fact that they inhibit ADP-induced platelet aggregation, and/or to capillary fragility. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal

**Source:** PsycINFO

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8. **Withdrawal of Selective Serotonin Reuptake Inhibitors (SSRIs) May Cause Increased Atrial Natriuretic Peptide (ANP) and Persistent Sexual Arousal in Women?**

**Citation:** Journal of Sexual Medicine, March 2006, vol./is. 3/2(376), 1743-6095;1743-6109 (Mar 2006)

**Author(s):** Goldmeier, David; Bell, Charlotte; Richardson, Daniel

**Abstract:** Comments on an article by Linda Freed (see record 2005-09660-016). The author notes that a sizeable number of women in her chat room sample had been on selective serotonin reuptake inhibitors (SSRIs). Here we would like to put forward a theory of how this might occur. In her case we suggested that raised atrial natriuretic peptide (ANP) might be the cause of at least some of her symptoms. When patients discontinue SSRIs they may develop a well-documented withdrawal syndrome. However, this withdrawal syndrome may be both severe and chronic and in some cases last for at least 18 months. We hypothesize that some women who have been on SSRIs in the past produce high levels of ANP. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

**Publication Type:** Journal; Peer Reviewed Journal

**Source:** PsycINFO

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9. **A review on hyponatremia associated with SSRIs, reboxetine and venlafaxine.**

**Citation:** International Journal of Psychiatry in Clinical Practice, March 2006, vol./is. 10/1(17-26), 1365-1501;1471-1788 (Mar 2006)

**Author(s):** Egger, C; Muehlbacher, M; Nickel, M; Geretsegger, C; Stuppaec, C

**Abstract:** Hyponatremia, defined as serum sodium below 135 mmol/l, is a potentially life-threatening condition and was shown to be more frequent in elderly and psychiatric patients. In the last years numerous case reports on SSRI- and venlafaxine-induced hyponatremia were published indicating a higher incidence than previously thought. Only few studies have been performed and the incidence reported varies widely from 4.6/1000 people to 25%. It is still unclear if any single SSRI shows a higher incidence of hyponatremia than the others. Some data suggest that venlafaxine may have a stronger association to hyponatremia than SSRIs. Risk factors include age, female sex, low body mass index, severe physical illness, history of former hyponatremia and co-medications known to induce hyponatremia, especially thiazide diuretics. Symptoms of hyponatremia are usually neuropsychiatric (e.g. restlessness, lethargy, cognitive impairment), and any worsening in psychiatric symptoms in patients with a corresponding risk-profile receiving SSRIs or venlafaxine should give cause to check serum electrolytes. Usually SSRi-induced hyponatremia occurs within approximately 30 days and is reported to improve after withdrawal of the drug. Further controlled studies to confirm the true incidence of hyponatremia due to SSRI or venlafaxine and to define predictors more precisely are needed. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal

**Source:** PsycINFO

**Full Text:** Available from EBSCOhost in International Journal of Psychiatry in Clinical Practice

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10. **Clinical Pharmacology, Clinical Efficacy, and Behavioral Toxicity of Alprazolam: A Review of the Literature.**

**Citation:** CNS Drug Reviews, 2004, vol./is. 10/1(45-76), 1080-563X;1527-3458 (Spr, 2004)

**Author(s):** Verster, Joris C; Volkerts, Edmund R

**Abstract:** Alprazolam is a benzodiazepine derivative that is currently used in the treatment of generalized anxiety, panic attacks with or without agoraphobia, and depression. Alprazolam has a fast onset of symptom relief (within the first week); it is unlikely to
produce dependency or abuse. No tolerance to its therapeutic effect has been reported. At discontinuation of alprazolam treatment, withdrawal and rebound symptoms are common. Hence, alprazolam discontinuation must be tapered. An exhaustive review of the literature showed that alprazolam is significantly superior to placebo, and is at least equally effective in the relief of symptoms as tricyclic antidepressants (TCAs), such as imipramine. However, although alprazolam and imipramine are significantly more effective than placebo in the treatment of panic attacks, Selective Serotonin Reuptake Inhibitors (SSRIs) appear to be superior to either of the two drugs. Therefore, alprazolam is recommended as a second line treatment option, when SSRIs are not effective or well tolerated. In addition to its therapeutic effects, alprazolam produces adverse effects, such as drowsiness and sedation. Since alprazolam is widely used, many clinical studies investigated its cognitive and psychomotor effects. It is evident from these studies that alprazolam may impair performance in a variety of skills in healthy volunteers as well as in patients. Since the majority of alprazolam users are outpatients, this behavioral impairment limits the safe use of alprazolam in patients routinely engaged in potentially dangerous daily activities, such as driving a car. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal
**Source:** PsycINFO

11. **SSRIs and Intraocular Pressure Modifications: Evidence, Therapeutic Implications and Possible Mechanisms.**

**Citation:** CNS Drugs, 2004, vol./is. 18/8(475-484), 1172-7047;1179-1934 (2004)

**Author(s):** Costagliola, Ciro; Parmeggiani, Francesco; Sebastiani, Adolfo

**Abstract:** SSRIs are the most commonly prescribed antidepressant drugs, in part because of their favourable safety profile compared with older antidepressants. However, the widespread use of SSRIs leads to an increased occurrence of rare adverse effects. This review, based on data from published experimental research, clinical studies and case reports, describes the role of serotonin in the control of intraocular pressure (IOP) and the evidence for IOP modifications in patients receiving SSRIs. In a small percentage of patients with depression, the cause of SSRI withdrawal has been the occurrence of ill-defined visual disturbances. It can be speculated that in some of these patients, the iatrogenic ocular alterations could have been due to changes in IOP. There have also been a limited number of case reports of acute attacks of glaucoma occurring during treatment with SSRIs. Although causality is not exactly specified, the relationship between SSRIs and this ocular adverse event is strongly implied. Nevertheless, in a small clinical study assessing the effect of a single dose of fluoxetine on IOP, the drug was shown to increase this parameter, although the effect was asymptomatic. The clinical signs of unexpected adverse drug effects are often disregarded, with the exception of those characterised by serious symptoms (such as acute angle-closure glaucoma in the case of IOP modifications). Also, the distribution of iridocorneal angle configurations in the general population implies that an adverse effect on IOP will be paucior asymptomatic in most patients (intermittent, sub-acute or progressive angle-closure glaucoma). As a result, it is likely that the incidence of SSRI-related IOP modifications is underestimated. Until the involvement of SSRIs in IOP modifications is better understood, ophthalmological consultations should be considered before starting and during treatment with any SSRI in patients with glaucomatous risk factors, especially those who are elderly. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal
**Source:** PsycINFO

**Full Text:** Available from EBSCOhost in CNS Drugs
Available from EBSCOhost in CNS Drugs

12. **WCA recommendations for the long-term treatment of generalized anxiety disorder.**

**Citation:** CNS Spectrums, August 2003, vol./is. 8/8(Supp1(53-61), 1092-8529 (Aug 2003)

**Author(s):** Allgulander, Christer; Bandelow, Borwin; Hollander, Eric; Montgomery, Stuart A; Nutt, David J; Okasha, Ahmed; Pollack, Mark H; Stein, Dan J; Swinson, Richard P

**Abstract:** What are the current recommendations for the long-term treatment of generalized anxiety disorder (GAD)? GAD is a common disorder with a lifetime prevalence of 4% to 7% in the general population. GAD is characterized by excessive, uncontrollable worry or anxiety about a number of events or activities that the individual experiences on more days than not over a 6-month period. Onset of GAD symptoms usually occurs during an individual's early twenties; however, high rates of GAD have also been seen in children
and adolescents. The clinical course of GAD is often chronic, with 40% of patients reporting illness lasting >5 years. GAD is associated with pronounced functional impairment, resulting in decreased vocational function and reduced quality of life. Patients with GAD tend to be high users of outpatient medical care, which contributes significantly to healthcare costs. Currently, benzodiazepines and buspirone are prescribed frequently to treat GAD. Although both show efficacy in acute treatment trials, few long-term studies have been performed. Benzodiazepines are not recommended for long-term treatment of GAD, due to associated development of tolerance, psychomotor impairment, cognitive and memory changes, physical dependence, and a withdrawal reaction on discontinuation. The antidepressant venlafaxine extended-release (XR) has received approval for the treatment of GAD in the United States and many other countries. Venlafaxine XR has demonstrated efficacy over placebo in two randomized treatment trials of 6 months' duration as well as in other acute trials. Paroxetine is the first of the selective serotonin reuptake inhibitors (SSRIs) to receive US approval for the treatment of GAD. Paroxetine demonstrated superiority to placebo in short-term trials, and investigations into the use of other SSRIs are ongoing. This suggests that other SSRIs, and serotonin and noradrenaline reuptake inhibitors, are likely to be effective in the treatment of GAD. Of the psychological therapies, cognitive-behavioral therapy (CBT) shows the greatest benefit in treating GAD patients. Treatment gains after a 12-week course of CBT may be maintained for up to 1 year. Currently, no guidelines exist for the long-term treatment of GAD. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO

Citation: CNS Spectrums, August 2003, vol./is. 8/8,Sufl4(7-16), 1092-8529 (Aug 2003)
Author(s): Greist, John H; Bandelow, Borwin; Hollander, Eric; Marazziti, Donatella; Montgomery, Stuart A; Nutt, David J; Okasha, Ahmed; Swinson, Richard P; Zohar, Joseph
Abstract: What are the latest psychotherapeutic and pharmacotherapeutic treatment recommendations for obsessive-compulsive disorder (OCD)? OCD is a relatively common disorder with a lifetime prevalence of ~2% in the general population. It often has an early onset, usually in childhood or adolescence, and frequently becomes chronic and disabling if left untreated. High associated healthcare utilization and costs, and reduced productivity resulting in loss of earning, pose a huge economic burden to OCD patients and their families, employers, and society. OCD is characterized by the presence of obsessions and compulsions that are time-consuming, cause marked distress, or significantly interfere with a person's functioning. Most patients with OCD experience symptoms throughout their lives and benefit from long-term treatment. Both psychotherapy and pharmacotherapy are recommended, either alone or in combination, for the treatment of OCD. Cognitive-behavioral therapy is the psychotherapy of choice. Pharmacologic treatment options include the tricyclic antidepressant clomipramine and the selective serotonin reuptake inhibitors (SSRIs) citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline. These have all shown benefit in acute treatment trials; clomipramine, fluvoxamine, fluoxetine, and sertraline have also demonstrated benefit in long-term treatment trials (at least 24 weeks), and clomipramine, sertraline, and fluvoxamine have United States Food and Drug Administration approvals for use in children and adolescents. Available treatment guidelines recommend first-line use of an SSRI (ie, fluoxetine, fluvoxamine, paroxetine, sertraline, or citalopram) in preference to clomipramine, due to the latter's less favorable adverse-event profile. Further, pharmacotherapy for a minimum of 1-2 years is recommended before very gradual withdrawal may be considered. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)
Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO

Citation: Journal of Clinical Psychiatry, 2002, vol./is. 63/Sufl4(9-16), 0160-6689 (2002)
Author(s): Rickels, Karl; Rynn, Moira
Abstract: Discusses pharmacological options in the treatment of generalized anxiety disorder (GAD) as well as treatment algorithms. The medications with the most evidence of efficacy in GAD are the benzodiazepines (BDs). BDs have a low incidence of side effects.
but may cause physical dependence, withdrawal, and sedation. Antidepressant drugs (ADs) are also efficacious in GAD but act less quickly than BDs. Tricyclic ADs may substantially reduce symptoms of anxiety but are not considered a first-line therapy because of their side effects. The extended-release formulation of venlafaxine and selective serotonin reuptake inhibitors (SSRIs) are also efficacious. While their association with sexual dysfunction may be intolerable for some adults, these drugs may be more appropriate than the BDs because their chronic use does not lead to dependence. Buspiron e also significantly reduces symptoms of GAD and is associated with less sexual dysfunction than SSRIs and less sedation than BDs. Combining AD and BD treatment and psychotherapy may lead to an increase in improvement in patients not responding to 1 treatment approach alone. The most effective treatment for managing the recurrent symptoms of GAD will remain unknown until more long-term studies using both drug and nondrug therapies are conducted. (PsycINFO Database Record (c) 2013 APA, all rights reserved)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

15. **Hyponatraemia and selective serotonin re-uptake inhibitors in elderly patients.**  
**Citation:** International Journal of Geriatric Psychiatry, May 2001, vol./is. 16/5(484-493), 0885-6230;1099-1166 (May 2001)  
**Author(s):** Kirby, Dianne; Ames, David  
**Abstract:** Hyponatraemia is an increasingly recognised adverse effect of selective serotonin re-uptake inhibitors (SSRIs). Its precise prevalence and incidence in the elderly are hard to determine because of confounding factors including other medications and medical conditions. Although hyponatraemia has been reported with all SSRIs and venlafaxine, most studies are small, retrospective, limited by confounding variables or are individual reports. The symptoms of hyponatraemia include confusion, delirium, somnolence, fluctuating consciousness and hallucinations. The risk of developing hyponatraemia while on an SSRI seems to increase with age, female sex, previous history of hyponatraemia and the concomitant use of other medications known to include hyponatraemia. Sodium concentrations of most patients with SSRI associated hyponatraemia return to normal within days to weeks of SSRI withdrawal. A few cases of SSRI rechallenge indicate that hyponatraemia may sometimes be a transient effect with tolerance developing over time. There is an urgent need for controlled, rigorous studies to confirm the extent of the association between SSRIs and hyponatraemia. It remains unclear whether any specific SSRI or venlafaxine has a stronger association with hyponatraemia than any other antidepressant. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

**Full Text:** Available from **EBSCOhost** in **International Journal of Geriatric Psychiatry**  
Available from **International Journal of Geriatric Psychiatry** in **Grantham Hospital Staff Library**

16. **Selective serotonin reuptake inhibitors and withdrawal symptoms: A review of the literature.**  
**Citation:** Human Psychopharmacology: Clinical and Experimental, July 1997, vol./is. 12/4(309-323), 0885-6222;1099-1077 (Jul-Aug 1997)  
**Author(s):** Therrien, Francois; Markowitz, John S  
**Abstract:** Presents a review of 1985-96 literature on withdrawal symptoms emerging following the discontinuation of selective serotonin reuptake inhibitor (SSRIs) antidepressants. 46 case reports and 2 drug discontinuation studies were retrieved from a MEDLINE search. All of the selective serotonin reuptake inhibitors were implicated in withdrawal reactions, with paroxetine most often cited in case reports. Withdrawal reactions were characterized most commonly by dizziness, fatigue/weakness, nausea, headache, myalgias and paresthesias. The occurrence of withdrawal did not appear to be related to dose or treatment duration. Symptoms generally appeared 1-4 days after drug discontinuation, and persisted for up to 25 days. Time of onset and duration of symptoms differed little among the agents. The pathophysiology/ pharmacology of withdrawal is unclear but may involve multiple neurotransmitter systems. It is concluded that all of the SSRIs can produce withdrawal symptoms and if discontinued, they should be tapered over 1-2 wks to minimize this possibility. Some patients may require a more extended tapering period. No specific treatment for severe withdrawal symptoms is recommended beyond reinstitution of the antidepressant with subsequent gradual tapering as tolerated.
17. Antidepressant withdrawal syndrome: Recognition, prevention and management.

Citation: CNS Drugs, April 1996, vol./is. 5/4(278-292), 1172-7047;1179-1934 (Apr 1996)

Author(s): Lejoyeux, Michel; Ades, Jean; Mourad, Isabelle; Solomon, Jacquelyn; Dilsaver, Steven

Abstract: Stresses that withdrawing patients from tricyclic antidepressants (TCAs), MAO inhibitors (MAOIs), and selective serotonin reuptake inhibitors (SSRIs) can produce somatic and psychological distress. Influenza-like syndromes, gastrointestinal adverse effects, arrhythmias, sleep disturbances, movement disorders, mania or hypomania, panic attacks, and delirium may follow antidepressant withdrawal. Currently, the etiology of withdrawal symptoms is not fully known. Withdrawal phenomena are usually prevented by gradually reducing the total daily dosage of the drug in question rather than abruptly discontinuing it. Antimuscarinic agents can be prescribed in order to alleviate the symptoms produced by the withdrawal of TCAs or MAOIs. To date, no drugs have been shown to be useful in the treatment of SSRI-associated withdrawal symptoms. The withdrawal syndrome associated with MAOIs may constitute a medical emergency. (PsycINFO Database Record (c) 2012 APA, all rights reserved)


Citation: Journal of Clinical Psychopharmacology, October 1996, vol./is. 16/5(356-362), 0271-0749;1533-712X (Oct 1996)

Author(s): Coupland, Nick J; Bell, Caroline J; Potokar, John P

Abstract: Studied reported withdrawal symptoms in a retrospective chart review of 362 patients treated in an outpatient clinic with the nonselective serotonin reuptake inhibitor clomipramine or with one of the selective serotonin reuptake inhibitors (SSRIs), fluoxetine, fluvoxamine, paroxetine, or sertraline. In 171 Ss who were supervised during medication tapering and discontinuation, the most common symptoms were dizziness, lethargy, paresthesia, nausea, vivid dreams, irritability, and low mood. When Ss with at least 1 qualitatively new symptom were defined as cases, these symptoms occurred significantly more frequently in Ss who had been treated either with one of the shorter half-life SSRIs, fluvoxamine or paroxetine (17.2%), or with clomipramine (30.8%), than in Ss taking one of the SSRIs with longer half-life metabolites, sertraline or fluoxetine (1.5%). Symptoms persisted for up to 21 days after onset, but were relieved within 24 hrs by restarting the medication. A role has been suggested for serotonin in coordinating sensory and autonomic function with motor activity. The authors suggest that this may lead to useful hypotheses about the pathophysiology of withdrawal symptoms from serotonin reuptake inhibitors. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

19. Drug holidays to counter sexual dysfunction.

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Author(s): Balon, Richard

Abstract: Comments on A. J. Rothschild's (see record 1996-09007-001) proposal of drug holidays as another strategy for alleviating the sexual dysfunction side effects of selective serotonin reuptake inhibitors (SSRIs). Caution should be taken when applying this approach because of possible withdrawal syndrome that may hamper the success of the drug holiday. Symptoms of withdrawal include insomnia, fatigue, and agitation. Withdrawal syndrome has been described after abrupt discontinuation of various SSRIs including sertraline, paroxetine, and fluvoxamine in patients with various diagnoses. (PsycINFO Database Record (c) 2012 APA, all rights reserved)