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Ninety-three cases of alcohol dependence following SSRI treatment

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Abstract.
BACKGROUND: There have been recent reports linking serotonin reuptake inhibitor use with increased alcohol consumption. A syndrome of alcoholism precipitated by a common treatment has clear implications for both research and treatment if it is a common phenomenon.
OBJECTIVE: To explore the profile of people affected, and drugs that might trigger the syndrome.
METHODS: We have selected reports to RxISK.org reporting the problem and cases linked to a blog posting outlining the syndrome and mined these for data on age, gender, drug of use, pattern of outcome on treatment, and impact of the problem.
RESULTS: The data make it clear that all treatments with significant effects on the serotonin reuptake system are likely to cause this problem. Both sexes, and all ages are affected and reports have come from a range of countries. While stopping treatment can lead to the problem clearing, a failure to stop can result in death.
CONCLUSIONS: SSRI induced alcoholism is likely to be a relatively common problem. Recognizing the problem can lead to a gratifying cure. A failure to recognize it can be fatal.

Keywords: SSRIs, alcohol dependence, antidepressants, adverse event databases

1. Background

We recently reported the case of Miss X who developed alcohol problems following treatment with paroxetine and subsequently citalopram over the course of several years. While on treatment she began to consume ever increasing amounts of alcohol with successively more severe consequences. She lost friends, her job, and she ended up with criminal convictions [1].

Convinced her SSRI was the problem, she was switched to another antidepressant but unfortunately another SSRI and the problem continued. Later switched to a 5HT3 receptor antagonist, mirtazapine, her problems cleared up. There has been no problem drinking since.

Her case was featured on RxISK.org (and DavdHealy.org) where it attracted over eighty comments. Many of these comments revealed that the person commenting had a comparable problem that had either resolved or was ongoing.

In addition, thirty-five people reported similar problems to the Adverse Events Database, RxISK.org.

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In total, between these two sites, 93 episodes of alcohol dependence linked to serotonin reuptake inhibitor drugs have been reported to us. This paper gives a breakdown of the characteristics of those affected.

2. Methods

The data in this article come from two sources. The first dataset stems from those who filed a full RxISK report on RxISK.org [2]. The second dataset comprises comments on posts on davidhealy.org and RxISK stories outlining the syndrome of alcohol dependence on SSRIs.

There were 35 people who reported to RxISK.org. Reports to RxISK.org enquire systematically for the reporter's age, sex and background along with their drug consumption and medical history. It takes them through a causality assessment as to whether the drug has caused the problem and gets them to assess the impact of the problem on their life.

The reports to RxISK are more comprehensive than comments to a blog posting and according we have more information on these cases and present data from this source to flesh out the core data extracted from both reporting processes in Appendix 1.

In response to the blog posting of Miss X's story on davidhealy.org and RxISK stories, there were over eighty comments. These comments are not as systematic as a RxISK report. However, we can extract from the material details of the age, sex and the drug involved and in the case of missing information have been able to supplement this through email contact with the person who posted the comment.

3. Results

In total there have been 93 episodes of SSRI linked alcohol problems reported from 79 people. Some people report the problem on more than one drug. The frequency of drug involvement is laid out in Table 1.

Of note, citalopram and escitalopram are essentially the same drug, as are venlafaxine and desvenlafaxine. Tramadol is closely related to venlafaxine.

Table 1
Number of reports per drug

Drug	Frequency (%) $n = 93$
Citalopram	27 (29)
Paroxetine	16 (17.2)
Fluoxetine	14 (15.1)
Escitalopram	10 (10.8)
Sertraline	10 (10.8)
Venlafaxine	10 (10.8)
Duloxetine	4 (4.3)
Tramadol	1 (1.1)
Desvenlafaxine	1 (1.1)
SSRI nos	1 (1.1)

Table 2
Gender of those reporting

Gender (% of *N*)	*N*	Age range	Mean
Female (65%)	33	17–57 yrs	37 yrs
Male (27%)	15	17–60 yrs	36 yrs

Table 3
Pattern of alcohol consumption linked to treatment

Pattern	Frequency (%) $n = 93$
1. Moderate drinker (pre and post AD use)	53 (57)
2. Minimal drinker (pre and post AS use)	10 (10.8)
3. Heavy drinker (pre and post AD use)	3 (3.2)
4. Ongoing AD and Ongoing alcohol cravings	21 (22.6)
5. Post AD alcohol cravings	1 (1.1)
6. Death	3 (5.4)

Table 4
Consequences of SSRI-induced alcoholism

Consequences of treatment	Cases (%)
Breakdown of relationships	16 (20.2)
Unemployment/job difficulties	4 (5.1)
Death	3 (3.8)
Compulsive shopping	3 (3.8)
No hangover effect from alcohol	3 (3.8)

The mean age of the 59 subjects for whom we have ages was 36.9 years with a range from 17 to 60 years.

Of the 79 subjects, 51 were female and 21 were male. Data on the sex of 7 subjects was missing – See Table 2.

The pattern of interactions between treatment and alcohol is laid out in Table 3. Subjects showed a number of patterns. They reported either being a moderate drinker whose drinking got worse on the SSRIs and returned to moderate levels when their antidepressant was stopped [1]; or a minimal drinker who returned to being a minimal drinker when the drug was stopped or reduced [2]; or a heavy drinker who developed an even greater problem on treatment and returned to their prior level of drinking when their treatment was stopped [3].

There were a number of patients or people who reported ongoing problems with ongoing antidepressant treatment and one person who reported post-SSRI alcohol cravings [4].

Over 70% of these cases show challenge de-challenge with the individual's alcohol consumption reverting to what it was prior to SSRI intake after the SSRI has been stopped or in one case reduced.

The consequences of this treatment induced alcoholism have been severe – see Table 4. Five individuals went on to die. At least four people have lost their job. Y number of people ended up with criminal problems. The vast majority of people talked about losing friends.

A number of people commented that certain treatments could help with the alcohol cravings that were caused. These include mirtazapine which is now under investigation as a possible treatment for alcoholism [3]. Another was acamprosate.

4. Discussion

This collection of 93 episodes of alcoholism linked to the use of drugs affecting the serotonin system builds on the previous case report of Miss X [1]. It would appear from this that treatment induced alcoholism is a relatively common problem.

They supplement the original case report in that they offer a large number of cases also showing challenge-dechallenge, as well as other cases showing the problem continuing on exposure to more than one SSRI. They make it clear that the problem affects both women and men, with indeed double the rates of reports from women as from men.

At present the data reported here offers a tight link between a specific action on the serotonin system and induced alcohol cravings. Of interest is that the problem has been reported on drugs that patients might not realise are primarily serotonin reuptake inhibitors such as tramadol, and desvenlafaxine, but not on drugs without effects on the serotonin system.

The link between serotonergic effects and cravings would be reinforced if it becomes clear that the tricyclic antidepressants that are serotonin reuptake inhibitors also cause the problem where drugs from this group without actions on the serotonin reuptake system do not.

It also appears that drugs that have opposing effects on the serotonin system, such as mirtazapine, can be helpful. It remains to be seen whether other drugs with comparable effects can be helpful.

It would also seem important to establish whether SSRIs and related drugs cause cravings for other substances from pain-killers to nicotine products or whether this is an alcohol specific problem.

Quite aside from the harm linked to excessive alcohol use in patients who would otherwise not drink, there is a need to establish the effects of SSRIs in patients with pre-existing alcohol problems in that many patients who abuse alcohol are viewed as being depressed, with their depression seen as either the cause of or a consequence of their alcohol use, and put on antidepressants [4–8]. For a proportion of patients this might be the worst thing to do.

Another group given antidepressants are women of child bearing years who are treated on the basis that treating a depression will reduce the likelihood that they will drink [9]. These data suggest that for some women, SSRI intake may increase the risk of drinking and damage to the fetus in this way.

Finally there would appear to be clear implications for genetic and other studies aimed at exploring the links between the serotonergic system and alcoholism [10–15]. This is an area of active investigation at present.

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Appendix 1
Reports to RxISK.org

No	Age	Sex	Drug	Dose	Side effects reported	Behavioural consequences	Other consequences
1	24	F	Paroxetine	20 mg	Alcohol Abuse Memory Loss Loss of Libido	Embarrassing, inappropriate behavior	Lost friends Affected relationships Withdrew
2	43	M	Paroxetine	30 mg	Blunted Affect Increased alcohol Lack of emotion Lack of empathy	Overtly social, careless, risky	Increased alcohol consumption Left job and had creative period
3	33	F	Paroxetine	20 mg	Alcohol Abuse Alcohol cravings	Risky behaviour	Friends and family distanced
4		F	Paroxetine	20 mg	Alcohol Abuse	Risky behaviour Sexual risks	
5	40	F	Paroxetine	10–20 mg	Anxiety Weight gain Alcohol cravings		
6	17	F	Paroxetine	10–30 mg	Alcoholism Blackouts Vertigo	Impulsiveness Lack of conscience	Suicidal Breaking Law Social activities changed Fighting with family
7	42	F	Setraline	50 mg	Alcohol Abuse Mania Weight gain	Disinhibition	Lacking motivation Increased spending Manic behaviour
8	60	M	Sertraline	25–100 mg	Depression Anxiety Alcohol Abuse	Increased sensitivity to criticism	Paranoia Loss of emotion
9	39	F	Setraline	50–100 mg	Insomnia Alopecia Alcohol use		Withdrawal, stopped engaging in social activities
10	50	M	Sertraline	50 mg	Loss of libido Erectile dysfunction Alcohol craving		Relationship with wife affected
11	28	F	Sertraline	50 mg	Alcohol intolerance	Blackouts	Lost friends

Appendix 1
(*Continued*)

No	Age	Sex	Drug	Dose	Side effects reported	Behavioural consequences	Other consequences
					Alcohol cravings	Confusion	Lost job Anxiety
12	17	M	Fluoxetine	10–20 mg	Substance Use Alcohol use	Smoking Cannabis	Apathetic, Unfocused Less social Withdrawn
13	45	F	Fluoxetine	20 mg	Weight gain Alcohol cravings		Anti social
14	17	M	Fluoxetine Paramax	20 mg Daily	Suicide Akathisia Disturbing dreams Amnesia Alcohol Abuse	Confused Agitated Aggressive Distress	Affected self-esteem Increased alcohol tolerance
15	26	M	Fluoxetine	20 mg	Euphoric mood Insomnia Alcoholism Tremors/shaking	Hypersexual Impulsive Intense emotions Gambling	Financially reckless Superior complex, Uninhibited behaviour Less feelings
16	39	F	Citalopram	10–20 mg	Affect Lability Nightmares Sleep walking Amnesia Alcohol interaction Loss of libido	Anger/rage Physical Assault Overdose Crying Sexual risky behaviour	Violent towards partner No memory of events Suspended from work
17	25	F	Citalopram	20 mg	Dissociative amnesia Alcohol interaction	Aggression Alcohol caused blackouts	Aggressive and abusive after small amounts of alcohol and blackouts
18	25	F	Citalopram	20 mg	Alcohol Abuse Akathisia Irritability	Overexcited Irritable	Problems with concentration
19	38	F	Citalopram	20–30 mg	Alcoholism/ Alcohol craving Disinhibition	Impulsive behaviour	Didn't suffer from hangovers

Appendix 1
(*Continued*)

No	Age	Sex	Drug	Dose	Side effects reported	Behavioural consequences	Other consequences
20	40	F	Citalopram	20 mg	Weight gain Alcohol use Insomnia	Uninhibited Violent Manic	Increased time alone
21	54	F	Citalopram	20–40 mg	Alcohol use		Weight loss
22	43	M	Citalopram	20–40 mg	Alcohol interaction	Alcohol craving Irritation Anger	Blackouts Less energy
23	28	M	Citalopram	20 mg	Alcoholism Amnesia	Blackouts	
24	57	F	Citalopram	10 mg	Alcoholism Alcohol Craving & Intolerance	Inhibited Sexual inhibition Also promiscuous	Motor skills affected Friendships affected
25	31	F	Citalopram	20 mg	Alcoholism Weight gain		Failed a course Employment affected Lost friends
26	39	F	Citalopram	20 mg	Alcohol abuse and cravings Emotion numbed	Dangerous, anti social behaviour	Arrested Relationships with family and friends impacted
27	48	F	Escitalopram	10 mg	Alcoholism	Aggression More risky behaviour	No hangovers Lost interest in hobbies Shame Relationships affected
28	41	F	Escitalopram	10 mg	Mania Alcohol cravings Alcohol Abuse Tremor Suicidal		Can no longer drive Prison
29	42	M	Escitalopram	10–20 mg	Impulsive Paranoia Alcohol abuse Anxiety	Uninhibited sexually Aggression Fearless Impulsive	Felt disconnected from the world Feel empty

Appendix 1
(*Continued*)

No	Age	Sex	Drug	Dose	Side effects reported	Behavioural consequences	Other consequences
					Loss of appetite	Agitated	
					Insomnia		
30			Escitalopram	10 mg	Alcohol use		
31	39	F	Duloxetine	20 mg	Compulsive shopping	Poor judgement	
					Hypomania	Excessive talking	
					Alcohol cravings	Agitated	
					Akathisia		
32	40	F	Duloxetine	60 mg	Loss of libido		Concentration affected
					Dizziness		Withdrawn and anti-social
					Alcoholism		
33	40	F	Duloxetine	60 mg × 2	Food cravings		Lost friends
					Alcohol cravings		
					Vivid dreams		
34	46	F	Venlafaxine	100 mg × 2	Depression	Loss of self-control	Divorce
					Akathisia		Debts
					Alcohol abuse		
35	41	F	Desvenlafaxine		Alcohol Problems	Manic on alcohol	Now alcoholic – but drug saved life
					Increase appetite	Poor work	
					hyperactivity		