A 37-year-old woman experienced a witnessed generalized seizure in the Emergency Department three hours after ingesting approximately 1400 mg of fluoxetine in a suicide attempt. Although the majority of fluoxetine ingestions are benign, seizures may occur after large intentional overdoses.

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CASE REPORT

Fluoxetine Overdose-Induced Seizure

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INTRODUCTION

Fluoxetine (Prozac®, Eli Lilly and Company, Indianapolis IN) is a selective serotonin reuptake inhibitor (SSRI) commonly used to treat depression and for other psychiatric indications. The majority of fluoxetine overdoses result in a benign clinical course. The largest published case series of fluoxetine overdoses found that the most common effects were tachycardia, drowsiness, tremor, nausea, and vomiting, and concluded that such overdoses typically are “minimally toxic”. Despite this suggestion that only mild to moderate symptomatology is to be expected, seizures, cardiac conduction abnormalities, and even fatalities have been associated with fluoxetine ingestions, although most of these cases involve co-ingested drugs or other confounding factors. We report the case of a witnessed, generalized seizure occurring three hours after a fluoxetine overdose in an otherwise healthy young woman.

CASE REPORT

A 37-year-old woman with a history of bulimia nervosa and depression ingested approximately seventy 20 mg fluoxetine capsules and 4-5 cans of beer in a self-professed suicide attempt. Shortly thereafter, she telephoned a friend who activated the EMS system. The patient’s prescribed medications were fluoxetine 20 mg daily and buspirone 15 mg twice daily. The patient stated that she had taken her buspirone only as directed, with the last dose on the morning of the fluoxetine overdose, about six hours earlier. She specifically denied ingesting any additional buspirone or any other medications. She admitted to “purging” herself daily for the last week. Other than some orthopedic surgical procedures, she denied any other significant past medical history, including seizures.

The paramedics arrived approximately 90 minutes post-ingestion and found the patient to be awake, alert, sitting up, and emotionally upset. The initial blood pressure was 142/106 mmHg, heart rate 120/minute. In the emergency department (ED) her vital signs were: temperature 37.2°C, pulse 91/min, blood pressure 132/72 mmHg, respiration 20/min, O₂ saturation 99% on room air. The emergency physician noted the patient to be alert and oriented, but with slurred speech and slow verbal response time. The patient had a non-focal neurologic exam without tremor, rigidity, or hyperreflexia, and the remainder of the physical examination was without noted abnormalities. The patient was given 50 g of activated charcoal, and blood and urine samples were obtained for baseline values and for quantitative serum acetaminophen and salicylate measurements. Serum chemistries showed sodium 138 mmol/L, potassium 4.2 mmol/L, chloride 105 mmol/L, bicarbonate 23 mmol/L, BUN 11 mg/dL, creatinine 0.6 mg/dL, glucose 81 mg/dL, salicylate 3.9 mg/dL, acetaminophen <1µg/mL, and ethanol 48 mg/dL. A qualitative urine pregnancy test was negative. An electrocardiogram revealed a normal sinus rhythm of 97 beats per minute with normal intervals (QRS 88 msec, QTc 461 msec).

Approximately three hours after the ingestion, the patient cried out and then experienced a generalized tonic-clonic seizure lasting 30 seconds witnessed by the ED personnel. The seizure resolved spontaneously, and the patient had a post-ictal period lasting five minutes. The patient received an intravenous loading dose of phenobarbital (620 mg [10mg/kg]) and was then transported without incident to a regional toxicology referral center.

On arrival to the intensive care unit, the patient was somnolent but easily arousable. Vital signs were: temperature 36.9°C, pulse 82/min, blood pressure 112/78 mmHg, respiration 24/min. A repeat physical examination was...
unremarkable including the neurologic exam. Additional
laboratory data obtained upon admission included serum
creatinine kinase (140 IU/L), calcium (8.8 mg/dL), and
a comprehensive urine drug screen (which combines the
enzyme-multiplied immunoassay technique, thin layer
chromatography, and gas chromatography/mass spectroscopy
to detect over 1500 drugs and metabolites) that showed
the presence of only phenobarbital, fluoxetine, ethanol,
and caffeine. The laboratory verified that buspirone can
be detected by this analysis. Quantitative serum levels of
fluoxetine, norfluoxetine, and buspirone were ordered on
admission. The fluoxetine level six hours after the ingestion
was 922 ng/mL (therapeutic = 50-480 ng/mL) and the
norfluoxetine level was 379 ng/mL (therapeutic = 50-450 ng/
ml). The quantitative buspirone level could not be determined
due to laboratory handling error. The patient was observed
overnight without any further seizure activity or other unusual
events. The psychiatry consultation and liaison service
evaluated the patient the following morning and arranged for
outpatient therapy. The patient was then discharged home in
stable condition.

DISCUSSION

Data from human and animal trials show fluoxetine to be
generally safe and with few drug interactions.10-12 Fluoxetine
overdose typically results in a benign clinical course, with
the most common symptoms being tachycardia, drowsiness,
tremor, nausea, and vomiting, and has therefore been
identified as “minimally toxic in doses up to 1,500 mg and
with combined plasma levels [fluoxetine plus norfluoxetine]
up to 1390 ng/mL.”1 With regard to potential neurotoxic
effects, considerable evidence exists that fluoxetine has
an anticonvulsant effect at therapeutic doses in humans
and animal models.13 Antidepressants may display both
anticonvulsant and pro-convulsant properties, with the
most important determining factor being the dose.14 In a
study of five different SSRIs taken in overdose, fluoxetine
had the lowest incidence of inducing seizures (1%, vs.
2% for sertraline, paroxetine, and citalopram, and 4% for
fluvoxamine).15 Not surprisingly then, there are few reports of
seizures associated with fluoxetine in the medical literature.
Many of these reports are confounded by co-ingestants and/or
underlying brain disease.2-5,8 Only a few cases of seizure after
isolated fluoxetine overdose in normal subjects have been
reported,6,7 and there is also a case occurring after escalation
of therapeutic dosing up to 60 mg/day.16

Evidence in the patient presented here for an acute
fluoxetine overdose is supported not only by history, but also
from the relatively high ratio of the parent substance compared
to norfluoxetine, its N-desmethylated metabolite. The seizure
does not appear to be related to serotonin syndrome, because
the patient did not exhibit autonomic instability, muscular
rigidity, or abnormal mental status (excluding the seizure
itself and a brief post-ictal period) as typically occur in that
disorder.17 The patient also consumed some ethanol during her
suicide attempt, but it is very unlikely that ethanol contributed
to her seizure. Firstly, she was only an occasional ethanol
consumer without a history of dependence or prior episodes
of withdrawal; in such a case, the presence of ethanol would,
if anything, act as an anticonvulsant. Secondly, she did not
exhibit signs of autonomic instability (e.g., diaphoresis,
hypertension) or tremor consistent with ethanol withdrawal.
She was initially tachycardic, but this is also commonly found
in cases of significant SSRI overdose.

Although acute fluoxetine overdose is believed to
cause the seizure in this patient, buspirone might potentiate
fluoxetine’s neurotoxicity. A seizure has been reported in a
patient receiving therapeutic doses of fluoxetine and buspirone
for obsessive-compulsive disorder.18 In contrast, a case series
of 11 patients on fluoxetine and buspirone does not describe
any seizures or other neurotoxicity.19 Caffeine overdoses
have also been reported to cause seizures,20 and caffeine was
detected in our patient’s urine. When questioned about this
finding, she reported that she consumed caffeine-containing
beverages (e.g. tea, soft drinks), but denied excessive
use. Although a serum caffeine level is not available for
this patient, she was not exhibiting symptoms of caffeine
intoxication such as tremor, agitation, hyperglycemia or
hypokalemia.21 She did have a mild tachycardia initially, but
this spontaneously resolved prior to the seizure. In order for
caffeine to be responsible for this seizure, one would expect
the patient to exhibit prominent symptoms of caffeine toxicity.
Thus, although the patient’s ingestion was not a completely
isolated fluoxetine overdose, since other xenobiotics were
detected, there is no evidence that any other drug contributed
significantly to her seizure.

CONCLUSION

We report the clinical course of a patient who had a
witnessed seizure following an acute fluoxetine overdose.
While the medical literature strongly suggests that most
fluoxetine overdoses are benign, emergency physicians need
to remain cognizant that intentional, high-dose fluoxetine
ingestions may induce seizures.

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