Sertraline Hydrochloride Withdrawal-Induced Unilateral Tinnitus: Case Study

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Abstract
Sertraline hydrochloride (Zoloft—Roeris Division, Pfizer Incorporated, New York) is an antidepressant medication that has numerous side effects, including dizziness, nausea, and tinnitus, documented during the period of medication. This presentation reports on Zoloft-induced unilateral tinnitus that resulted from withdrawal of the medication in a male patient with bilateral hereditary sensory hearing loss and concomitant clinical depression.

Key Words: Bipolar disorder, depression, mania, sensory hearing loss, serotonin, tinnitus, Zoloft

This case study reports the development of unilateral "chirping" tinnitus, which erupted following the patient's attempts to cease the use of psychiatric medications.

This 40-year-old male patient had an 8-year history of bipolar disorder. Bipolar disorder is the result of a chemical inability within the brain to properly use serotonin. Serotonin is a vasoconstrictor present in high concentrations in the central nervous system, particularly the hypothalamus and basal ganglia. Bipolar disorder is characterized by manic episodes, which are periods of elevated, expansive, or irritable mood for at least 1 week (Diagnostic and Statistical Manual of Mental Disorders, 1994) alternating with depression. Beck (1967) further explains manic episodes as that of inflated self-esteem or grandiosity, a decreased need for sleep, a need to talk constantly or rapidly, with motor agitation and/or the excessive involvement in pleasurable activities with a high potential for painful consequences. Since not all patients overtly exhibit the manic component, the disease is sometimes only diagnosed as clinical depression.

Clinical depression is the presence of

...persistent depressed or dysphoric mood that usually interferes with daily function-

ing (nearly every day for at least 2 weeks) and includes at least 4 of the following symptoms: change in appetite; change in sleep; psychomotor agitation or retardation; loss of interest in usual activities or decreased sexual drive; increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration; and a suicide attempt or suicidal ideation. (Physician's Desk Reference, 1994, pg. 2001)

Clinical depression can be differentiated from societal or event depression in that it does not require a specific event such as divorce, loss of employment, death of a friend or family member, etc. to become manifest.

One medication commonly used to treat clinical depression is sertraline hydrochloride (Zoloft), which is an orally administered antidepressant available in 50- or 100-mg tablets. Up to 200 mg per day can be prescribed to treat depression. Zoloft inhibits the central nervous system neuronal uptake of serotonin with little effect on norepinephrine (a catecholamine vasoconstrictor hormone stored in the adrenal medulla and secreted in response to hypotension or physical stress (Stedman's Medical Dictionary, 1995) or dopamine (a sympathetic nervous system neurotransmitter produced in the substantia nigra and transmitted to the putamen and caudate nucleus (Mosby's Medical Dictionary, 1998).

While tinnitus has been reported in 1.4 percent of the subjects taking Zoloft during clinical trials, 1.1 percent of the subjects taking a placebo
also reported tinnitus (Physician’s Desk Reference, 1994).

A variety of adverse reactions have been reported with the discontinuation of Zoloft. These include agitation, insomnia, somnambulism (sleepwalking), dizziness, headache, tremors, anorexia, nausea, fatigue, diarrhea, and ejaculatory delay.

**PATIENT**

A male 40-year-old professional had an 8-year history of bipolar disorder manifested primarily in clinical depression. He did not report any other neurologic symptoms such as seizures or event-related depression. One parent is diagnosed as manic depressive and one sibling is paranoid schizophrenic. The patient reported that he had been physically and emotionally abused as a child. The patient reported several aborted attempts at suicide and had near-daily suicidal thoughts prior to beginning treatment. In addition, he manifested feelings of worthlessness, excessive fatigue, difficulty sleeping, and loss of interest in various activities. He did not manifest mania or extreme happiness; however, the consulting psychiatrist felt that the depth of the patient’s depression was severe enough that any substantial indication of happiness might be a manic episode. Psychiatric care consisted of the use of medication to control the symptoms while psychological care was instituted to provide support therapy to reduce the risk of suicide.

Prior to consulting a psychiatrist, the patient had been taking 100 mg of Zoloft prescribed by his primary care physician for approximately 1 year for depression. Since he continued to have daily episodes of suicidal thoughts, feelings of worthlessness, increased fatigue, and insomnia, he sought additional mental health care. The psychiatrist increased the patient’s daily dosage of Zoloft to 200 mg (maximum dosage). In addition, the patient was placed on 1000 mg of divalproex sodium (Depakote) used to treat petit mal seizures, 12 mg of perphenazine (Trifalon) for psychoses or neuroses concomitant with depression, and 0.5 mg of lorazepam (Ativan), an anti-anxiety agent to be used as needed (Physician’s Desk Reference, 1994).

In addition to the bipolar disorder, the patient has had bilateral congenital moderate to severe sensory hearing loss since childhood with good to excellent speech recognition. A Loudness Growth by 1/2 Octave Band Test (Allen et al., 1990) revealed steeply sloping loudness contours consistent with cochlear pathology (Table 1). Distortion-product otoacoustic emissions were absent in each ear. No other site of lesion tests were performed. The patient wore bilateral behind-the-ear hearing aids with shell earmolds and pressure vents. The manic depressive parent and a different sibling than the paranoid schizophrenic sibling are also hearing impaired.

**TINNITUS**

The patient was a long-time tinnitus sufferer prior to the use of Zoloft. His previous tinnitus varied in pitch and loudness and was sporadic. Previous tinnitus was described as either tonal or hissing. A magnitude estimation scale was used to determine the perceived loudness of the tinnitus. The patient was asked to rate the loudness of the tinnitus on a 0 to 10 scale with 0 = no tinnitus and 10 = intolerable tinnitus. The before-Zoloft tinnitus never exceeded a magnitude estimate of 3 to 4 without amplification and was not perceived with amplification.

Various narrow and wide-band noise maskers were used in an attempt to mask the Zoloft-induced tinnitus and to determine if the chirping tinnitus was present in both ears but only perceived louder in the right ear. With masking levels to up to 100 dB SPL presented to the right ear, the patient denied hearing tinnitus in the left ear.

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<tr>
<th>Pure-Tone Thresholds</th>
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<tr>
<th>Loudness Growth Octave Band Minimum and Maximum Values</th>
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<td>Right: Minimum</td>
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The approximate frequency of the Zoloft tinnitus was derived by having the patient match the tinnitus to octave and half-octave pure tones provided by an audiometer. The audiologist presented a tone and asked the patient to report whether his tinnitus was higher or lower in pitch than the stimulus tone. The audiologist repeated the process by attempting to bracket (testing above and below) the reported frequency of the tinnitus. The patient reported that the tinnitus approximated the pitch of an 8000-Hz tone as the lower frequency (6000-Hz) tone was too low and the higher frequency (12,000 Hz) was too high. This series was repeated two times to verify the frequency selected. He described the tinnitus as a “chirping” type of sound that arrived in a pattern of three beats with each beat approximately 500 msec in duration with approximately 500 msec between beats. After the completion of a three-beat series there was an off period of approximately 1 second before the series began again. The entire pattern would then repeat itself over and over again.

The loudness was estimated to be at 7 to 8 on the 0 to 10 magnitude estimation scale when he did not wear his hearing aid but the rating was reduced to a 2 to 3 with amplification. No measures of the approximate sound pressure level of the tinnitus via loudness matching were attempted.

WITHDRAWAL COURSE

Seven months after beginning the psychiatric and psychological therapy previously described, the patient ceased all medications without medical advice. The patient reported that he did not want to be taking medication all of the time. The psychiatrist reported that this is a common mistake of patients with bipolar disorder. They feel that the medication is no longer needed when they are in a manic phase, only to “crash” again during the subsequent depressive phase.

Within 48 hours of ceasing all medications, the chirping tinnitus erupted. He tolerated the tinnitus for approximately 2 weeks before seeking help. After consulting with the psychiatrist and the audiologist, the patient agreed to resume only the Zoloft at 200 mg. The tinnitus disappeared within 72 hours. On his own, he began to systematically decrease the dosage of the Zoloft on a weekly basis in 50-mg steps. Five weeks later, he stopped the Zoloft entirely and reported to the audiologist that the chirping tinnitus resumed within 48 hours at the 7 to 8 magnitude estimate.

The patient was encouraged to resume taking his medication at the 200-mg level; however, he resumed the Zoloft at 150 mg and began reducing the dosage in 50-mg steps on a 2-week reduction cycle. Eight weeks later, he stopped the Zoloft again and reported to the audiologist that the tinnitus returned within 48 hours.

The patient resumed 50 mg of Zoloft and the tinnitus disappeared within 48 hours. At this point, he failed to return for follow-up regarding his tinnitus; however, the audiologist phoned the patient. The audiologist was told that the patient continues to get chirping tinnitus daily but only at a 1 to 2 magnitude estimate as long as he maintains at least 50 mg of Zoloft daily.

The above information was reported by the patient to the audiologist and is believed to be accurate. The patient was a professional person and intellectually coherent even though he was depressed. Since his Zoloft caplets were 100 mg each and had a line dividing them in half, it was fairly easy for the patient to monitor his dosages. At no time did he evidence any confusion about wanting to be rid of his medications and also be rid of the tinnitus. Apparently, he was able to find a satisfactory compromise where he was taking very little medication and experiencing little tinnitus.

DISCUSSION

According to the Physician’s Desk Reference (1994), peak serum plasma concentrations of Zoloft occur within 4.5 to 8.4 hours postdosing with average plasma concentrations decreasing by one half in 26 hours. With this in mind and with the patient’s consistent report of the eruption of tinnitus within 48 hours of cessation of the medication (when the plasma concentrations would have been reduced by three-quarters), it would support the conclusion that withdrawal of Zoloft and the consequent reduction in plasma concentrations induced the eruption of the tinnitus. The fact that the patient reported a substantial reduction or elimination of the tinnitus when he ingested only the Zoloft would support the conclusion that the withdrawal of Zoloft perpetuated the tinnitus. While it is not possible to state whether the combination of medications used was instrumental in the initial development of the tinnitus, the fact that the Zoloft alone could control the presence of the tinnitus strongly implicates the Zoloft as a pri-
mary etiologic factor. Since Zoloft is a central nervous system medication, it is assumed that the tinnitus is centrally based, but one cannot rule out that the bloodborne Zoloft may have resulted in a chemical change within the cochlea; however, it is not clear why the patient experienced tinnitus in just one ear. Both a central nervous system etiology or a bloodborne chemical change in the cochlea would intuitively suggest the presence of bilateral tinnitus; however, the patient steadfastly reported chirping tinnitus only in the right ear.

Chronic intractable tinnitus by itself can be emotionally upsetting. When severe tinnitus is added to concomitant suicidal ideation, there is a risk of exacerbating a troubling condition. Extreme care must be exercised by the audiologist to ensure that all possible options for reduction or elimination of the tinnitus are implemented. Although it may not be possible to eliminate the tinnitus, continued counseling by an appropriate mental health professional may prevent a tragedy. Under no circumstances should such a depressed patient be told “to live with it” as they may choose not to do so.

Additionally, this case suggests that it may be incorrect to assign all tinnitus to cochlear pathology and to treat all tinnitus accordingly.

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REFERENCES


