INTRODUCTION

Mirtazapine is a tetracyclic piperazinoazepine analogue of mianserin. It is a tetracyclic noradrenergic and specific serotonergic antidepressant, which acts as an antagonist of central presynaptic alpha-2-adrenergic autoreceptors and heteroreceptors, as well as a potent antagonist of postsynaptic 5-HT2 and 5-HT3 receptors (1,2).

Mirtazapine is an orally administered drug and indicated for the treatment of major depressive disorder. It is a safe and well-tolerated drug for use in daily clinical practice (3). Deafness, tinnitus, otitis media, ear pain, taste loss, parosmia, and vertigo are some possible side effects of mirtazapine related with otorhinolaryngology (4). Although deafness and tinnitus described as possible and infrequent adverse drug reaction in the product information of mirtazapine, this association and clinical features has not been described in literature. Herein, we report clinical and audiological characteristics of unilateral sudden hearing loss (SHL) that occurred after the introduction of mirtazapine, without resolution after discontinuation of the drug.

CASE REPORT

A 22-year-old male patient who had been taking mirtazapine 30 mg/day for the treatment of depression was admitted to our clinic with complaints of tinnitus and SHL in the left ear. Complaints occurred within 24 hours...
after the first dosage of mirtazapine. He did not have any personal or familial history of diseases associated with SHL, ear surgery, or drug abuse. His vital signs were checked and measured as normal. Otoscopy was normal for both ears. Results of a physical and neurological examination were unremarkable. The laboratory results were normal or negative.

The conventional (0.25 to 8.0 kHz) audiometry and tympanometric screening were performed. The pure-tone audiometry tests showed the mean hearing thresholds changed to 35 dB HL relatively flat sensorineural hearing loss at 250-8000 Hz frequencies with a good speech discrimination in left ear. Tympanometric screening showed normal middle ear functions bilaterally.

Within 24 hours of the first dosage the patient developed unilateral SHL and tinnitus without vertigo. The absence of clinical, laboratory and radiological evidence of a possible cause for sudden hearing loss and tinnitus, an association between mirtazapine and SHL and tinnitus was suggested.

A conservative therapy including bed rest, low salt diet, avoidance of noise exposure, and elevation of the head of bed were ordered. The patient received a standard course of oral corticosteroid (Deflazacort Tablets 90mg and taper) and B-complex vitamin supplementation. Weekly otological and audiological examinations were performed. Recovery of hearing sensitivity was measured using standard audiometry.

Mirtazapine was discontinued and there was a noticeable reduction in the degree of tinnitus after approximately 24 hours. But SHL continued to deteriorate for 4 weeks. The SHL was persisted with an audiogram confirming a 35 dB HL relatively flat sensorineural hearing loss in left ear. The patient is still under clinical follow-up. Conservative and medical treatments offered no relief from SHL.

**DISCUSSION**

Mirtazapine is a good choice in treatment of major depression with its rapid onset antidepressant activity and favorable tolerability (5). In the treatment of major depressive disorder, the effective dose range was generally 15-45 mg/day (4,6). The starting dose for mirtazapine is 15 mg/day, administered in a single dose. The most common side effects of mirtazapine are drowsiness, dry mouth, increased appetite, weight gain, and dizziness. These side effects tend to improve with time (2,7,8). Mirtazapine has a relatively low incidence of side effects related with otorhinolaryngology (9).

Many different classes of drugs are known to produce otoxicity. Many hypotheses have been developed to explain SHL etiology, including blood flow disturbances, membrane rupture of the inner ear, toxic and metabolic causes, etc. (10,11). The mechanism by which mirtazapine causes this adverse drug reaction is unclear. Further studies are needed to explain the mechanisms responsible for the mirtazapine-induced SHL. Mirtazapine-induced hearing loss appears to be irreversible. The onset of otoxicity can be very rapid, possibly complete within 24 hrs. SHL occurred with the use of first dose of the drug and this reaction seemed to be dose-independent. Tinnitus, a sensation of noise in the absence of an external stimulus, was accompanied to SHL.

The spontaneous recovery rates for SHL are generally high (11). Conservative and medical treatments are also beneficial for SHL (11,12). Different factors such as the absence of vertigo, the presence of tinnitus, etc. may positively influence the prognosis of SHL (13). Different treatment approaches have been described, but there is no specific medicine to treat SHL associated with medications. Stopping the offending medication may reverse hearing loss or prevent it from worsening (10). Among the used treatments, corticoids and hyperbaric oxygen therapy seem to have universal acceptance and they are the only ones with confirmed efficacy (14,15). Previous reports describe the adoption of a wait and see strategy in selected cases of SHL with good prognostic factors and moderate hearing loss (16). In our case, our patient had multiple good prognostic factors, but we did not follow a "wait-and-see" approach. He had a very poor response to both conservative and medical treatments. The patient is still under clinical follow-up.

In conclusion, although mirtazapine is a relatively safe antidepressant, with the increased use of drugs in treating depression, the importance of this side effect cannot be overemphasized. SHL is a serious and irreversible adverse effect of mirtazapine. Therefore, the risk of hearing loss should be taken into consideration when initiating mirtazapine therapy and use of the drug should be discontinued at the first appearance of otological complaints.
References:


