Sudden Hearing Loss Associated with Mirtazapine Therapy: A Case Report

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ÖZET:

Mirtazapin tedavisi ile ilişkili ani işitme kaybı: Bir olgu sunumu

Mirtazapin mianserinin bir tetrasiklik piperazinoazepin analoğudur ve majör depresif bozukluk tedavisinde kullanılmaktadır. Günlük klinik uygulamada iyi tolere edilen ve güvenli bir ilaçtır. Mirtazapinin kulak burun boğaz ile ilişkili yan etkilerinin görülme oranı göreceli olarak düşüktür. Yirmi iki yaşında erkek hastaya major depresyon tanısı ile mirtazapin tedavisi düzenlenmişti. Hastada ilacın ilk dozunu aldıktan sonraki ilk 24 saat içinde vertigonun eşlik etmediği ani işitme kaybı ve kulak çınlaması gelişti. Eşlik eden bir hastalığının veya ilaç tedavisinin olmaması bununla birlikte klinik, laboratuvar ve radyolojik incelemelerde bu durumu açıklayacak olası bir neden tespit edilememesi sebebiyle ani gelişen işitme kaybı ve kulak çınlamasının mirtazapin tedavisine bağlı olarak geliştiği değerlendirildi. Bu yazıda mirtazapin'e bağlı gelişen ani işitme kaybının klinik ve odiyolojik özellikleri tanımlandı. Hekimler bu muhtemel yan etki konusunda dikkatli olmalıdır. Hastalar otolojik yan etkiler açısından uyarılmalı ve ilaç kullanımı işitme kaybının görülmesiyle birlikte kesilmelidir.

Anahtar sözcükler: Mirtazapin, ani işitme kaybı, kulak çınlaması, yan etki

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ABSTRACT:

Sudden hearing loss associated with mirtazapine therapy: a case report

Mirtazapine is a tetracyclic piperazinoazepine analogue of mianserin and indicated for the treatment of major depressive disorder. It is a safe and well-tolerated drug for use in daily clinical practice. Mirtazapine has a relatively low incidence of side effects related with otorhinolaryngology. A 22-year-old male patient with major depression was prescribed mirtazapine. Within 24 hours after the first dosage the patient developed a sudden hearing loss and tinnitus without vertigo. Since there was neither concomitant medication use nor another medical illness, in addition to the absence of clinical, laboratory, and radiological evidence of a possible cause for sudden hearing loss and tinnitus, an association between mirtazapine and sudden hearing loss and tinnitus was suggested. In this report, we identify clinical and audiological characteristics of mirtazapine induced sudden hearing loss. Physicians should be aware of this possible adverse effect. Patients should be informed about the signs and symptoms of otological side effects and use of the drug should be discontinued at the first appearance of sudden hearing loss.

Key words: Mirtazapine, sudden hearing loss, tinnitus, side effect

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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 ototoxicity. 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 ototoxicity can be very rapid, possibly complete within 24 hrs. SHL occured 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:

1. Stimmel GL, Dopheide JA, Stahl SM. Mirtazapine: an antidepressant with noradrenergic and specific serotonergic effects. Pharmacotherapy 1997;17:10-12.

2. Frazer A. Pharmacology of antidepressants. J Clin Psychopharmacol 1997;17:2-18.

3. Ozcankaya R, Acar A. The comparison of amitriptyline and mirtazapine side effects on depression treatment. Klinik Psikofarmakoloji Bülteni- Bulletin of Clinical Psychopharmacology 2001;11:17-27

4. Battal S, Cetin M. Basic principles in drug treatment of depression. Klinik Psikofarmakoloji Bülteni- Bulletin of Clinical Psychopharmacology 1998; 8 :202-214

5. Celikel FC, Cumurcu BE, Etikan I. Onset of Action and Tolerability of Mirtazapine in Major Depression: Case Series. Klinik Psikiyatri Dergisi, 2006: 9 :89-98.

6 Agargun MY, Ebrinc S. Mirtazapine: A Review. Klinik Psikofarmakoloji Bülteni- Bulletin of Clinical Psychopharmacology 1998; 8: 59-68.

7. Preskorn SH. Selection of an antidepressant: mirtazapine. J Clin Psychiatry 1997;58(Suppl 6):S3-S8.

8. Burrows GD, Kremer CM. Mirtazapine: clinical advantages in the treatment of depression. J Clin Psychopharmacol 1997;17:34-39.

9. Remeron Drug Description. URL:Http://www.rxlist.com/remeron-drug.htm. RxList Inc. 2008.

10. Aftab A, Quraishi S. Aetiological causes of reversible sensorineural hearing loss. The Internet Journal of Otorhinolaryngology 2006: Volume 4 Number 2.

11. Penido NO, Ramos HVL, Barros FA, Cruz OL, Toledo RN. Clinical, etiological and progression factors of hearing in sudden deafness. Rev Bras Otorrinolaringol 2005;71:633-638

12. Haberkamp TJ, Tanyeri HM. Management of idiopathic sudden sensorineural hearing loss. Am J Otol 1999; 20: 587-595.

13. Mamak A, Yilmaz S, Cansiz H, Inci E, Güçlü E, Dereköylü L. A study of prognostic factors in sudden hearing loss. Ear Nose Throat J. 2005 ;84:641-644

14. Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss. A double-blind clinical study. Arch Otolaryngol 1980, 106: 772-776.

15. Cekin E, Cincik H, Ulubil SA, Gungor A. Effectiveness of hyperbaric oxygen therapy in management of sudden hearing loss.J Laryngol Otol. 2009; 13:1-4.

16. Dursun E, Dogru S, Cincik H, Cekin E, Gungor A, Poyrazoglu E. Iloprost-induced sudden hearing loss. J Laryngol Otol. 2007;121:609-610