Introduction: Bell's palsy is a neurological condition manifests with acute unilateral neuropathy of 7th cranial nerve. The cause is not clear. However, some infections, immune system responses and ischemic causes are suggested as etiologies. We report 2 cases with Bell’s palsy while using quetiapine plus sertraline, in the absence of concurrent prescriptions which have been reported Bell's palsy as an adverse effect.

Cases Presentation:

First patient was an Iranian 54 years old male with Major Depressive Disorder who has been treated by sertraline 100mg per day for 1 year. His main manifestations was depressed mood, fatigue, insomnia, irritability, suicidal ideas and social isolation. He presented the classical manifestations of peripheral Bell’s palsy only 3 days after initiation of quetiapine 50mg per night. Brain imaging such as Magnetic Resonance Imaging (MRI) and Diffusion Weighted Imaging (DWI) was performed. Also other investigations for infective and immune causes were done. All of them showed normal results.

The second case was an Iranian 20 year old female diagnosed as Major Depressive and Body dysmorphic disorder patient. She was being treated by sertraline 100 mg/daily plus quetiapine 25md per night for 15 months. She also presented peripheral type of Bell’s palsy while using this combination therapy. Neurological investigations also performed and all results were normal. She recovered after reduction of quetiapine dosage to 12.5 mg per night and prescription of acyclovir and dexamethasone by our neurologist colleague.

Discussion:

Based on our search there is no reported correlation between psychiatric medications and Bell’s palsy. First explanation about our cases is an accidental correlation but also the short time correlation with initiation of treatment and presenting Bell’s palsy in first case and recovery of second one after reduction of quetiapine dosage are supporting the idea that the combination of sertraline and quetiapine may causes Bell’s palsy. Some articles have mentioned that antipsychotic drugs may have a weak antibiotic agent role and specially may demonstrate an inhibitory effect on neurotropic viruses, such as herpes simplex. Sertraline may also acts as an antibacterial agent. Reduction of protecting human microbiota may explain our observations.

Conclusion:

Combination of sertraline and quetiapine may cause Bell’s palsy and clinicians should consider neurological adverse effects of this common combination.

**ABSTRACT**

Introduction: Bell’s palsy is a neurological condition manifests with acute unilateral neuropathy of 7th cranial nerve. The cause is not clear. However, some infections, immune system responses and ischemic causes are suggested as etiologies. We report 2 cases with Bell’s palsy while using quetiapine plus sertraline, in the absence of concurrent prescriptions which have been reported Bell's palsy as an adverse effect.

Cases Presentation: First patient was an Iranian 54 years old male with Major Depressive Disorder who has been treated by sertraline 100mg per day for 1 year. His main manifestations was depressed mood, fatigue, insomnia, irritability, suicidal ideas and social isolation. He presented the classical manifestations of peripheral Bell’s palsy only 3 days after initiation of quetiapine 50mg per night. Brain imaging such as Magnetic Resonance Imaging (MRI) and Diffusion Weighted Imaging (DWI) was performed. Also other investigations for infective and immune causes were done. All of them showed normal results.

The second case was an Iranian 20 year old female diagnosed as Major Depressive and Body dysmorphic disorder patient. She was being treated by sertraline 100 mg/daily plus quetiapine 25md per night for 15 months. She also presented peripheral type of Bell’s palsy while using this combination therapy. Neurological investigations also performed and all results were normal. She recovered after reduction of quetiapine dosage to 12.5 mg per night and prescription of acyclovir and dexamethasone by our neurologist colleague.

Discussion: Based on our search there is no reported correlation between psychiatric medications and Bell’s palsy. First explanation about our cases is an accidental correlation but also the short time correlation with initiation of treatment and presenting Bell’s palsy in first case and recovery of second one after reduction of quetiapine dosage are supporting the idea that the combination of sertraline and quetiapine may causes Bell’s palsy. Some articles have mentioned that antipsychotic drugs may have a weak antibiotic agent role and specially may demonstrate an inhibitory effect on neurotropic viruses, such as herpes simplex. Sertraline may also acts as an antibacterial agent. Reduction of protecting human microbiota may explain our observations.

Conclusion: Combination of sertraline and quetiapine may cause Bell’s palsy and clinicians should consider neurological adverse effects of this common combination.
Introduction

Bell’s palsy is a neurological condition that manifests with an acute unilateral neuropathy of the seventh cranial nerve [1, 2]. Based on the first published issue, its etiology remains unknown [3]; however, some conditions, such as infections, immune system responses, and ischemic incidents are suggested as its etiologies [4]. Among all the reported etiologies for Bell’s palsy, there was no drug-induced one. However, in this article, we presented two cases that seemed to be caused by a combination of pharmacotherapy. Quetiapine is an atypical antipsychotic which has a greater binding affinity for serotonin 5-HT2 receptors compared to dopamine D2 receptors. Quetiapine, compared to other antipsychotic drugs, is well-tolerated and tends to cause fewer adverse effects, especially neurological types, such as acute dystonia, tardive dyskinesia, akathisia, and parkinsonism, during acute and long-term treatment [5]. Sertraline is a Selective Serotonin Reuptake Inhibitors (SSRI) in the central nervous system. The role of SSRIs, like sertraline in the treatment of several psychiatric conditions, such as Major Depressive Disorder (MDD), Obsessive-Compulsive Disorder (OCD), and anxiety disorders, is well established. It is considered among the safest treatments, as well as better tolerated and better accepted by patients to manage the disorders mentioned above with a low incidence of neurological complications [6].

In this study, we described two patients undergoing treatment for MDD by sertraline combined with quetiapine. These patients, in the absence of concurrent prescriptions, developed Bell’s palsy, which led us to report it as a rare adverse effect of this combination therapy.

Case 1

The first patient was a 54-year-old Iranian male with MDD. Moreover, she was presented with depressed mood, fatigue, insomnia, irritability, suicidal ideation, and social isolation without any psychotic features, i.e. initiated about two years earlier. He reported no history of medical problems, such as heart diseases, diabetes mellitus, seizure, current viral or bacterial infections, or immunological diseases. He also reported no use of recreational drugs other than tobacco in the past 10 years. He had two children suffering from disabling Obsessive-Compulsive Disorder (OCD).

Furthermore, he experienced some episodes of exacerbation, i.e. his primary precipitating stressor. His family and the patient reported no major problem in his personal history, other than chronic irritability. The patient had been treated with sertraline (100 mg/d) for one year. After adding 50 mg quetiapine per night to his previous medications to treat insomnia and achieving better therapeutic outcomes in depression symptoms, the patient presented the classical manifestations of Bell’s palsy after 3 days of administration. To better find the cause, a neurological assessment was performed on the patient, including brain imaging; Magnetic Resonance Imaging (MRI) and Diffusion-Weighted Imaging (DWI). Other investigations for infective and immune causes were also conducted and all the obtained results were normal. The patient then took some medications for treating Bell’s palsy. The treatment consisted of acyclovir and dexamethasone. We also discontinued quetiapine immediately. However, after all the procedures, the patient did not have full remission, and some symptoms, like left eye ptosis, remained after one year from presenting symptoms, which improved after physiotherapy.

Case 2

The second case was a 20-year-old Iranian female diagnosed with MDD and Body Dysmorphic Disorder (BDD). The patient was presented by depressed mood, hopelessness, anhedonia, and a lack of refreshing sleep. There was no evidence of psychotic features. She was on treatment with 100 mg sertraline daily and 25 mg quetiapine for 15 months. She reported no other medical problems, such as thyroid, cardiovascular or immunological diseases, or seizure before this course. There was no history of substance abuse for the patient. She also had a dizygotic twin suffering from MDD. Concerning her personal life, her mother mentioned that she was socially isolated, and her intimate friend was her sister. Her intellectual and educational performance was acceptable, and she was a student of laboratory sciences. The patient presented peripheral Bell’s palsy after these 15 months while using this combined therapy. She reported no reasonable cause for the manifestation, such as current infection, or taking a new medication, or traumatic accidents. Neurological investigations, including complete neurological evaluation and MRI, were also performed, and the relevant results were in normal ranges. Her quetiapine dosage was decreased to 12.5 mg per night, and she was treated with acyclovir and dexamethasone by our neurologist colleague. The patient achieved full remission within two weeks of quetiapine dose reduction, and the remission persisted in our last one-year follow-up.
Discussion

Bell’s palsy is a temporary unilateral facial paralysis resulting from damage or trauma to the facial nerves by unknown cause; it is presented in acute manifestation even in a few hours [1-3]. When Bell’s palsy occurs, the function of the facial nerve is disrupted [7], causing an interruption in sending the signals to the facial muscles. This interruption results in facial weakness or paralysis. Bell’s palsy occurs when the nerve that controls the facial muscles is swollen, inflamed, or compressed, resulting in facial weakness or paralysis [8, 9]. The etiology of this damage remains unknown.

There is no reported correlation between these two psychiatric medications (quetiapine and sertraline), and Bell’s palsy. In these cases, however, we could conduct a relationship between these medications and Bell’s palsy. In the first case, Bell’s palsy occurred shortly after the treatment initiation, and no other cause was found for this incidence. In the second case, we observed a significant development in the patient’s symptoms after reducing the quetiapine dosage. Some studies mentioned that antipsychotic drugs may have a weak antibiotic role [10, 11], and may demonstrate an inhibitory effect on neurotropic viruses, like herpes simplex [12]. Based on these articles and our observations, we could theorize that quetiapine and sertraline, as antibacterial agents, could reduce the protecting human microbiota.

In some recent investigations, some psychiatric conditions, such as depression and obsession symptoms, were found to have a reciprocal relationship with inflammation [13, 14]. Additionally, high levels of peripheral inflammatory markers (e.g., C-reactive protein, tumor necrosis factor-alpha, & interleukin) were observed among depressed patients with no other physical comorbidities. Accordingly, these studies could indicate the probable effects of inflammation on depression. These findings could further support our hypothesis.

Conclusion

A physician should be aware that combination therapies with antipsychotic drugs could have some adverse effects, i.e. unclear and require further investigations. Our reported cases generated Bell’s palsy as a susceptible adverse effect of quetiapine and sertraline combination therapy in patients with MDD. However, it might be a random co-occurrence. Given the correlation between quetiapine dosage reduction and symptoms of relief in these two cases, we suggested further investigations to explore similar cases.

Ethical Considerations

Compliance with ethical guidelines

Informed consent was obtained from both of patients and all data were reported anonymously.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declared no conflicts of interest.

References

[1] Runge MS, Andrew Greganti M, editors. Netter’s internal medicine. 2nd Edition. Philadelphia, PA: Saunders/Elsevier; 2009. https://books.google.com/books?id=j9L7wAEACAAU&dq
[2] Fuller G, Morgan C. Bell’s palsy syndrome: Mimics and chameleons. Practical Neurology. 2016; 16(6):439-44. [DOI:10.1136/practn
[3] Bird TD, Nicolaus A. Friedreich’s description of peripheral facial nerve paralysis in 1798. Journal of Neurology, Neurosurgery, and Psychiatry. 1979; 42(1):56-8. [DOI:10.1136/jnnp.42.1.56] [PMID] [PMCID]
[4] Adour KK. Current concepts in neurology: Diagnosis and management of facial paralysis. The New England Journal of Medicine. 1982; 307(6):348-51. [DOI:10.1056/NEJM198208053070605] [PMID]
[5] Dev V, Raniwalla J. Quetiapine: A review of its safety in the management of schizophrenia. Drug Safety. 2000; 23(4):295-307. [DOI:10.2165/00002018-200023040-00003] [PMID]
[6] Barth M, Kriston L, Klostermann S, Barbui C, Cipriani A, Linde K. Efficacy of selective serotonin reuptake inhibitors and adverse events: Meta-regression and mediation analysis of placebo-controlled trials. British Journal of Psychiatry. 2016; 208(2):114-9. [DOI:10.1192/bjp.bp.114.150136] [PMID]
[7] Niparko JK, Mattax DE. Bell’s palsy and herpes zoster oticus. In: Johnson RT, Griffin JW, eds. Current Therapy in Neurologic Disease. 4th Edition. St Louis, MO: BC Decker; 1993.
[8] Kim IS, Shin SH, Kim J, Lee WS, Lee HK. Correlation between MRI and operative findings in Bell’s palsy and Ramsay Hunt syndrome. Yonsei Medical Journal. 2007; 48(6):963-8. [DOI:10.3349/ymj.2007.48.6.963] [PMID] [PMCID]
[9] Fisch UJ, Esslen E. Total intratemporal exposure of the facial nerve. Pathologic findings in Bell’s palsy. Archives of Otolaryngology. 1972; 95(4):335-41. [DOI:10.1001/archotol.1972.00770080529008] [PMID]
[10] Nehme H, Saulnier P, Ramadan AA, Cassisa V, Guillet C, Eveillard M, et al. Antibacterial activity of antipsychotic agents, their association with lipid nanocapsules and its impact on the properties of the nanocarriers and on antibacterial activity. PLoS One. 2018; 13(1):e0189950. [DOI:10.1371/journal.pone.0189950] [PMID] [PMCID]

[11] Jeyaseeli L, Dasgupta A, Dastidar SG, Molnar I, Amaral L. Evidence of significant synergism between antibiotics and the antipsychotic, antimicrobial drug flupenthixol. European Journal of Clinical Microbiology & Infectious Diseases. 2012; 31(6):1243-50. [DOI:10.1007/s10096-011-1435-3] [PMID]

[12] Jones-Brando LV, Buthod JL, Holland LE, Yolken RH, Torrey EF. Metabolites of the antipsychotic agent clozapine inhibit the replication of human immunodeficiency virus type 1. Schizophrenia Research. 1997; 25(1):63-70. [DOI:10.1016/s0920-9964(97)00007-8] [PMID]

[13] Ghazizadeh-Hashemi M, Ghajar A, Shalbafan MR, Ghazizadeh-Hashemi F, Afarideh M, Malekpour F, et al. Palmitoylethanolamide as adjunctive therapy in major depressive disorder: A double-blind, randomized and placebo-controlled trial. Journal of Affective Disorders. 2018; 232:127-33. [DOI:10.1016/j.jad.2018.02.057] [PMID]

[14] Shalbafan M, Mohammadinejad P, Shariat SV, Alavi K, Zeinodini A, Salehi M, et al. Celecoxib as an adjuvant to fluvoxamine in moderate to severe obsessive-compulsive disorder: A double-blind, placebo-controlled, randomized trial. Pharmacopsychiatry. 2015; 48(4-5):136-40. [DOI:10.1055/s-0035-1549929] [PMID]