Gangisetty sneha *et al.* / *International Journal of Pharmacy & Therapeutics*, 5(3), 2014, 227-229.

e- ISSN 0976-0342
Print ISSN 2229-7456

International Journal of Pharmacy & Therapeutics

Journal homepage: www.ijptjournal.com

IJPT

OLANZAPINE INDUCED BILATERAL PEDAL EDEMA- A CASE REPORT

Gangisetty sneha*, Koppula Shilpa, Nallani Venkata Rama Rao, Ramarao Nadendla

Department of Pharmacy Practice, Chalapathi Institute of Pharmaceutical Sciences, Guntur - 522034, Andhra Pradesh, India.

ABSTRACT

A case of olanzapine- induced bilateral pedal oedema in a 40 year old male patient with a diagnosis of schizophrenia of paranoid type is discussed. The exact mechanism of olanzapine to cause bilateral pedal oedema is not known; a number of possible mechanisms are discussed. It is suggested that the clinicians should remain vigilant to promptly recognize this uncommon adverse reaction of olanzapine. Naranjo's casuality assessment algorithm was used to assess the adverse effect and it indicated olanzapine as probable cause of bilateral pedal edema.

Key Words:- Schizophrenia, Olanzapine, Bilateral Pedal Edema.

INTRODUCTION

Schizophrenia is one of the most complex and challenging of psychiatric disorders. It represents a heterogeneous syndrome of disorganized and bizarre thoughts, delusions, hallucinations, inappropriate affect, and impaired psychosocial functioning. Schizophrenia most commonly has its onset in late adolescence or early adulthood and rarely occurs before adolescence or after the age of 40 years (Joseph TD, 2011).

Schizophrenia includes the following subtypes:

- Paranoid-type schizophrenia is marked by delusions of persecution or conspiracy and is often accompanied by auditory hallucinations.
- Disorganized-type schizophrenia is marked by disordered thought processes, manifested in disorganized speech and behavior, and includes flat affect (absence of appropriate emotional responsiveness).
- Catatonic-type schizophrenia is marked by extremes in movement and behavior ranging from hyperactive agitation to complete lethargy and immobility.

Corresponding Author

Gangisetty sneha
Email:- gangisettysneha@gmail.com

- Undifferentiated-type schizophrenia is a category used when symptoms do not clearly fall into one of the above subtypes.
- Residual-type schizophrenia is used to describe patients who have had a history of schizophrenia but whose symptoms have diminished or become less severe (Hemminqs G, 1990).

TREATMENT OPTIONS FOR SCHIZOPHRENIA

Pharmacotherapy is the mainstay of treatment in schizophrenia, and it is impossible in most patients to implement effective psychosocial rehabilitation programs in the absence of antipsychotic treatment (Lehman AF *et al*., 2004)

COMMONLY USED ANTIPSYCHOTIC MEDICATIONS

A. First generation antipsychotics (FGAs) (Rajiv Tandon *et al*., 2010)

I. Phenothiazines

Chlorpromazine, chlorproethazine, levomepromazine, promazine, triflupromazine. Mesoridazine, piperacetazine, pipoptiazine, sulforidazine, Fluphenazine,

II. Butyrophenones
Haloperidol, benperidol, bromperidol, droperidol, fluanisone, melperone, trifluperidol.
III. Thioxanthenes
Thiothixene, chlorprothixene, clopenthixol, flupenthixol, zuclopenthixol
IV. Dihydroindolones
Molindone, oxypertine
V. Dibenzoxazepines
Loxapine, clotiapine
VI. Diphenylbutylpiperidines
Pimozide, fluspirilene, penfluridol
VII. Benzamides
Sulpiride, nemonapride, sultopride, tiapride
VIII. Iminodibenzyl
Clocapramine, mosapramine
B. Second Generation antipsychotics (SGAs)
I. Benzo (diaze- or thiaze-) pines
Asenapine, Clozapine, Olanzapine, Quetiapine, Zotepine
II. Indolones and diones
Aripiprazole, iloperidone, paliperidone, perospirone, risperidone, sertindole, ziprasidone
III. Benzamide
Amisulpride

ANTIPSYCHOTIC MEDICATION CHOICES

Second-Generation Antipsychotics

Second-generation antipsychotics (SGAs) (with the exception ofclozapine) have become first-line agents in the treatment of schizophrenia. The major advantage of atypical antipsychotics can be their lower risk of neurologic side-effects, particularly effects on movement.

FIRST GENERATION ANTIPSYCHOTICS

However, in first episode schizophrenia, SGAs are often considered first-line treatments because of the risk of tardive dyskinesia with FGAs. This can be of particular significance in individuals with their first psychotic break, as they seem particular susceptible to extrapyramidal side effects (Moore TA *et al*., 2004).

Antipsychotic Drug Therapy- Mechanism of Action

All antipsychotic drugs tend to block D2 receptors in the dopamine pathways of the brain. This means that dopamine released in these pathways has less effect. Excess release of dopamine in the mesolimbic pathway has been linked to psychotic experiences. It is the blockade of dopamine receptors in this pathway that is thought to control psychotic experiences (Marder SR *et al*., 2007)

OLANZAPINE

Olanzapine is an atypical antipsychotic that has high affinity for serotonin (5-HT2A, 5-HT2C), dopamine (D1–4) muscarinic (M1–5), histamine (H1), adrenergic (α1) receptors and weak affinity for β-adrenergic and GABAA receptors (Stahl SM, 2000). While the common side effects of olanzapine are weight gain and somnolence (Deshauer D *et al*., 2006.) The less common side effects include dry mouth, dizziness, constipation, dyspepsia, and increased appetite; akathisia, tremors and peripheral oedema (3-6%) are among the rare side effects (Martindale, 2005).

Results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study indicate that olanzapine, compared with quetiapine, risperidone, ziprasidone, and the FGA perphenazine, has modest superiority in maintenance therapy when treatment persistence is the primary clinical outcome (Lieberman JA *et al*., 2005).

Possible mechanisms that olanzapine causes edema, (Ng B *et al*., 2003).

- Blocks alpha 1 receptors: peripheral vasodilation and decreased SVR.
- Blocks M1, H1, and 5-HT2 receptors: prevents increase in IP3, then have down regulation of ATP-dependent calcium pump which can reduce smooth muscle contractility resulting in vasodilation and edema.
- Blocks 5-HT2 receptors: increases cyclic AMP which relaxes vascular smooth muscle by phosphorylation of myosin light chain kinase inhibition (Yovtecheva SP and Yazel JJ, 2000).
- Olanzapine has a very low incidence of extrapyramidal side effects when used within the approved dose range of 10 to 20 mg daily.

CASE REPORT

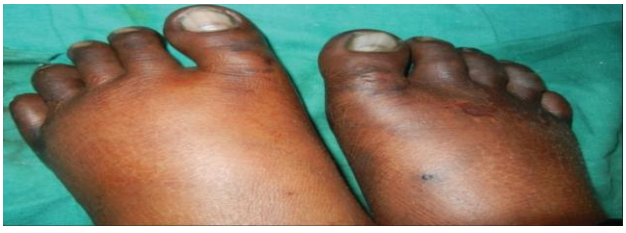
A 40 yrs male patient was admitted in psychiatry department on Jan 2014 with chief complaints of aggressive and bizarre behavior since 20 days. Aggressive behavior in the form of beating and scolding his mother and others who lives in the neighbourhood and bizarre behavior in the form of wearing 3-4 shirts on one another, writing on walls with a stick. Hearing voices and his wife who was dead is talking to him. He used to urinate and defeacate on bed. His social habits include he is alcoholic since 8yrs and stopped 4-5 months back and had financial disputes which made him to stay at home for about 2 months later started coming out of the house and from then bizarre behavior started.

Based on the above condition he was diagnosed with schizophrenia of paranoid type by physician and was prescribed with tab olanzapine 10mg B.D , tab trihexyphenidyl 2 mg O.D, Tab diazepam 5mg O.D after 10days of therapy he developed bilateral pedal edema.

His physical examination including cardiac and respiratory examination was done. There were no signs of cardiac failure, pulmonary oedema, varicose or spider veins on the legs or ankles. His blood pressure was recorded on different occasions and it was with in the normal range. The results of ECG, complete blood counts, liver function tests, renal functions, electrolytes were normal.

Measures taken for the management includes

- He was refered to department of medicine were his B.P was 130/80mm of hg with presence of tenderness. He was prescribed with Tab. Propanolol 40mg B.D.
- His caregiver (mother) was told to provide salt restricted diet.



DISCUSSION

In this case, a pre-existing tendency to develop edema was exacerbated by olanzapine. This exacerbation was dose related, but it can be managed effectively with a diuretic i.efrusemide of 20mg is sufficient. In our case, managing the edema had to be weighed against discontinuing the olanzapine. After considering the alternatives, it was better continuing olanzapine, coupled with more attention to lifestyle modification, was the best choice.

Here in this condition the patient was prescribed with propanolol instead of a diuretic as he had chief complaint of nocturnal eneuresis. He was treated with both olanzapine and propanolol simultaneously and the edema resolved within 5 days. Taking all these informations in to consideration, a causality assessment was done by using naranjo's causality assessment scale and the naranjo score was found to be 5 (probable 5-8) (Naranjo CA *et al*., 1981).

CONCLUSION

While olanzapine-related edema can be reversed with a diuretic, little is known about the long-term efficacy or safety of this intervention. Prompt recognition and intervention with discontinuation of the offending agent is important for this potentially serious, seemingly idiosyncratic, vascular complication.

REFERENCES

Deshauer D, Erwin L, Karagianis J. Case Report: Edema related to olanzapine therapy. *Can Fam Physician*, 52, 2006, 620–621.

Hemminqs G. Causes of schizophrenia. *Schizophrenia Bulletin*, 16(4), 1990, 663-671.

Joseph TD, Robert LT, Ary CY, Gary R, Matzke, Barbara G, Wells L, Michael P. Pharmacotherapy-A Pathophysiologic Approach. 8th ed., 2011, 2254-2261.

Lehman AF, Lieberman JA, Dixon LB, *et al*. American Psychiatric Association Practice Guidelines; Work Group on Schizophrenia. Practiceguideline for the treatment of patients with schizophrenia, 2nd ed. *Am J Psychiatry*, 161(2 Suppl), 2004, 1–56.

Lieberman JA, Stroup TS, McEvoy JP, *et al*. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med*, 353, 2005, 1209–1223.

Marder SR, West B, Lau GS, *et al*. Aripiprazole effects in patients with acute schizophrenia experiencing higher or lower agitation: a post hocanalysis of 4 randomized, placebo controlled clinical trials. *Journal of Clinical Psychiatry*, 68(5), 2007, 662-8.

Martindale. The Complete Drug Reference (34th Edition). In: Clowers W, editor. Great Britain: Suffolk 2005.

Moore TA, Buchanan RW, Buckley PF, *et al*. The Texas Medication Algorithm Project antipsychotic algorithm for schizophrenia: 2006update. *J Clin Psychiatry*, 68, 2004, 1751–1762.

Naranjo CA et al. Amethod for estimating the probability of adverse drugreactions. *Clin Pharmacol Ther*, 30, 1981, 239 – 245.

Ng B, Postlethwaite A, Rollnik J. Peripheral oedema in patients taking olanzapine. *Int Clin Psychopharmacol*, 18, 2003, 57–59.

Rajiv Tandon, Henry A. Nasrallah, Matcheri S. Keshavan. Schizophrenia, Just the Facts, 5. Treatment and prevention Past, present, and future. *Schizophrenia Research*, 122, 2010, 4-10.

Stahl SM. Antipsychotic Agents. Essential Psychopharmacology(2nd Edition); Cambridge University Press, 2000.

Yovtecheva SP, Yazel JJ. Olanzapine-Induced Bilateral Pedal Edema: A Case Report. *Gen Hosp Psychiatry*, 22(4), 2000, 290-291.