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OLANZAPINE INDUCED PEDEL EDEMA

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ABSTRACT

Olanzapine is commonly used atypical antipsychotic drug for schizophrenia and other psychotic disorders. Pedal edema is a rare side effect of olanzapine. As the definitive causes and further consequences of pedal edema due to olanzapine are not known, it is important to further study this side effect. This is a case report of two cases of pedal edema secondary to olanzapine. In both cases systemic causes of pedal edema were ruled out. On reducing the dose of olanzapine, pedal edema regressed and completely resolved after stopping the drug. So cause of edema can be attributed to olanzapine therapy.

Introduction:

Olanzapine, an atypical antipsychotic drug, is approved for treatment of schizophrenia, bipolar mania, maintenance therapy of bipolar disorder and psychosis in demented patients.[1] It is a selective monoaminergic antagonist with high affinity to serotonin (5-HT2A, 5-HT2C), dopamine (D1–4), muscarinic (M1–5), histamine (H1) and adrenergic (α1) receptors; and weak affinity to GABA-A and β-adrenergic receptors[2,3]. Most frequent side effects with olanzapine include constipation, dyspepsia, weight gain, drymouth, dizziness, somnolence, asthenia and insomnia, metabolic syndrome, extra pyramidal side effects[1]. In premarketing trials, peripheral edema was reported as an infrequent side effect, which affected 3% of the 532 olanzapine treated patients, as compared to 1% of the 294 subjects on placebo[1]. The following two cases demonstrate edema due to olanzapine.

Case History:

CASE 1

A 28 year old female patient reported with complaints of suspiciousness, fearfulness, withdrawn behavior, poor personal hygiene, poor oral intake, and muttering, since three months. According to DSM IV TR guidelines4, she was diagnosed to have schizophreniform Disorder. On admission clinical systemic examination and all baseline investigations i.e. complete blood count, random blood sugar, liver function test and renal function test were within normal range. The patient was prescribed olanzapine 10mg/day (5mg BD), which was increased to 15 mg/day (5mg TDS) on day 7. On 10th day, she complained of swelling of both feet associated with pain and burning sensation. And hence, all baseline investigations and chest X-ray, ECG, electrolytes, thyroid function test and urine routine and microscopy examination were done, which turned out normal. On 12th day after physician's opinion, diclofenac sodium 50mg BD was given for pain in sole. On day 17 frusemide was started with 80 mg per day. After seven days of frusemide treatment, edema improved markedly. But, with reduction in the dose of frusemide edema increased again.

Olanzapine was tapered and stopped, as no other cause for edema could be found. The edema disappeared over 10 days. She was then prescribed risperidone 4 mg per day and on subsequent follow up, it was found that the edema did not recur.

A repeat challenge with 5 mg of olanzapine was performed with omission of risperidone. Olanzapine rechallenge again resulted in edema within 4 days. The edema resolved spontaneously within a week of stopping olanzapine and did not require further diuretic treatment. Olanzapine was omitted with resumption of risperidone 4 mg per day. As patient was not having any psychotic symptoms for last three and a half months, risperidone was also omitted.

CASE 2:

A 37-year-old male patient presented with withdrawal symptoms due to alcohol. The history and mental status examination revealed fearfulness, aggressive behavior, work impairment, visual and auditory hallucinations, referential ideas and irritability since 1 month. According to DSM IV TR guidelines[4,] he was diagnosed as a case of Alcohol Dependence, Alcohol withdrawal syndrome and Alcohol induced psychotic disorder with prominent hallucinations. His withdrawal symptoms were treated with lorazepam 8mg on day 1 with gradually tapering to 2mg on day five. He was prescribed olanzapine 10 mg at bed time from third day of admission, for his psychotic symptoms. After 10 days of admission, patient was discharged with same treatment. During first follow up after 15 days, he complained of occasional fearfulness, ideas of reference and auditory and visual hallucinations. After one and half months of starting the treatment, patient complained of bilateral pedal edema. Clinical systemic examination, renal function tests, liver function tests, thyroid function tests and cardiac parameters were within normal limits. Based on experience of previous case & review of literature of pedal edema due to olanzapine, olanzapine was omitted and patient was treated with risperidone 4 mg per day. The edema reduced and disappeared over 7 days. A repeat challenge with 5 mg of olanzapine resulted in edema within 4 days, the edema resolved spontaneously within a week of stopping olanzapine. On subsequent follow up, the edema did not recur, and Risperidone was also discontinued after 1 month as patient was not having any psychotic symptoms.

Discussion:

In both the cases discussed above, since the edema regressed when olanzapine was tapered and stopped, edema can be attributed to olanzapine therapy. D. Deshauer et al, mentioned that patient was given low dose olanzapine along with frusemide for 5 months, after stoppage of Frusemide edema reappear, edema resolved when Olanzapine was discontinued[5.] In this case report, edema regressed with frusemide and completely resolved on stopping olanzapine. Further on repeat challenge with olanzapine, edema reappeared and again disappear after omitting olanzapine. Hence we can interpret that olanzapine has led to edema in both the patients. Ng B et al (2003) gives the following theoretical explanation of this phenomenon[6]:

1. Olanzapine blocks α1 receptors that peripherally result in vasodilation and decreased vascular resistance, which predisposes to edema.
2. The post receptor mechanisms for M1, H1 and 5-HT2 receptors include inositol-1, 4, 5-triphosphate (IP3), and diacylglycerol (DAG). The activation of these receptors increases IP3 and DAG. At the molecular level, IP3 binds to endoplasmic reticulum receptors, and causes a rapid release of calcium in favour of the calcium–calmodulin complex, which binds to enzymes regulating the ATP-dependent calcium pump. Olanzapine-induced blockade of these receptors can prevent the physiological increase of IP3, down regulate the ATP-dependent calcium pump, and secondarily reduce smooth muscle contractility, resulting in vasodilation and edema.
3. Olanzapine-induced 5-HT2 receptor blockade can potentially increase cyclic adenosine monophosphate (cAMP), which relaxes vascular smooth muscle through phosphorylation of myosin light chain kinase inhibition. A high cAMP plasma concentration has been found in patients with idiopathic edema in both the recumbent and upright positions.

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There is a possibility that the edema is not frequently found unless the patient spontaneously complaints or the physician intentionally looks for it. It is suggested that special care be taken when prescribing olanzapine to patients who are otherwise predisposed to develop edema[6.] Other antipsychotics also share the same mechanisms, it is necessary to rigorously monitor the adverse events of this group as a whole[7]. As side effect persists with continuation of olanzapine and disappears after omitting it, discontinuing olanzapine appears to be the best strategy.

REFERENCE

1. Zyprexa production leaßet; 2005. last accessed on 2010 Feb . | Available from:http://www.lilly.com.au/common/CMI/ZYPREXA%20.pdf. | 2. Stahl SM (2008). Antipsychotic Agents.Essential Psychopharmacology, 3rdedn. Cambridge University Press; pp. 327-451. | 3. Sadock BJ, Sadock VA.Kaplan and Sadock.s synopsis of Psychiatry. 10th ed. Philadelphia: Lippincott Williams and Wilkins; 2007. p. 1094. | 4. American Psychiatric Association Diagnostic and Statistical Manual of mental disorders 4th ed. Washington DC. American Psychiatric Association 2000. | 5. Deshauer D, Erwin L, Karagianis J. Edema related to Olanzapine therapy | Canadian Family Physician 2006;52: 620-1 | 6. Ng B, Postlethwaite A, Rollnik J. Peripheral oedema in patients taking Olanzapine. IntClinPsychopharmacol 2003;18:57-9. | 7. V Nayak, B Chogtu, V Devaramane, P.V. Bhandary: Pedal edema with olanzepine Indian J Pharmacol | Feb 2009 | Vol 41 | Issue 1 | 49-50