

A case Report On Duloxetine Poisoning



Medical Science

KEYWORDS :

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Case description

A 19 year old male medical student presented to Vadilal Sarabhai hospital with complain of palpitation and diaphoresis after taking heavy dose of duloxetine (15 tabs of 20 mg). Patient was prescribed the medicine for exam related anxiety and depression from private side. On examination patient was having heart rate of 128 per min and blood pressure of 158/100mm of Hg and pupils were dilated and temperature was 104 degree ferenheite. ECG showed sinus tachycardia mild QT prolongation.

Patient was immediately admitted to emergency room. A ryle's tube inserted and single dose of activated charcoal given to the patient and blood samples are drawn for routine and toxicological examination. For hyperthermia he was given cold water tepid sponging. During the primary treatment patient had an episode of general tonic clonic convulsion which was treated by intravenous administration of lorazepam and anti epileptic was not started.

When patient recovered from post ictal phase. Detailed neurological examination carried out, which showed occasional blepharospasm (focal myoclonus), resting tremors and rigidity in lower extremity. Cerebellar signs were also positive in lower limb which was evident by positive knee-heel test. However it was normal for hand coordination test.

Reports showed Normal Haemogram (Hb-11 gm%, Total WBC count-11,200/cumm, Platelet count-2.14 lacs/cumm) and normal all sera report except for clinically non significant hyponatremia (Random blood sugar 76 mg%, creatinine-0.98 mg%, urea-24 mg%, Sodium-126, potassium-4.5, and normal liver function profile). The value of CPK total was higher than normal.

He showed dramatic improvement over 24 hours. The next day heart rate was 90/min and blood pressure was 128/90mm Hg and ECG was showing normal sinus rhythm and patient's neurological assessment was completely normal. Patient was shifted to general ward and discharged from there on the very same day. Further recovery was completely uneventful and patient was counselled for suicide prevention.

Discussion:

Duloxetine is classified as an SNRI (serotonin and norepinephrine reuptake inhibitor). Venlafaxine and desvenlafaxine are other drugs of this group. These agents are non selective inhibitors of serotonin and norepinephrine reuptake with a very small dopamine reuptake inhibition. These drugs have no direct effect on pre synaptic and post synaptic neurotransmitter receptor.

The side effect profile is like that of selective serotonin reuptake inhibitors (SSRI). These includes headache, dizziness, weakness, fatigue, tremor and nervousness. Extra pyramidal side effects occurs because of varying degree effect on dopaminergic system involvement. It includes dystonic reaction, akathisia, dyskinesia, hypokinesia and even drug induced parkinsonism. GI complaints, such as nausea, diarrhoea, constipation, vomiting and anorexia. Other side effects less commonly reported are dry mouth, increased

sweating, blurred vision, hyponatremia and hypoglycemia.

Acute overdose toxicity:

SNRIs (serotonin/norepinephrine reuptake inhibitors) cause sympathetic nervous system stimulation via inhibition of norepinephrine reuptake, which predispose patient to tachycardia, hypertension, diaphoresis, tremor and mydriasis. Most of these effects are of moderate severity and can be usually managed with supportive care alone. Generalized seizure appear to be more common than SSRI. Patients frequently show alteration in level of consciousness, with moderate sedation being fairly common but coma is extremely rare.

ECG abnormalities are commonly reported following intentional overdose. Sinus tachycardia is the most common ECG abnormality observed. QRS widening and QT interval prolongation have also been reported. Although symptoms are more severe than SSRIs, the overall survival rate very favourable.

Serotonin syndrome:

Serotonin syndrome is potentially life threatening adverse drug reaction to serotonergic drugs. It can be produced by any drug or, more commonly, by a combination of drugs that increases central serotonin transmission. Serotonin syndrome is characterized by exposure to serotonergic medication plus alteration in cognition and behaviour, autonomic nervous system dysfunction. The stimulation of specific postsynaptic serotonin receptors is required for full expression of serotonin syndrome. The 5HT_{2A} is believed to be the primary receptor for this.

The important aspects of serotonin syndrome are that on one hand the diagnosis is very challenging because of nonspecific symptomatology. Mild cases are often misdiagnosed as other psychiatric and medical disorder and severe cases as neuroleptic malignant syndrome. On the other hand emergency physician inadvertently precipitate serotonin syndrome without proper recognition of patients at risk of developing serotonin syndrome by administering tramadol like drugs. Most studies overestimate the incidence and underestimate the severity.

Myoclonus is the most common finding in serotonin syndrome. A very important feature, because myoclonus is rarely seen in other condition that mimic serotonin syndrome.

Interestingly muscle rigidity when present is especially prominent in the lower extremities. Patient with ataxia should be carefully evaluated for lower extremity hypertonia. Seizures are always generalized and short lived. Hyperthermia is of moderate severity but if temperature is greater than 41 degree centigrade, is a marker of poor prognosis. Hypertension is twice more common than hypotension and is a marker of good prognosis.

There is no confirmatory laboratory test for serotonin syndrome that's why clinical suspicion is very important. It is also noteworthy that only 10% patients of serotonin syndrome have history of excessive inappropriate dose. Most of them are on standard therapeutic doses. Diagnosis is especially missed if patient is taking

SSRI or SNRI for indications other than depression.

The initial treatment consist of discontinuing all the drugs that can cause this syndrome and providing appropriate supportive care. But all patients with this disorder should be admitted and approximately 25% patient will require endotracheal intubation and ventilator support. 11% mortality rate has been noted in various studies. The most common cause of death is hyperthermia.

At present, there is no acceptable guideline for the use of serotonin antagonist in serotonin syndrome. Benzodiazepenes are non specific antagonists and can be used to decrease patient discomfort and promote muscle relaxation. Cyproheptadine appear to be the most effective antiserotonergic in humans. Unfortunately it is available only as an oral formulation. The initial dose is 4 to 12 milligrams per oral. Cyproheptadine therapy should be discontinued if no therapeutic symptomatic benefit observed after 32 milligram dose. Patients who respond to therapy should be given 4 milligrams every 6 hours till next 48 hours to prevent recurrence. Chlorpromazine is an antagonist of 5HT_{2A} receptor. Theoretically it is the best agent to treat serotonin syndrome and also available in parenteral form but it also blocks dopamine receptors which can promote muscle rigidity, lower seizure threshold and can exacerbate neuroleptic malignant syndrome.

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REFERENCE

- 1) Tintinalli's Emergency medicine 7th edition | 2) Harrison's textbook of internal medicine, 18th edition | 3) Mills KC: serotonin syndrome: a clinical update. Crit care Clin 13:764, 1997 | 4) Kortzan JA, Maclean R, Wade W et al: prevalence and pattern of concomitant use of serotonin reuptake inhibitors and other anti depressant in high cost poly pharmacy cohort. Clin Ther 24:237, 2007 | 5) Hedenmalm K, Guzey C, Dahl ML et al: risk factors for extrapyramidal symptoms during treatment with SSRI. J clin psychopharmacol 26:192, 2006. | 6) Isbister GK, Bowe SJ, Dawson AH, Whyte IM: relative toxicity of SSRI in overdose. J toxicol clin tox 42:277, 2004. | 7) Deecher DC, Beyer CE, Johnston G et al: desvenlafexin anew SNRI. J Pharmacol Exp Ther 318:657, 2006. | 8) Perahia DG, Pritchett YL, Kajdasz DK, et al: a randomized, double blind study of venlafexine and duloxetine in patient with major depressive disorder. J Psychiatr Res 42:22, 2008 |