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A Case of Serotonin Syndrome: Toxicity and Management of Overdose of Escitalopram - Case Report and Review of Literature

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Key Words:

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Abstract:

The serotonin syndrome is a potentially life-threatening adverse drug reaction that results from therapeutic drug use, intentional self-poisoning, or inadvertent interactions between drugs. It is identified through a particular dose-relevant spectrum of the clinical finding, that related to the serotonin free level (5-hydroxytryptamine [5-HT]), or the activation of 5-Ht receptor (predominantly 5-HT2A subtypes and the 5-HT1A), that further involves changes of mental state, autonomic hyperactivity and neuromuscular abnormalities. Critical serotonin syndrome is barely and in generally precipitated through the frequent initiation of multiple serotonergic drugs. Yet this specific syndrome could further arise afterwards single serotonergic drug initiations in the susceptible individual, the overall addition of third or second agents towards the long-standing doses of serotonergic drug maintenance or else afterwards an overdose.

Here we present a case of Escitalopram induced serotonin syndrome. A 24 year old female, in postpartum period, had alleged consumed multiple tablets of Escitalopram. The patient was admitted to ICU and treated. Patient improved over a period of 48 hours and was later discharged.

Here we present a case of Escitalopram induced serotonin syndrome. A 24 year old female, in postpartum period, had alleged consumed 4500 mg of Escitalopram. She was brought to emergency department of the hospital in a semi-conscious state. All the necessary measures were taken as per poisoning protocol, stomach wash given and the patient was later admitted to ICU and managed. Patient improved over a period of 48 hours and was later shifted to ward. A Psychiatrist opinion was taken and was diagnosed to be having post-partum depression. The patient was later discharged with follow-up medications.

1. Introduction

The syndrome of serotonin sometimes defined and elaborated as clinical triad of the mental changes such as neuromuscular activities and autonomic hyperactivity, yet not all the findings and indications are frequently presents among the all kinds of patient's alongwith this disorder. (table 1).[1,2] Excess serotonin signs are staying in a particular range from diarrhea and tremor within the mildcase towards delirium, hyperthermia and neuromascular rigidity in some life threatening case. The clinical difficulty is much mild symptoms, which might be overlooked beside drug addition with the proeterotonergic effect and causative agent dose might provoke and influence a rapid clinical deterioration.

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Altered mental status	-Agitation -Anxiety -Disorientation -Restlessness -Excitement
Neuromuscular abnormalities	-Tremors -Hyperreflexia -Clonus -Bilateral Babinski sign -Akathisia
Autonomic hyperactivity	-Tachycardia -Hypertension -Hyperthermia -Tachypnea -Mydriasis -Diaphoresis -Vomiting -Diarrhoea

Spectrum of Clinical Findings: (Table 1)

A noticeable amount of drugs along with drug combinations has properly associated through serotonin syndrome which is elaborated in table 2. These involves SSRIs, anti-migraine agents, antiemetics, weight-reduction agents, herbal products, abuse drugs, antibiotics, over-the-counter cough medicines, opiate analgesics, monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants; the medication withdrawal has further associated with this syndrome.[3-14]

Table 2. Drugs implicated in serotonin syndrome
– Selective serotonin-reuptake inhibitors: sertraline, paroxetine, fluoxetine, fluvoxamine, and citalopram
– Selective serotonin-reuptake inhibitors: sertraline, paroxetine, fluoxetine, fluvoxamine, and citalopram
– Monoamine oxidase inhibitors: phenelzine, moclobemide, clorgiline, and isocarboxazid

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Table 2. Drugs implicated in serotonin syndrome

– Anticonvulsants: valproic acid
– Analgesics: meperidine, fentanyl, tramadol, and pentazocine
– Antinausea medications: ondansetron, granisetron, and metoclopramide
– Migraine medications: triptans
– Antibiotics: linezolid and ritonavir
– Cough suppressants: dextromethorphan
– Drugs of abuse: methylenedioxymethamphetamine (MDMA aka "ecstasy"), lysergic acid diethylamide (LSD)
– Supplements and herbal products: tryptophan, St. John's wort, ginseng

A single SSRI therapeutic dose has been caused the serotonin syndrome.[5] However, the drug addition which inhibit the CYP3A4 and cytochrome isoforms CYP2D6 towards the therapeutic SSRI schemes had been associated through the condition.[7,15,16] Serotonergic agents administration among the five weeks, afterwards discontinuation of the fluoxetine therapy had created a particular drug culminating communication within serotonin syndrome, in all probability those outcome of the fluoxetine demethylation towards the norfluoxetine , however, a specific serotonergic metabolite alongside half-life longer serum compared to the s parent compound .[17] Particular drug similarly MAOIs , which are nonselective or irreversible or a subtype A of inhibit monoamine osidase, that are much strongly associated with extreme syndrome cases, in a particular extreme case of syndrome, generally when those agents are utilized in mixing with the SSRIs, dextromethorphan, mepiridine or methylenedioxymethamphetamine (MDMA, or "ecstasy").[4,6,18,19,20]

The syndrome of serotonin encloses specific ranges of the clinical findings and indications. Patients having the mild cases might afebrile yet can had tachycardia, beside a proper physical monitoring and examination, which is notable for the autonomic indications and findings and detection such as mydriasis, diaphoresis and shiverings (Fig. 2). The neurologic examination might discover the hyperreflexia, myoclonous as well as intermittent tremor.

A representative and proper example of medium cases of serotonin syndrome include various kinds of vital sign of abnormalities such as hyperthermia, hypertension and tachycardia. A core gig temperature such as 40 degree Celsius is common among intoxication. One of the most common characteristics of physical examinations are the sounds of hyperactive bowel, normal skin color, diaphoresis and mydriasis. Despite of fact that, the clonus and hyperreflexia has been seen within a medium cases might be greater among the lower extremities compared to upper extremities; patellar deep-tendons reflexes sometimes elaborate clonus for the numerous seconds afterwards a individual tap of this tendon. While on the other hand, brachioradialis reflex is barely enhanced. The Patients might be exhibit the ocular clonus which is horizontal. Various kinds of changes within the mental status involved slight pressured speech, hypervigilance as well mild agitations.

In comparison to, a specific extreme syndrome case of serotonin patients might had tachycardia and the hypertension which might abruptly degenerate within the frank shock. However, such kinds of patients might has hypertonicity, mascular rigidity as well as agitated delirium. However, the enhancement of the muscle tone is much more considerably much greater among lower extremities. The muscle hyperactivity might create a central temperature, which is higher than 41 degree Celsius among the few life-threatening cases. On the other hand, Laboratory abnormalities which arise in extreme cases involves disseminated

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intravascular coagulopathy, renal failure, seizures, elevated levels of creatinine and serum aminotransferase, rhabdomyolysis and metabolic acidosis.

For better delineating those symptoms and signs which mainly refer serotonin syndrome, this clinical indication and findings in the 2222 sequential self-poisoning consecutive cases with the serotonin drugs was rigorously assessed according to the information and data through detailed toxicology registry.[21] Those major findings and decisions which has statistically signifant connation with syndrome diagnosis , that were mainly neuromuscular. It involves shivering, peripheral hypertonicity, spontaneous clonus, ocular clonus, myoclonus, inducible clonus, and hyperreflexia. [21] These main findings was then it get compared with the "gold standard", the assignment of the serotonin syndrome diagnosis through a medical toxicologist.[21] Autonomic derangements was tachycardia among admission, diarrhea, presence of the bowel sound, diaphoresis and mydriasis. [21] Abnormalities in the mental status, which are significantly in combination with serotonin syndrome were delirium and agitation. [21]

Hyperthermia was mainly caused through the muscular hypertonicity, which defined and elaborated in this study paper, as a more than 38 degree Celsius temperature, that was not as powerfully get along with the serotonin syndrome diagnosis, yet it occurred severely in some intoxicated patients.[21 The onset symptoms is generally fast, alongside clinical findings and sometimes it occurs within minutes after self-poisoning or medication changes. [22] Approximately 60 percent patients along with syndrome of serotonin present among six hours afterwards the utilization of changing in dosing, an overdose and general uses of medication.[22] Patients with the slight manifestations might represent with chronic or subacute symptoms, where the extreme cases might progress rapidly towards the death. The syndrome of serotonin is not particularly believed towards spontaneously resolve as long the participating agents get carry to be administrated.

2. Case Report

A 24 year old female patient with lack of medical history beside recent history of the delivery of a healthy male baby 4 months ago was brought to casualty department in an altered sensorium. Upon further enquires she was found to have consumed multiple tablets of Escitalopram, a total dose of 4500mg. Stomach wash given. Patient admitted to ICU.

We used Hunter Toxicity Criteria to diagnose serotonin syndrome.[21]

To fulfil the Hunter Criteria, a patient must have taken a erotogenic agent and meet ONE of the following conditions:

*Spontaneous clonus

*Inducible clonus PLUS agitation or diaphoresis

*Ocular clonus PLUS agitation or diaphoresis

*Tremor PLUS hyperreflexia

*Hypertonia PLUS temperature above 38ºC PLUS ocular clonus or inducible clonus

Continuous cardiac monitoring done with supportive care. QT interval was recorded regularly in ECG which was normal. On examination the patient was delirious, pupils dilated, deep tendon reflexes exaggerated, ankle clonus was present. A loading dose of Magnesium sulphate 2 gm IV was given prophylactically. And Cyproheptadine 12 mg stat followed by 2 mg bid dose was administered through nasogastric tube. Patient improved over 48 hours after admission. Laboratory parameters monitored regularly, all within normal limits during the course of hospital stay. A Psychiatrist consultation was taken before discharge, was diagnosed to be having Post-partum Depression. She was started on a small dose of oral Benzodiazepine. Tolerated the medication well. She was later discharged and followed up. Patient is doing well now.

3. Discussion

Serotonin syndrome is a fatal condition unless treated on time. Hence it is very important to identify the manifestations of the disease and treat at the earliest. Patient on serotinergic drugs should be on regular follow up. If more than one serotinergic drugs are used, always use with caution. If the patient develops even the mildest form of symptoms of serotonin syndrome it is best to stop the treatment with the drug and switch to alternate pharmacological options.

For mild symptoms: Patient may present with twitching, tremors and anxiety. Treatment is to stop the of-

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fending agents and giving supportive care to the patient with intravenous fluids, correction of vital signs and treating with a benzodiazepine. Patients should be admitted and kept under observation for 12-24 hours.

For moderate to severe symptoms: Patients can present with irritability, confusion, altered sensorium. Examination may reveal hyperreflexia, clonus, hypertension, tachycardia, mydriasis, hyperthermia. Patients can have tonic clonicseizures.It is advisable to admit the patient in Intensive Care Unit. In severe cases, patients should be paralyzed, sedated and intubated. Standard cooling measures should be used for hyperthermia.

There are no standard guidelines for treatment of serotonin syndrome. Serotonin antagonists like Cyproheptadine (5-HT2A antagonist), Chlorpromazine (5-HT1A and 5-HT2A antagonist) have been used in managing cases of serotonin syndrome.

In our patient we have used Cyproheptadine which is a potent 5-HT2A antagonists. Since the drug is only available in tablet form, it was powdered and adistered via nasogastric tube. Dose administered was 12 mg, followed by 2mg bid.

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