

# SEROTONIN SYNDROME IN A POSTOPERATIVE CARDIAC SURGICAL PATIENT

- A Case Report -

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## Abstract

Depression is common in patients with ischemic heart disease. According to mental health survey approximately one fifth of the patients with angiographic evidence of coronary artery disease have major depression<sup>1</sup>. It is well recognized that stigmatization of mental disorders leads to stigmatized individuals to avoid treatment or to conceal treatment. We report a case of serotonin syndrome that occurred during postoperative period in a patient who underwent coronary artery bypass grafting. The patient was receiving 60 mg/day fluoxetine since the last four years which she and her attendants concealed during the preoperative evaluation. To our knowledge this is the first case in a postoperative patient reported in biomedical literature. We suggest that history taking should be done with special emphasis on antidepressant drug intake in patients suffering from coronary artery disease. If serotonin syndrome occurs in these patients aggressive and timely management can save the patient.

## Case Report

A 57 year old female admitted to our coronary care unit with the complaint of severe chest pain radiating to left arm and diaphoresis. She was a known hypertensive and on oral metoprolol 100mg/day since the last seven years period. On examination she was found to be tachypneic, pulse rate 110/minute, regular, normal volume, blood pressure 165/95 mmHg. Examination of other systems revealed no abnormalities. Her biochemical parameters were found to be within normal limits. Troponin-T value was found to be strongly positive. After initial stabilization, she underwent coronary angiography and found to be suffering from triple vessel disease with > 80% blockade of all the major coronary vessels. Surgical correction was planned and she was taken for it one week later.

She was premedicated with one tablet diazepam 10 mg the night before, 5 mg in the morning orally and injection of morphine sulfate 0.2 mg/kg and phenergan 25 mg intramuscularly one hour before surgery. One tablet metoprolol 50 mg was continued on the morning of surgery. The anaesthesia and induction and maintenance regimen included thiopentone sodium, midazolam, fentanyl, rocuronium and pancuronium. Coronary artery bypass grafting was done under moderate

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hypothermia and cold blood cardioplegia. The patient was weaned off successfully from cardiopulmonary bypass under the cover of nitroglycerine infusion and shifted to postoperative cardiac surgical intensive care unit. She was extubated six hours after surgery. She was found to be comfortable, breathing normally, blood pressure of 118/68mmHg, pulse rate 67/minute, SaO<sub>2</sub> 97% in room air. Two hours later she was found to be agitated, had sudden increase in blood pressure to 200/100mmHg and diaphoresis. As the last dose of fentanyl was administered three hours before extubation, pain factor was considered and she was administered 1 µ/kg body weight fentanyl to get a quick relief from symptoms. However instead of relief she developed myoclonus, headache, nausea and vomiting. An infusion of nitroglycerine 1 µ/kg/hour was started to reduce the blood pressure. A possibility of neurological complication related to cardiopulmonary bypass was thought and an emergency CT scan of the head was done which revealed no abnormality. In the mean while the family members were informed regarding the problem and the possible outcome. This time her husband revealed the fact that she was under fluoxetine 60 mg/day therapy since the last eighteen weeks. At this point of time a possibility of serotonin syndrome was diagnosed. Injection of diazepam 5 mg was administered intravenously and cyproheptadine 20 mg orally to reduce the symptoms. The improvement in symptoms was noticed within four hours and complete resolution was happened within 30 hours period. Fluoxetine therapy was resumed after 36 hours with a reduced dose of 40 mg/day after a psychiatric consultation. The remaining postoperative course was uneventful and she was discharged from hospital on 8<sup>th</sup> postoperative day.

## Discussion

The stigma of mental illness has often been considered a potential cause for reluctant willingness to seek help for mental problems, avoid the treatment or to hide the treatment. Among the mental illnesses, clinical depression is a very common psychological problem especially in patients suffering from coronary artery disease.<sup>2</sup> Medications used for depression are increasing in number and effectiveness, meaning more patients may benefit. While antidepressant medications

help the illness that, until a few years ago, had never been treatable with drugs before, keeping track of all possible adverse effects and drug interactions from these medications is becoming more difficult.

All antidepressants have potential side effects, although not every one will experience all of them or to same degree<sup>3</sup>. Serotonin re-uptake inhibitors (SSRIs) are a family of antidepressants considered to be the current standard of drug treatment for major depression. Fluoxetine was the first selective serotonin re-uptake inhibitor to be widely available for treatment of depression and numerous other neuropsychiatric disorders. Its attributes have been described in numerous scientific papers, and it has been the subject of a considerable volume of lay press. Fluoxetine is generally safe and well-tolerated. Common adverse events reported with the recommended dose of 20 mg/day are referable to the gastrointestinal system and the nervous system. The approved dose range is up to 80 mg/day, and when higher doses are used, adverse events are more common<sup>4</sup>. It is an inhibitor of cytochrome P450 (CYP) 2D6 and other CYP enzymes, which increases the potential for drug interactions. However, most of these are not clinically important.

These antidepressants have fewer adverse events than the tricyclic antidepressants or MAOIs.<sup>5</sup> Among all the side effects serotonin syndrome is a potentially life threatening complication of SSRI therapy. The syndrome is produced most often by the concurrent use of two or more drugs that increase brainstem serotonin activity and is often unrecognized without specific nature of its symptomatology. The physiopathological hypothesis is principally supported by excess stimulation of the central (5HT1a) serotonin receptors. This syndrome is characterized by alterations in cognition, behavior, autonomic nervous system function and neuromuscular activity<sup>5</sup>. The symptoms can be: mild (may or may not concern the patient); moderate (toxicity which causes significant distress and deserves treatment, but is not life-threatening); or severe (a medical emergency characterized by rapid onset of severe hyperthermia, muscle rigidity and multiple organ failure). Diagnosis of serotonin toxicity is often made on the basis of the presence of at least three of Sternbach's 10 clinical features<sup>7</sup>. Prevention of the syndrome and its early discovery is essential.

Several non-selective anti-serotonin treatments have been tested without much success. Withdrawal of the imputable drugs often resolves the symptoms within 24 hours. Symptomatic and supportive care remains the pillar to treatment. While reviewing the literature regarding the treatment of serotonin syndrome, the authors gather some evidence suggesting the efficacy of chlorpromazine and cyproheptadine in the treatment of serotonin syndrome. The evidence for cyproheptadine is less substantial, perhaps because the dose of cyproheptadine necessary to ensure blockade of brain 5-HT<sub>2</sub> receptors is 20-30 mg, which is higher than that used in the cases reported to date (4-16 mg)<sup>8</sup>. Our patient responded to a dose of 20 mg cyproheptadine and 5mg diazepam. There are few

case reports supporting serotonin syndrome caused by fluoxetine but none in a postoperative patient or with the use of fentanyl<sup>9,10</sup>.

Due to the increasing availability of agents with serotonergic activity, physicians need to be more aware of serotonin syndrome. The following case highlights the complex nature in which serotonin syndrome can arise, as well as the proper recognition and treatment of a potentially life-threatening yet easily avoidable condition. The authors also give importance to the fact that history taking in a patient suffering from coronary artery disease should emphasize on the antidepressant medication intake.

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