Naltrexone Induced Serotonin Syndrome

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Background*:* Serotonin syndrome resulted from hyperactivity of serotonin in nervous system and is potentially life threatening. Tramadol is known as one it's causing factors. Administration of Naltrexone is associated with a significant increase in the ratio of 5-HIAA/5-HT and DOPAC/DA in the frontal cortex and dorsal hippocampus respectively. We present a rare case with some signs of serotonin syndrome and withdrawal syndrome which simultaneously use naltrexone, tramadol and benzodiazepine in the realm of opium addiction.

Case Report: A 41 years old man who was admitted due to loss of consciousness and seizure.

In simultaneous usage of naltrexone, tramadol and benzodiazepine in an addicted person, and in the case of sever agitation which was resistance to routine treatments, serotonin syndrome beside withdrawal syndrome should be considered and its treatment should be done as soon as possible.

Conclusion: In simultaneous usage of naltrexone, tramadol and benzodiazepine in an addicted person, and in the case of sever agitation which was resistance to routine treatments, serotonin syndrome beside withdrawal syndrome should be considered and its treatment should be done as soon as possible.

►*Implication for health policy/practice/research/medical education:*
Naltrexone Induced Serotonin Syndrome

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1. Introduction:

Serotonin syndrome resulted from excessive activity of serotonin in the nervous system and is potentially life threatening. Tramadol is known as one of the causes of this syndrome. We present this case as rare case with some signs of serotonin syndrome and withdrawal syndrome which simultaneously use naltrexone, tramadol and benzodiazepine in the realm of opium addiction (1, 2).

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2. Case Report:

The patient is a 41 years old man which was admitted on 13.9.2012, at 6 pm, with agitation in toxicity emergency center. In taken history, he was found in the bathroom with loss of consciousness and seizure in the morning and transferred to hospital by his entourage. He was addicted to opium and using Tramadol from 8 years

ago. Empty cartridges of benzodiazepine and tramadol were found beside him. In clinical examination, loss of consciousness (Glasgow Coma Scale (GCS)=10-11.15) and severe agitation was found. Pupils were mydriasis with low response to light and he was sweating. Tachycardia was detected with normal sound (s1 and s2). Lung sound was normal. Abdomen was not tenderness and normal bowel sound (BS) was sound. In Neurologic examination, no myoclonus appeared. Deep tendon reflex (DTR) of both sides was normal and symmetric. The reflex of sole (Babinski) was downward and symmetrical in both sides. Ecchymosis was evident on right and left arm and also on right foot. In ECG, sinus Tachycardia had presented and urine screen shows positive Benzodiazepine (BZD).

Blood Pressure (BP): 100.65 mmHg
Pulse Rate (PR): 105 per minute
Respiratory Rate (RR): 14 per minute
Temperature (T): 37.5°C
Blood Sugar (BS): 107 milligrams (mg) with glucometer

Toxicity management had done for patient. Foley catheter prepared. Diazepam was ordered for agitation. Chest X ray (CXR) and brain computerized tomography (CT) was requested and patient was admitted in intensive care unit (ICU).

CXR on 14.10.2012: Lung with normal appearance. No pneumonia and nodule was seen.

Brain CT on 14.10.2012: No hemorrhage or abnormal changes was seen. In Cranial CT, no rapture or displacement was seen.

On 14.10.2012, Diazepam, Ranitidine, Plazil, and methadone were ordered for patient. He went under oxygen therapy with mask. Glucometer was ordered each 6 hours and he went under I/O chart.

Because of severe agitation morphine was ordered for patient and he went under Midazolam treatment. His agitation was continued. Chlorpromazine was ordered for him and he discomforted from his catheter. He became calm after using lidocaine in sterile form in urine duct.

Urine Analysis:

Potential of Hydrogen (PH): 6 Red
Blood Cell: Many
Arterial Blood Gas: Acceptable
Specific Gravity: 1025
Bacteria: Few
Blood: +3
White Blood Cell (WBC): 6-8 per Microliter (µl)

On 14.9.2012, agitation continues. Drug orders were prescribes. He was febrile and was suffering from restlessness and insomnia. He received serum treatment for 4 liters in 24 hours, because of rabdomiolisis. Urine culture (U/C) and Blood culture (B/C) was requested.

On 15.9.2012, agitation reduced but he had rabdomiolisis. He was also febrile. He received dextrose water 5% in 24 hours with Lasix and potassium in the serum. Diclofenac Suppository was ordered.

WBC: 20.4 per Microliter (µl)
Potassium (K): 3.2 milligram (mg)
Blood Urea Nitrogen (BUN): 19 mg/dL
Creatine phosphokinase (CPK): 18839 U/L (units per liter)
Calcium (Ca): 8.4 mg
Creatine (Cr): 0.9 mg/dL
Creatine phosphokinase, muscle band (CPKMB): 167 U/L (units per liter)
PH: 2.3
Aspartate aminotransferase (AST): 274 U/L
Alanine aminotransferase (ALT): 85 U/L

On 16.9.2012, WBC: 19.1 per Microliter (µl)
Ca: 8 mg
CPK: 5559 U/L (units per liter)
Natrium (Na): 135 mg
AST: 123 U/L
K: 3.4 mg
ALT: 6 U/L

On 17.9.2012, his fever still persists but his general condition was acceptable and he answers the questions well.

WBC: 14.3 per Microliter (µl)
CPK: 5024 U/L (units per liter)
Ca: 9.8 mg
Na: 140 mg
K: 3.9 mg
ABG: Acceptable
Vital sign: Stable

On 18.9.2012, he transferred to the ward.
WBC: 11.700 per Microliter (µl)
AST: 117 U/L
Urine Culture (U/C): -
ALT: 69 U/L
CPK: 2538 U/L
On 19.9.2012, his general condition was well and tests were normal and under physician suggestion he was discharged.

3. Discussion:

In this case, despite using tramadol, oral benzodiazepine and inhaled opium, only benzodiazepines can be detected urine screening test, that according to the high false negative test and the lack of a gas chromatographic mass spectrophotometry, the accuracy of using these drugs is relied only on the history which taken from patient. Based on Sternbach diagnostic criteria, we need 3 signs of the 10, in the field of serotonergic substance for diagnosing serotonin syndrome. These 10 signs are agitation, diaphoresis, hyper reflex, ataxia, confusion, hypomania, myoclonus, shivering and tremor (2), (4).
Diagnostic criteria for serotonin syndrome due to Gold frank Sare in two groups, (major & minor) that at least 4 major symptoms or 3 major plus 2 minor symptoms is necessary to diagnosis (9).In this case, 4 major symptoms (Altered level of consciousness, elevated mood, sweating and fever) and 4 minor symptoms (restlessness, insomnia, mydriasis and tachycardia) was seen which can be diagnostic for serotonin syndrome. One case of SS due to using naltrexone is reported that FDA approved him. (8)
In this report our patient was suffered from serotonin syndrome; although there were other signs such as mydriasis and tachycardia. Despite using benzodiazepine, the patient's temperature was not above than 38.5 and musculoskeletal symptoms such as myoclonus and tremor were masked (2). Incidence and duration of symptoms in the case of chronological fact, as well as the lack of response to benzodiazepines and continuation of rhabdomyolysis, makes it more probable diagnosis of serotonin syndrome (4). Although naltrexone is antagonistic of opium, and has the capacity of withdrawal syndrome, but above mentioned signs in patient, shows serotonin syndrome.

4. Conclusion:

In simultaneous usage of naltrexone, tramadol and benzodiazepine in an addicted person, and in the case of sever agitation which was resistance to routine treatments, serotonin syndrome beside withdrawal syndrome should be considered and its treatment should be done as soon as possible.

References

1. Takeshita J. Serotonin syndrome associated with tramadol. prim care companion J clin psychiatry. 2009;11(5):173.
2. Frank CH. Recognition and treatment of serotonin syndrome. MFC J. 2008;54(7):988-992.
3. Sanson R. Tramadol. Psychiatry (Edgmont) j. 2009;6(4):17-21.
4. Ables A. Prevention diagnosis and management of serotonin syndrome. American family physician j. 2010;81(9):1139-1141.
5. Dimatelis J, Russell VA. The effects of lobe line and naltrexone on methamphetamine-induced place preference and striatal dopamine and serotonin levels in adolescent rats with a history of maternal separation. Springer for Research & Development. 27(3): 351-361.
6. Sharma TR, Chan WC, Gintzler AR. Effect of chronic naltrexone administration and its withdrawal on the regional activity of neurons that contain norepinephrine, dopamine and serotonin. Brain Res. 1988;442(2):379-86.
7. Isenberg D, Wong SC, Curtis JA. Serotonin syndrome triggered by a single dose of suboxone. Am J Emerg Med. 2008;26(7):840:3-5.
8. eHealthMe-Real World Drug Outcomes. http://www.ehealthme.com
9. Hoffman R, Nelson L, Howland M, et all. Goldfranks manual of Toxicologic Emergencies. New York: McGraw-Hill companies. 2007;607-559.