

UC Irvine

Clinical Practice and Cases in Emergency Medicine

Title

Serotonin Syndrome Triggered by Increasing the Dose of Quetiapine

Permalink

<https://escholarship.org/uc/item/0m32v39j>

Journal

Clinical Practice and Cases in Emergency Medicine, 5(3)

Authors

Miyamatsu, Yayoi
Tanizaki, Ryutaro

Publication Date

2021

DOI

10.5811/cpcem.2021.5.52505

Supplemental Material

<https://escholarship.org/uc/item/0m32v39j#supplemental>

Copyright Information

Copyright 2021 by the author(s). This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

Serotonin Syndrome Triggered by Increasing the Dose of Quetiapine

Yayoi Miyamatsu, MD*
Ryutaro Tanizaki MD, PhD*†

*Nabari City Hospital, Department of Internal Medicine, Nabari, Japan
†Mie University School of Medicine, Department of Community Medicine, Nabari, Japan

Section Editor: Rick McPheeters, DO

Submission history: Submitted March 18, 2021; Revision received May 12, 2021; Accepted May 10, 2021

Electronically published August 5, 2021

Full text available through open access at http://escholarship.org/uc/uciem_cpem

DOI: 10.5811/cpcem.2021.5.52505

Case presentation: An 85-year-old woman with a history of depression treated with polypharmacy including selective serotonin reuptake inhibitor presented to the emergency department with head, and upper and lower limb tremors four hours after increasing the dose of quetiapine from 12.5 milligrams (mg) per day to 25 mg/day. She was diagnosed with serotonin syndrome (SS), and all medications except clonazepam were discontinued. The symptoms subsided within 48 hours.

Discussion: The use of atypical antipsychotics alone seldom increases the risk of SS. However, combining atypical antipsychotics with serotonergic agents increases the risk of SS because the activity of serotonin receptor subtype 1A is relatively enhanced. This report suggests that physicians should be aware that even a small increase in quetiapine could pose a risk of developing SS. [Clin Pract Cases Emerg Med. 2021;5(3):365–366.]

Keywords: *serotonin syndrome; quetiapine; tremor; neuroleptic malignant syndrome.*

CASE PRESENTATION

An 85-year-old woman presented to the emergency department with acute head and upper and lower limb tremors and agitation. She had a long history of major depressive disorder and insomnia, which were treated with escitalopram 20 milligrams (mg) per day, mirtazapine 30 mg/day, sulpiride 20 mg/day, olanzapine 2.5 mg/day, quetiapine 12.5 mg/day, and clonazepam 5 mg/day. Her symptoms occurred four hours after the dose of quetiapine was increased from 12.5 to 25 mg/day by her psychiatrist to improve her insomnia. All doses had remained unchanged except for that of quetiapine. Physical examination revealed fever of 39.1°C, tachycardia, agitation, mydriasis, deep tendon hyperreflexia, and symmetrical tremor of the head, and upper and lower limbs that lasted for 15 seconds and repeated at five-second intervals (video).

There was no muscular rigidity. Laboratory findings showed normal white blood cells, C-reactive protein, and creatinine phosphokinase levels. A computed tomography of the head was performed and did not reveal any significant abnormalities. Serotonin syndrome (SS) was then diagnosed

based on the Hunter Serotonin Toxicity Criteria,¹ and she was admitted to our hospital. All medications except clonazepam were discontinued, and the symptoms subsided within 48 hours.

DISCUSSION

Serotonin syndrome is related to overstimulation of a serotonin receptor subtype 1A (5-HT_{1A}), commonly caused by the use of serotonergic agents.¹ Quetiapine is an atypical antipsychotic agent that exhibits serotonergic receptor 5-HT_{2A} antagonism, which has a short half-life and is often used to manage agitation and psychotic symptoms in hyperactive delirium.² The use of atypical antipsychotics alone seldom increases the risk of SS; specifically, there is a lower risk of SS on treatment with quetiapine because it is a significantly weaker 5-HT_{2A} antagonist than other atypical antipsychotics.³ However, combining atypical antipsychotics and serotonergic agents increases the risk of SS because the activity of 5-HT_{1A} is relatively enhanced.

Furthermore, because quetiapine also exhibits a dopaminergic D2 receptor antagonism, which may cause

neuroleptic malignant syndrome (NMS),⁴ it was necessary to differentiate between SS and NMS in this patient. In general, agitation, diarrhea, mydriasis, myoclonus, and hyperreflexia are more frequent in SS, whereas dysphagia, hypersalivation, incontinence, hyperthermia, akinesia, lead pipe rigidity, and rhabdomyolysis are characteristics of NMS.⁵ Thus, it is not challenging to differentiate between SS and NMS in a patient with typical symptoms. However, it should be noted that atypical NMS, which lacks typical NMS symptoms, cannot be excluded based on the symptoms alone. The significant difference between SS and NMS is time to onset. Neuroleptic malignant syndrome generally appears within seven days following the introduction of a neuroleptic agent, whereas SS develops rapidly within 24 hours following the introduction of a serotonergic agent.⁵ In this patient, the diagnosis of SS was made because of rapid onset four hours after increasing the dose of quetiapine, in addition to her symptoms being consistent with the Hunter criteria.¹

Management of SS mainly involves supportive care, the discontinuation of serotonergic drugs, and treatment with benzodiazepines. Immediate sedation, neuromuscular paralysis, and orotracheal intubation are performed in severe cases.³ In this patient, all medications except clonazepam were discontinued, and the symptoms resolved within 48 hours. Although quetiapine has a lower risk of SS than other atypical antipsychotics, physicians should be aware that even a small increase in quetiapine could pose a risk of developing SS.

Video. An agitated patient, repeatedly calling the unidentified name “Etsuko,” and demonstrating intermittent tremor of her head, and upper and lower limbs after escalation of her quetiapine dose

Patient consent has been obtained and filed for the publication of this case report. The authors attest that their institution does not require Institutional Review Board approval for publication of this case report. Documentation on file.

REFERENCES

1. Dunkley EJ, Isbister GK, Sibbritt D, et al. The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. *QJM*. 2003;96(9):635-42.
2. Hatta K, Kishi Y, Wada K, et al. Antipsychotics for delirium in the general hospital setting in consecutive 2453 inpatients: a prospective observational study. *Int J Geriatr Psychiatry*. 2014;29(3):253-62.
3. Boyer EW and Shannon M. The serotonin syndrome. *N Engl J Med*. 2005;352(11):1112-20.
4. Trollor JN, Chen X, Sachdev PS. Neuroleptic malignant syndrome associated with atypical antipsychotic drugs. *CNS Drugs*. 2009;23(6):477-92.
5. Birnes P, Coppin D, Schmitt L, et al. Serotonin syndrome: a brief review. *CMAJ*. 2003;168:1439-42.

*CPC-EM Capsule *Pending**

What do we already know about this clinical entity?

Serotonin syndrome is commonly caused by serotonergic agents.

What is the major impact of the image(s)?

Even a small increase in quetiapine could cause serotonin syndrome in patients taking serotonergic agents.

How might this improve emergency medicine practice?

Physicians in the emergency department can recognize that even a small increase in quetiapine could pose a risk of developing serotonin syndrome.

Address for Correspondence: Ryutaro Tanizaki, MD, PhD, Ise Municipal General Hospital, Department of Internal Medicine, 3038, Kusubecho, Ise, Mie, 516-0014, Japan. Email: rtanizaki@hospital.ise.mie.jp.

Conflicts of Interest: By the CPC-EM article submission agreement, all authors are required to disclose all affiliations, funding sources and financial or management relationships that could be perceived as potential sources of bias. The authors disclosed none.

Copyright: © 2021 Miyamatsu et al. This is an open access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) License. See: <http://creativecommons.org/licenses/by/4.0/>