

Serotonin syndrome in a 27-year-old female in the context of therapeutic titration of sertraline

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Serotonin syndrome is a life-threatening medical emergency that can result from serotonergic drugs used to treat neuropsychiatric disorders. Serotonin acts on receptors throughout the body, and at an excess level can result in the triad of symptoms associated with serotonin syndrome: altered mental status, autonomic nervous system instability, and neuromuscular hyperactivity.¹

We report a case of serotonin syndrome in a 27-year-old female admitted to our inpatient psychiatric unit with major depressive disorder and worsening suicidal ideation, undergoing a therapeutic titration of the selective serotonin reuptake inhibitor, sertraline. Given the patient's persistent symptoms of depression and suicidal ideation, on hospital Day 6, the patient was started on sertraline (50 mg), added to prior-to-admission medications of trazodone (50 mg), and lisdexamfetamine (70 mg). Two days after the initiation of sertraline (50 mg), she reported abdominal pain and hand tremors that lasted most of the day and resolved without treatment. The patient reported having similar symptoms from past antidepressant medication trials.

Given her symptoms, the treatment team waited until their resolution on Day 9 of her hospitalization to increase her sertraline to 100 mg daily. The next day, we increased her dose of lamotrigine to 300 mg daily. Two days later, on hospital Day 12, her dose of sertraline was increased to 150 mg daily; she reported tolerating the dose increase. On hospital Day 13, the patient reported new-onset bilateral hand tremor. In addition to her bilateral hand tremors, the patient had dilated pupils, diaphoretic palms, clonus in the left ankle,

and bilateral hyperreflexia at the knees and ankles. The patient's new symptoms were concerning for serotonin syndrome.

The diagnosis of serotonin syndrome is clinical, with no specific set of laboratory tests to confirm it. However, The Hunter Serotonin Toxicity criteria is a validated measure that can be used to diagnose serotonin syndrome with a sensitivity of 84% and a specificity of 97%.² The Hunter criteria necessitate the following: (1) recent addition or increase of a serotonergic drug; (2) rule out other potential medical causes; and (3) no recent changes to a neuroleptic substance, as well as \geq three of the following signs: mental status changes, agitation, myoclonus, hyperreflexia, diaphoresis, shivering, tremor, diarrhea, incoordination, and fever.²

Our patient met the criteria, with symptoms of palmar diaphoresis, myoclonus, hyperreflexia, and tremor. The differential diagnosis for serotonin syndrome is broad and includes anticholinergic syndrome, malignant hyperthermia, and neuroleptic malignant syndrome.¹ To differentiate these conditions from serotonin syndrome, the causative agent and signs and symptoms are key components. Anticholinergic syndrome is associated with the use of anticholinergic agents and is characterized by fever, mydriasis, dry mouth, delirium, and urinary retention. Serotonin syndrome is characterized by hyperreflexia and hyperactive bowel sounds. In contrast, anticholinergic syndrome is associated with normal reflexes and hypoactive bowel sounds.¹

Malignant hyperthermia is a result of a reaction to inhalational anesthetic agents resulting in hyperthermia. Malignant hyperthermia results in skeletal muscle rigidity and hyporeflexia.¹ Neuroleptic malignant syndrome traditionally develops over the course of several days in response

to neuroleptic drugs, resulting in altered mental status, bradykinesia or akinesia, muscular rigidity, and hyperthermia. A distinguishing factor between neuroleptic malignant syndrome and serotonin syndrome is the presence of bradykinesia in the former and hyperkinesia in the latter.¹

Due to our concern for serotonin syndrome, we treated the patient with 8 mg of cyproheptadine, an antihistamine drug commonly used to treat serotonin syndrome,³ and consulted the internal medicine team. The patient was transferred to the medical unit and diagnosed with serotonin syndrome, given her symptoms of tremors and hyperreflexia. During her hospitalization on the medical unit, she received an additional 4 mg of cyproheptadine, and sertraline and trazadone were discontinued. On hospital Day 16, she was deemed medically stable and appropriate for return to the inpatient psychiatric unit for further management of her depressive symptoms; she was started on bupropion to treat her symptoms of depression and suicidal ideation.

The combination of multiple drugs to target specific psychiatric symptoms is a common practice in the care of patients.¹ Medical practice aims to integrate patient symptoms and treatment responses to develop a care plan. In our patient, the serotonergic drugs used for disease management were within approved therapeutic ranges; however, the patient developed serotonin syndrome. This case provides insight into a rare response to common therapeutic drugs seen in the inpatient psychiatric setting. Furthermore, it highlights the importance of being aware of the signs and symptoms of serotonin

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syndrome even in the setting of therapeutic dose ranges of serotonergic drugs, and of integrating collaborative care plans from multiple teams within the hospital setting to ensure optimal patient outcomes. **MM**

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Primary care, the PSA test, and excess surgery: Does da Vinci robot acquisition lead to more prostatectomy?

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The prostate-specific antigen (PSA) is commonly ordered by primary care providers (PCPs) and may lead to unnecessary surgery, especially in the setting of new and expensive treatment modalities. The da Vinci robot has been widely adopted for radical prostatectomy (RP) after FDA approval in 2001. Prior work has associated acquisition of the robot with an increased absolute number of RPs at the state and regional level. We examined this association nationally using population-based RP rates from the Dartmouth Atlas, data which are derived from fee-for-service Medicare patients.

Methods

Publicly available age- and race-adjusted RP rate data for all 306 hospital referral regions (HRRs) of the Dartmouth Atlas were obtained for a pre-robotic period selected from 1999 to 2001 and a post-robotic period selected from 2008 to 2010. Total number of male Medicare beneficiaries in each HRR were also obtained (denominator for creating the da Vinci robot rate). Total da Vinci robot counts in each of the 306 HRRs were provided by Intuitive Surgical for 2008 only, and for each HRR, the total robot count was turned into a rate per 100,000 male Medicare beneficiaries. The HRR RP rate change was created by subtracting pre- and post-robotic RP rates. The HRR da Vinci robot rate change was created by using the 2008 da Vinci robot rate with an assumption that the pre-robotic rate was 0. HRRs with fewer than 26,783 male Medicare beneficiaries (50th percentile) were excluded to eliminate unstable or suppressed RP rates. Simple linear regression was used to assess association between the two variables. Two sensitivity analyses were done and excluded

HRRs with a population less than 49,735 (75th percentile) and 86,605 (90th percentile). Confounders such as urologist supply and disease burden were not addressed in this study.

Results

From 1999 to 2010, the national RP rate per 100,000 male Medicare beneficiaries declined from 1.64 to 1.32. A total of 222 (72.5%) HRRs had at least one robot in 2008. Of 306 HRRs, 153 were excluded due to suppressed or unstable RP rates. A total of 153, 76, and 30 HRRs had more than 26,783, 49,735, and 86,506 males, respectively. No association was found between RP rate change and the da Vinci robot rate change among 153 HRRs ($r^2 < .012$, $b1 < 1.4$, $p = .18$) and 76 HRRs ($r^2 < .007$, $b1 < .94$, $p = .48$). However, among 30 HRRs, for every 1 per 100,000 increase in the da Vinci robot, 4.9 per 100,000 more RPs were done in the post-robotic period compared to the pre-robotic period ($r^2 < .15$, $b1 < 4.9$, $p = .03$).

Conclusion

Acquisition of the da Vinci robot did not appear to increase the utilization of RP within HRRs with a male Medicare population between 26,783 to 85,605 (123 HRRs). However, in the 30 most densely populated HRRs (population size >85,605), including Minneapolis, robot acquisition was associated with increased RP rates in the post-robotic era. PCPs in these 30 HRRs should be mindful of these findings when ordering a PSA test. **MM**

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