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### Education module for serotonin syndrome with 24-hour dose monitoring intervention.

Jonathon Blake Hicks

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**Education module for serotonin syndrome with 24-hour dose monitoring intervention**

by

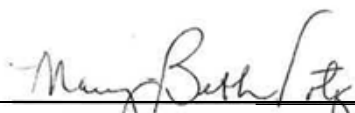
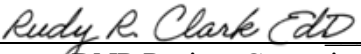
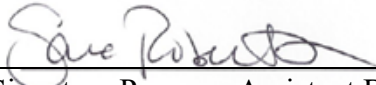
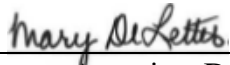
Jonathon Blake Hicks

Paper submitted in partial fulfillment of the  
requirements for the degree of

Doctor of Nursing Practice

School of Nursing, University of Louisville

August 30, 2020

 _____ Signature DNP Project Chair	_____ 7/30/20 _____ Date
 _____ Signature DNP Project Committee Member	_____ 7/30/20 _____ Date
 _____ Signature Program Assistant Dean	_____ 8/6/20 _____ Date
 _____ Signature Associate Dean for Academic Affairs	_____ 8/6/20 _____ Date

### Acknowledgments

I would like to acknowledge God for prompting me to further my education and pursue my potential. This work could not have been completed without the support of my wife Andrea and son Thane. They have been supportive and tolerant of the hours devoted to furthering my education. Dr. El-Mallakh for recognizing potential and urging me to further my education. Dr. Coty has been instrumental in helping me organize this manuscript and without her guidance it would have been exceedingly more difficult. Dr. Clark as my co-chair was helpful in manuscript revision and flow. Tammy Evanow NP for assisting me in finding an organization to implement this study. My psychiatric cohort: Luke Houser, Ashley Ricketts, and Shannon Williams have been supportive and encouraging through the entire program. Members of the acute care cohort: Jessica Duffy and Brittany Durbin have been assets in the non-psychiatric coursework.

### Dedication

This body of work is dedicated to my wife's grandmother Doris Biesel. She had been misdiagnosed with serotonin syndrome in a long-term care facility.

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### Abstract

Background: Serotonin Syndrome (SS) is recognized by a combination of mental status changes, neuromuscular hyperactivity, and autonomic hyperactivity (Volpi-Abadie, Kaye, & Kaye, 2013). Despite the severity and commonality of SS, it is an under reported and an under treated condition (Boyer, 2018). The purpose of this project was to 1) implement an education module on SS using a pretest and posttest design to increase LTC staff knowledge, and 2) evaluate the effectiveness (e.g., confidence level, satisfaction) of the intervention among nursing staff. Method: An education module was implemented focusing on recognizing and treating SS in aging adults. A pretest-posttest design was used to measure participant knowledge of SS. Participants consisting of nursing staff at a long-term care (LTC) facility (i.e., CNAs, LPNs, and RNs) completed a questionnaire at the end of the project to assess the effectiveness of the intervention. Results: There was a significant increase in knowledge from pretest to posttest with a pretest mean of 2.92 and a posttest mean of 6.61. Summary: Providing an educational module to LTC staff on SS facilitated an increase in LTC providers' knowledge of patients at risk for developing SS, and increased assessment frequency of LTC residents at risk for SS.

*Key words:* serotonin syndrome, serotonin toxicity, education, long-term care

**Education module for serotonin syndrome with 24-hour dose monitoring intervention**

Serotonin syndrome (SS) is a condition that can be brought on by single dose serotonergic medication, overdose of a serotonergic medication, or interaction between two or more serotonergic medications. SS is recognized by a combination of mental status changes, neuromuscular hyperactivity, and autonomic hyperactivity (Volpi-Abadie, Kaye, & Kaye, 2013). Despite the severity and commonality of SS, it is an under reported and often under treated medical condition (Boyer, 2018).

Serotonin is a neurotransmitter known to play a large role in multiple mental status changes such as: aggression, pain, sedation, anxiety, and depression. Serotonin is derived from tryptophan and is converted by enzymes to 5-HT (serotonin) (Dunkley, Isbister, Sibbritt, Dawson, & Whyte, 2003). Serotonin functions in the brain as a modulator for attention, anxiety, depression, sexual behavior, appetite, thermoregulation, migraines, and aggression (Volpi-Abadie, Kaye, & Kaye, 2013). SS occurs when there is an over-abundance of serotonin in the central nervous system (CNS) (Werneke, Jamshidi, Taylor, & Ott, 2016). Over the last 60 years, both psychiatric and medical communities have had difficulty in recognizing the symptoms and subsequently treating SS. The first recognized case of SS was in 1955 and continues to serve as a model case study. In 1984, a patient died from complications of SS. While it was speculated that the patient had SS well before she presented to the hospital, it was also clear that lack of symptom recognition lead to her mortality (Learner, 2009). The term “serotonin syndrome” is sometimes used inappropriately to describe adverse effects from medications that do not and cannot cause SS. These instances contribute to confusion in determining incidence and lead to a poor understanding of SS. Consequently, life threatening manifestations of SS are being overlooked and do not receive the necessary medical treatment (Gillman, 2006).

### **Problem Description**

SS is a rare disorder that can be fatal with just a single dose of medication containing serotonin (Gillman, 2006). The risk for developing SS increases when two or more serotonergic agents are used together (Werneke et al., 2016). Under recognition of SS can lead to mental status changes, autonomic hyperactivity, and neuromuscular hyperactivity; hospitalization, and death. The incidence and prevalence of SS are thought to be on the rise due to an increasing number of serotonergic medications being used in practice. The Toxic Exposure Surveillance System in 2004 reported 8,187 people diagnosed with SS resulting from the use of selective serotonin reuptake inhibitors (SSRIs), and of those diagnosed, 103 died from SS (Truschel, 2019). SS can be attributed to all serotonergic medications not specifically to SSRIs. The severity of SS ranges from mild to life threatening. SS can be misdiagnosed as medical conditions such as epilepsy, drug overdose, anxiety/panic attack, gastroenteritis, and as the syndrome worsens to sepsis, neuroleptic malignant syndrome (NMS), delirium or dementia, (Ables, & Nagubilli, 2010; Macfarlane, Bergin, & Peterson, 2016). Aging adults are especially at risk for SS due to their potential for polypharmacy, comorbidities, and changes to their metabolism (Poeschla, Bartle, & Hansen, 2011)

### **Theoretical Framework**

Malcolm Knowles' Adult Learning theory will serve as the theoretical framework for this EBP scholarly project. Knowles is credited as being the "father of andragogy," Andragogy is a method for teaching adult learners. Adult Learning theory makes assumptions about the design of learning: (1) adults need to know the reasons why they have to learn, (2) adults learn best by experience, (3) adults approach learning via a problem-solving method, and (4) adults learn best when the material is of immediate value (Knowles, 1984). Adult Learning theory postulates that



adult learners are self-directed, have experience with the topic under study, and are willing to learn. The educational model developed for this EBP project will include case studies, role playing, simulations and self-evaluation in accordance with Adult Learning theory. An on-site education module will facilitate evaluation of nursing staff knowledge of SS, which addresses the learner's reasons for learning, experience, and immediate value. The instructor will have a facilitator role instead of a grader role; this allows learners to move at a comfortable pace and learn material rather than memorize material

### **Setting and Organizational Assessment**

The sample for this project was long term care (LTC) staff consisting of registered nurses (RNs), licensed practical nurses (LPNs), and certified nursing assistants (CNAs) working in an LTC/personal care facility in an urban setting in northcentral Kentucky. This project was approved by the University of Louisville's Human Subject's Protection Program/Institutional Review Board (IRB) as a quality improvement project, and was reviewed and approved by the LTC facility prior to implementing the EBP project.

### **Purpose**

The purpose of this project was not to treat SS in LTC facilities but to increase nursing staff knowledge about and identification of residents at risk for SS. The purpose of this project was to 1) implement an education module on SS using a pretest and posttest design to increase LTC staff knowledge, and 2) evaluate the effectiveness (e.g., confidence level, satisfaction) of the intervention among nursing staff. The intent of this evidence-based practice (EBP) project was to increase knowledge regarding SS to assist nursing staff in their recognition of SS conditions and symptoms, and to incorporate an evidence-based 24-hour dose monitoring protocol when a serotonergic medication was started or increased.

### **Intervention**

The intervention consisted of an onsite learning educational module developed for this project that incorporated case studies, and focused on SS symptom recognition and treatment among nursing staff in an LTC setting. SS is an unexpected negative result from serotonergic medications. Steinman et al. (2011) suggested that prescribing decisions are important but adverse drug events (ADEs) do not always result from improper medication choices. The factors of ADEs like SS are complicated and it is difficult to predict how a resident will respond to medications. Drug receptor genotypes, p450 enzymes, and concurrent prescribed drugs are factors that can affect ADEs. These factors make it impossible to confidently predict the type and/or severity of ADEs. While Steinman et al. (2011) does not advocate for idle or speculative prescribing, they do advocate for proper dosing and symptom management. In the United States, 54% of ADE-related hospitalizations were attributed to medications that required monitoring, which raised an important question about medications that have ADEs but do not require monitoring (e.g., serotonergic agents). The crucial mechanism in their study was a dose monitoring system (Steinman et al). In Steinman's study, after a resident was prescribed a medication, health care providers implemented a monitoring system. While prescribers make the drug decision, other health professionals such as nurses or nurse aids play a critical role in dose monitoring. There are not specific laboratory tests for SS but understanding serotonergic medications that put the patient at risk and using a dose monitoring system can assist in recognizing and treating SS successfully. Steinman et al. also placed emphasis on actions to take in response to ADEs. In an LTC, using a dose monitoring intervention for SS can aid nursing staff in identifying a change in patient behavior and alert the physician to initiate treatment. Outcome goals for this EBP project were to (1) increase LTC providers' confidence

of recognizing and assessing patients at risk for developing SS, (2) implement a dose monitoring intervention in LTC residents at risk for SS, and (3) evaluate the satisfaction of the intervention with the nursing staff.

**Participants**

Participants (N=13) ranged in age from 24-75 years (M=46), consisted of nursing assistants (n=5), CNAs (n=2), LPNs (n=5), and RN (n=1). The majority of participants have been employed at the facility less than 5 years (n=10) see table 1.0. Participants were asked to complete a demographic questionnaire, pretest to evaluate participants’ knowledge on SS, education module on SS, posttest, intervention implementation of a 24-hour dose monitoring form for residents at risk for developing SS, and a satisfaction questionnaire.

Table 1.0

*Demographic*

Variable	n	%
Age in years		
20-39 years	6	46.2
40-59 years	5	38.5
>60 years	2	15.3
Education		
Highschool	5	38.5
CNA	1	7.7
Associates	5	38.5
Bachelors	2	15.4
Role		
Nursing assistant	5	38.5
CNA	2	15.4
LPN	5	38.5
RN	1	7.7
Years at LTC facility		
0-5 years	10	76.9
6-15 years	2	15.4
>16 years	1	7.7

### **Data Collection**

Participants were provided with an opaque envelope (envelopes were numbered 1-20). Each envelope contained: demographic questionnaire, pretest, Hunter's Criteria Decision Tree (HCDDT) along with a 24-hour dose monitoring form complete with signs and symptoms of SS ranging from mild to severe, common serotonergic medication list, posttest, and satisfaction questionnaire. These forms were created specifically for this project except for the HCDDT which was used with permission from the author of the Hunter Serotonin Toxicity Criteria scale (see Appendix A). Envelopes were passed out by DNP student at random to participants at the beginning of the EBP project. The demographic questionnaire and pretest were completed and placed back in the envelope prior to reviewing the education module, and the posttest was completed at the completion of the education module. These forms were returned to the DNP student following completion of the education module before beginning the intervention phase. The satisfaction surveys were kept by the participants in the corresponding envelopes and were completed at the end of the intervention phase. The envelopes were then collected by the staff educator and provided to the DNP student.

Participants' data (N=13) were collected from the demographic questionnaire, pretests and posttests, and the satisfaction survey. Data were also collected from the 24-hour dose monitoring form. When the client started or had an increase in a serotonergic agent, a 24-hour dose monitoring form was placed in the paper MAR binder and the communication binder at the nurse's station with the Hunter Criteria Decision Tree (HCDDT) to alert the staff to assess for SS. There were eleven (n=11) events in which the 24-hour dose monitoring forms were completed (out of a total 15 events in which either a serotonergic medication was added or increased). Data were collected from February 1, 2020 through March 2, 2020. The 24-hour dose monitoring

form reported on eight medications sertraline (Zoloft), mirtazapine (Remeron), ondansetron (Zofran), tramadol (Ultram), bupropion (Wellbutrin), trazodone, doxepin (Silenor), and venlafaxine (Effexor); and four diagnosis depression, nausea, insomnia, and pain.

### **Measurement**

The demographic questionnaire was developed for this project and consisted of four items. Additionally, the satisfaction questionnaire which assessed participants' satisfaction and confidence in assessing for SS and incorporating HCDDT as part of participants practice was also developed for this project and consisted of two Likert-type questions and five open ended questions. The HCDDT developed by Dunkley et al., (2003) highlights the autonomous symptoms associated with predicting SS. These symptoms consist of: clonus (spontaneous, inducible, or ocular movement), agitation (akathisia), diaphoresis, tremors, and hyperreflexia. With additional revisions, the Hunter Serotonin Toxicity Criteria was reformatted to include high temperature and rigidity which are indicative of life-threatening SS. Dunkley et al. (2003) conducted a univariate analysis to confirm the criteria as statistically significant predictors of SS. The Hunter Scale was compared to the Sternbach Scale in an assessment trial conducted by Dunkley et al. (2003). They determined that the Hunter Scale was 97% specific and 84% sensitive for determining SS compared to the Sternbach Scale, which reported a 97% specificity and 69% sensitivity.

### **Results**

A paired samples t-test was conducted to evaluate the impact of an education module on caregivers' knowledge regarding identifying at risk persons for serotonin syndrome and assessing those individuals. The pretest and posttest developed for this project consisted of eight (8) questions. The caregiver's knowledge increased significantly from pretest ( $M=2.92$ ) to

posttest (( $M=6.61$ ),  $t=8.59$ ,  $p<.0001$ ). The mean increase between pretest to posttest was 3.69 with a 95% CI ranging from 2.75 to 4.62. The magnitude of effect was large ( $\eta^2 = .86$ ). The topics assessed on the pre/posttests consisted of knowledge concerning serotonin syndrome such as what serotonin regulates in the body, knowledge of SS onset conditions, risk factors, and symptoms of SS.

The questions in the pretest and posttest ranged in question style from true/false, multiple choice, and select all that apply. Item 8 which was a 'select all that apply' question focused on symptoms of SS and was observed to be the most challenging question resulting in 0% correct in the pretest. Following the educational module, at post-test there was a noticeable improvement to 46% correct for this question.

Participants also completed 24-hour dose monitoring forms on those patients who were started on a serotonergic medication or if the serotonergic medication dosage was increased. Assessments consisted of three intervention time periods: 1-hour after serotonergic medication was started or increased, 12-hours after medication was started or increased, and 24-hours after medication was started or increased. The HCDDT was completed in 73% ( $n=11$ ) of the events in which a serotonergic medication was started or increased. In four other events (26.6%) in which serotonin was added or increased, a monitoring form was not completed by nursing staff (i.e., RN, LPNs). A review of the completed monitoring forms ( $n=11$ ) found that the 1-hour assessment was completed 100% of the time, the 12-hour assessment was completed 36% of the time, and the 24-hour assessment completed 100% of the time. Out of a possible 33 assessments (i.e., 1-hour, 12-hour, and 24-hour), the staff performed 26 assessments for a 79% completion rate. It is important to note, that while SS assessments were performed by the nursing staff (i.e.,

RN and LPNs), the HCDDT was only utilized in 45% of the assessments with the staff using their own assessment skills to evaluate for SS in the LTC patients.

A review of the two (2) questions on the satisfaction survey: one (1) addressing participants' confidence in assessing SS and, the second assessing if they believed they could correctly use the HCDDT showed RN and LPNs strongly agreed (30.8%) and agreed (15.4%) to the two statements. For nursing assistants/CNAs, 53.8% indicated they neither agreed nor disagreed with these statements. None of the open-ended questions were answered by the participants.

## **Discussion**

### **Interpretation**

The findings indicated that there was a significant increase in knowledge among nursing staff concerning signs and symptoms of SS from pretest to posttest. Implementation of the intervention showed an increase in assessments of SS in residents at risk from 0 to 73%. These findings are consistent with other research findings; even though the literature on SS education-specific studies is sparse. Douglas, Haydon, and Wollin (2016) evaluated a pain identification education module used by nursing staff and non-nursing staff in LTC facilities. The authors found an 8.2% increase in knowledge and a 25.4% increase in a documented routine pain assessment by nursing staff in the intervention group.

Interestingly, the findings for those events (n=11) that met the criteria for implementing the HCDDT, showed 100% of the time patients were assessed at the 1 hour and 24-hour time period, but not the 12-hour time period (36%). One explanation for the decrease in 12-hour assessments may be that these assessments fell during the patients' sleep hours and therefore were not awoken by nursing staff to conduct the SS assessment. While the staff implemented

assessments for at risk residents, they only utilized the HCDT 45% of the time predominantly during the 1-hour assessment time period per the 24-hour dose monitoring form. One explanation could be that they relied on their own assessment skills after the education module instead of using the HCDT. Another explanation could be that additional education is needed on the use of the HCDT, and/or the importance of using an evidenced based tool like the HCDT was not emphasized enough in the education module.

A review of the satisfaction survey revealed that only the two Likert-type questions were completed by the participants. The five open ended questions were left unanswered by all participants. The Likert-type questions were directed towards knowledge and assessment skills which may have only been useful to the RN or LPN staff as they were the ones implementing the HCDT intervention. Even though the nursing staff indicated that they were comfortable in assessing SS and were comfortable with the HCDT, they did not utilize the HCDT in over half of the assessments. Douglas, Haydon, and Wollin (2016) in their work developed a pain evaluation tool to assess residents' perception of the quality of their pain management, utilized an open-ended comment section for staff to evaluate the intervention and received a 60% response rate. Comments by participants in this study suggested that it was more difficult to implement with residents diagnosed with dementia (Douglas et al., 2016). This may be the case for this EBP project, as SS monitoring was implemented in a facility with a large population of patients with dementia. Additionally, this project implemented a new assessment design instead of consolidating or revising an existing protocol which may have contributed to the varying degree of use of the HCDT by nursing participants. Additionally, adding questions that included the CNAs scope of practice may have provided useful information about their role in identifying SS in LTC patients considering CNAs often have more contact with patients during a work shift due



to their responsibilities with helping patients with their ADLs (e.g., hygiene, meals, turning schedules, and answering call lights).

### **Limitations**

The sample size was small (N=13), which precluded the findings from being generalized beyond the sample. Additionally, over 50% of the participants (n=7) were nursing assistants and CNAs. CNAs and NAs did not participate in the project beyond the education module, as LPNs and RNs were responsible for implementing the HCDDT and monitoring patients on serotonergic medications for SS. Tailoring an observation protocol for CNAs and NAs to assist in the assessment of patients to notify licensed nurses (LPNs and RNs) of changes in patients' baseline behavior could be a first step in involving all nursing staff in identifying and treating SS. Another limitation included the attrition of two (n=2) licensed nurses who left the facility during the implementation phase of this EBP project. Additionally, agency nurses working in a PRN status were not included in the EBP project as they began working in the facility midway through the implementation of the project and thus did not participate in the 24-hour monitoring of SS. It is also important to note that many of the patients were stable on their medications and therefore, not incur many medication changes. Further, the DNP student did not have access to patients' medical records to determine if serotonergic medications were started or increased, and subsequently had to rely solely on the 24-hour monitoring binder created for this project. Lastly, this project did not include a post-intervention follow up test. An additional posttest one to two months after the completion of the project may have been helpful to evaluate nursing staff knowledge retention. Though the mean knowledge score increased to 83% after completion of the education module, there was not a posttest to determine post intervention knowledge retention over time.

## Conclusion

Boyer (2018) reported SSRIs are the most first line treatment for depression as well as are effective in treating anxiety related conditions. SSRIs are also the most implicated group of medications regarding SS. Treating symptoms of depression and anxiety are important with all populations. This can be difficult with patients in LTC facilities because many of those residents may also be diagnosed with dementia. Adverse drug events (such as SS) cannot always be prevented but they can be recognized early through increasing staff knowledge of serotonin related symptoms and incorporating appropriate monitoring for SS.

The purpose of this project was not to treat SS in LTC facilities but to increase nursing staff knowledge about and identification of residents at risk for SS. This project determined that an education module was a viable method for delivering relevant content to learners. Additionally, this EBP project led to several desired outcomes: (1) increase in LTC nursing staff knowledge of patients at risk for developing SS, (2) implementation of a dose monitoring intervention in LTC facilities for residents at risk for SS, and (3) evaluation of the effectiveness of the intervention with the nursing staff. This project initiated a practice change that increased assessments of at-risk residents for developing SS. Prior to the implementation of this EBP project, the facility did not have a SS assessment protocol prior, nor did they have the tools and resources (e.g., education module with case studies; Hunter Serotonin Toxicity Criteria decision tree) to implement said protocol. The results of this project will be disseminated through a publishable manuscript in a psychiatric/mental health nursing journal, and at the University of Louisville Doctorate of Nurse Practitioner poster session.



### References

- Ables, A. Z., & Nagubilli, R. (2010). Prevention, recognition, and management of serotonin syndrome. *American Family Physician, 81*, 1139-1142.
- Boyer, E. (2018). Serotonin syndrome. Retrieved from <https://www.uptodate.com/contents/serotonin-syndrome-serotonin-toxicity>
- Douglas, C., Haydon, D., & Wollin, J. (2016). Supporting staff to identify residents in pain: A controlled pretest-posttest study in residential aged care. *Pain Management Nursing, 17*(1), 25-37. doi:10.1016/j.pmn.2015.08.001
- Dunkley, E., Isbister, G., Sibbritt, D., Dawson, A., & Whyte, I. (2003). The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. *Qjm, 96*(9), 635–642. doi: 10.1093/qjmed/hcg109
- Gillman, P. K. (2006). A review of serotonin toxicity data: implications for the mechanisms of antidepressant drug action. *Biol Psychiatry, 59*. doi:10.1016/j.biopsych.2005.11.016
- Learner, B. (2009). A life-changing case for doctors in training. Retrieved from <https://www.nytimes.com/2009/03/03/health/03zion.html>
- Koo, E., Mcnamara, S., Lansing, B., Olmsted, R. N., Rye, R. A., Fitzgerald, T., & Mody, L. (2016). Making infection prevention education interactive can enhance knowledge and improve outcomes: Results from the targeted infection prevention (TIP) study. *American Journal of Infection Control, 44*, 1241-1246. doi:10.1016/j.ajic.2016.03.016
- Knowles, M. S., (1984) *Andragogy in action. Applying modern principles of adult education.* San Francisco: Jossey Bass

Macfarlane, B., Bergin, J., & Peterson, G. M. (2016). Assessment and management of serotonin syndrome in a simulated patient study of Australian community pharmacies.

*Pharmacology Practice (Granada)*, 14(2), 703. doi:10.18549/PharmPract.2016.02.703

Poeschla, B. D., Bartle, P., & Hansen, K. P. (2011). Serotonin syndrome associated with polypharmacy in the elderly. *General Hospital Psychiatry*, 33(3). doi:

10.1016/j.genhosppsy.2010.11.015

Steinman, M. A., Handler, S. M., Gurwitz, J. H., Schiff, G. D., & Covinsky, K. E. (2011).

Beyond the prescription: Medication monitoring and adverse drug events in older adults. *Journal of the American Geriatrics Society*, 59(8), 1513–1520. doi:

10.1111/j.1532-5415.2011.03500.x

Truschel, J. (2019). Serotonin syndrome (Toxicity): Symptoms, causes & treatment. Retrieved from <https://www.psycom.net/serotonin-syndrome>.

Volpi-Abadie, J., Kaye, A. M., & Kaye, A. D. (2013). Serotonin syndrome. *The Ochsner Journal*, 13, 533-40.

Werneke, U., Jamshidi, F., Taylor, D. M., & Ott, M. J. B. N. (2016). Conundrums in neurology: Diagnosing serotonin syndrome – a meta-analysis of cases. *16(1)*, 97.

doi:10.1186/s12883-016-0616-1

**Appendix A**

## Permission to use Hunter Serotonin Toxicity Criteria

**From:** Hicks,Jonathon Blake <jonathon.hicks@louisville.edu>  
**Sent:** Tuesday, 29 October 2019 1:38 AM  
**To:** geoffrey.isbister@newcastle.edu.au  
**Subject:** Permission to use the Hunter Serotonin Toxicity Criteria

Dr. Isbister,

My name is Jonathon Blake Hicks I am a Doctorate Nurse Practitioner student at the University of Louisville in Kentucky USA. I would like to respectfully ask for your permission to use the Hunter Serotonin Toxicity Criteria for my doctorate project. My project is a learning module with case studies and a 24-hour dose monitoring form consisting of the Hunter Criteria decision tree. The project will take place in a long-term care facility to increase the frequency of assessments on residents taking new/recently increased serotonergic agents.

Regards

Jonathon Blake Hicks RN BSN DNPstudent University of Louisville

**From:** geoff.isbister@gmail.com <geoff.isbister@gmail.com>  
**Sent:** Monday, October 28, 2019 7:44 PM  
**To:** Hicks,Jonathon Blake <jonathon.hicks@louisville.edu>  
**Subject:** RE: Permission to use the Hunter Serotonin Toxicity Criteria

No problems  
Geoff

**Appendix B**

## Hunter's Criteria Decision Tree

## Hunter Serotonin Toxicity Criteria

Hunter Serotonin Toxicity Criteria: Decision Rules
<ul style="list-style-type: none"><li>• Spontaneous clonus – yes-&gt; serotonin syndrome<ul style="list-style-type: none"><li>○ Else if/no</li></ul></li><li>• Inducible clonus -yes-&gt; Serotonin syndrome<ul style="list-style-type: none"><li>○ Else if/no</li></ul></li><li>• Ocular clonus with agitation or diaphoresis -yes-&gt; serotonin syndrome<ul style="list-style-type: none"><li>○ Else if/no</li></ul></li><li>• Tremor and hyperreflexia -yes-&gt; serotonin syndrome<ul style="list-style-type: none"><li>○ Else if/no</li></ul></li><li>• Hypertonia, fever &gt;100.4 F, and ocular or inducible clonus -yes-&gt; Serotonin syndrome<ul style="list-style-type: none"><li>○ No</li></ul></li><li>• Not serotonin syndrome</li></ul>
Decision rules for predicting serotonin toxicity. <i>*Included with permission from G.K. Isbister via email correspondence October 28, 2019.</i>

**Appendix C**

**Medications/substance associated with Serotonin Syndrome**

Medications/substance associated with Serotonin Syndrome				
Antidepressants				
SSRI	SNRI	MAOI	TCA	Misc.
<ul style="list-style-type: none"> <li>• Citalopram (Celexa)</li> <li>• Escitalopram (lexapro)</li> <li>• Fluoxetine (Prozac)</li> <li>• Fluvoxamine (Luvox)</li> <li>• Paroxetine (Paxil)</li> <li>• Sertraline (Zoloft)</li> </ul>	<ul style="list-style-type: none"> <li>• Duloxetine (Cymbalta)</li> <li>• Venlafaxine (Effexor)</li> <li>• Desvenlafaxine (Pristiq)</li> </ul>	<ul style="list-style-type: none"> <li>• Isocarboxazid (Marplan)</li> <li>• Phenelzine (Nardil)</li> <li>• Tranylcypromine (Parnate)</li> </ul>	<ul style="list-style-type: none"> <li>• Amitriptyline (Elavil)</li> <li>• Amoxapine (Asendin)</li> <li>• Clomipramine (Anafranil)</li> <li>• Desipramine (Norpramin)</li> <li>• Doxepin (Silenor)</li> <li>• Imipramine (Tofranil)</li> <li>• Nortriptyline (Pamelor, Aventyl)</li> <li>• Protriptyline (Vivactil)</li> <li>• Trimipramine (Sumontil)</li> </ul>	<ul style="list-style-type: none"> <li>• Trazodone (Desyrel)</li> <li>• Mirtazapine (Remeron)</li> <li>• bupropion (Wellbutrin)</li> </ul>
Non-antidepressant				
Antimigraine	Antiemetics	Antianxiety	Mood stabilizer	Antibiotic
<ul style="list-style-type: none"> <li>• Almotriptan (Axert)</li> <li>• Eletriptan (Relpax)</li> <li>• Frovatriptan (Frova, Migard)</li> <li>• Naratriptan (Amerge)</li> <li>• Rizatriptan (Maxalt)</li> <li>• Sumatriptan (Imitrex)</li> <li>• Zolmitriptan (Zomig)</li> </ul>	<ul style="list-style-type: none"> <li>• metoclopramide (Reglan)</li> <li>• Ondansetron (Zofran)</li> </ul>	<ul style="list-style-type: none"> <li>• Buspirone (Buspar)</li> </ul>	<ul style="list-style-type: none"> <li>• Lithium (Eskalith, Lithobid)</li> <li>• Divalproex Sodium (Depakote)</li> <li>• Carbamazepine (Tegretol)</li> </ul>	<ul style="list-style-type: none"> <li>• Linezolid</li> </ul>
Analgesic	Amphetamines	Other Opiates	Drugs of abuse*	Misc
<ul style="list-style-type: none"> <li>• Cyclobenzaprine (Flexeril)</li> <li>• Fentanyl</li> <li>• Meperidine (Demerol)</li> <li>• Tramadol (Ultram)</li> </ul>	<ul style="list-style-type: none"> <li>• Dextroamphetamine (Dexedrine)</li> <li>• Methamphetamine</li> </ul>	<ul style="list-style-type: none"> <li>• Levorphanol (Levo Dromoran)</li> <li>• Methadone</li> <li>• Tapentadol (Nucynta)</li> <li>• Tramadol (Ultram)</li> <li>• oxycodone</li> </ul>	<ul style="list-style-type: none"> <li>• Ecstasy</li> <li>• Cocaine</li> </ul>	<ul style="list-style-type: none"> <li>• St. john's wort – herbal</li> <li>• Dextromethorphan – OTC cold medicine</li> </ul>
Information obtained through references (Ables, & Nagubilli, 2010; Boyer, 2018; MacKay, Dunn, & Mann, 1999; Volpi-Abadie, Kaye, & Kaye, 2013). *drugs not included elsewhere				



**Appendix D**

## Pretest/Posttest

1. A Serotonergic agent MUST be present for serotonin syndrome to occur?
  - a. True
  - b. False
  
2. Serotonin syndrome ranges from mild to severe?
  - a. True
  - b. False
  
3. Once you have Serotonin Syndrome, you have it forever.
  - a. True
  - b. False
  
4. What are the three (3) types of clonus? (select one answer)
  - a. Spontaneous, inducible, ocular
  - b. Temporal, peripheral, inducible
  - c. Cranial, temporal, vascular
  
5. Serotonin regulates: (select one answer)
  - a. Memory, anxiety, depression
  - b. Pain, anxiety, depression, aggression, sleep
  - c. Sleep and depression
  - d. Depression only
  
6. Serotonin syndrome occurs within: (select one answer)
  - a. 24 hours
  - b. 2 days
  - c. 1 week
  - d. 1 month
  
7. Risk factors for developing serotonin syndrome (select all that apply)
  - a. An increase in serotonergic medication
  - b. Adding serotonergic medications
  - c. 2 or more anti-psychotic medications
  - d. Use of illicit drugs like cocaine or ecstasy
  - e. High blood pressure
  - f. Insomnia
  - g. Herbal supplements that increase serotonin
  
8. Symptoms of serotonin syndrome may include (select all that apply)
  - a. Clonus
  - b. Fever
  - c. Lethargy
  - d. constipation

- e. Muscle rigidity
- f. Increase agitation
- g. Heavy sweating
- h. Increased alertness

**Appendix E**

Serotonin Syndrome 24-hour monitoring form

Serotonin Syndrome 24-hour monitoring

Name and dose of medication(s) \_\_\_\_\_ Date and time given \_\_\_\_\_

Reason for medication \_\_\_\_\_

Person administering medication \_\_\_\_\_

Any adverse effects within 1 hour after administering \_\_no\_\_ yes

If yes, define \_\_\_\_\_

12-hour assessment: \_\_no\_\_ yes

If yes, define \_\_\_\_\_

24-hour response: Date and time \_\_\_\_\_

Serotonin Syndrome symptoms noted: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Hunter's Criteria decision tree used \_\_\_\_no\_\_\_\_yes

Suspected Serotonin Syndrome \_\_\_\_no\_\_\_\_yes

If yes, who was notified \_\_\_\_\_ nurse \_\_\_\_\_ prescriber

Person completing monitoring \_\_\_\_\_

Common symptoms:

- ▶ **Mild-**
  - ▶ presentation may include tremor, twitching, anxiety, hyperreflexia, tachycardia, diaphoresis, and gastrointestinal distress
- ▶ **Moderate-**
  - ▶ may present with increased agitation and restlessness. Hyperreflexia intensifies and clonus of the lower extremities. Diarrhea, nausea, vomiting, tachycardia, hypertension, and fever.
- ▶ **Severe-**
  - ▶ Has progressed to **life-threatening** that can lead to multiorgan failure. Presentation includes muscle rigidity, fever, increased confusion or change in baseline, delirium and possible seizure.

**Appendix F**

Satisfaction Questionnaire

Satisfaction Statement	Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
I feel confident in assessing a resident for serotonin syndrome					
I feel confident in using the Hunter Serotonin Toxicity Criteria decision tree to assess for serotonin syndrome					

**Your responses are important. Please answer the following questions.**

- What do you see as the strengths of the SS intervention?
  
- What do you see as the limitations of the SS intervention?
  
- What do you recommend to improve SS intervention?
  
- How has your practice changed as a result of the SS intervention?
  
- Please provide any additional comments.

## Appendix G

### Education Module Outline

- Objectives
  - **Identify key terms**
    - **Mental status changes** in Serotonin Syndrome can include
      - anxiety, agitation, delirium, restlessness, and disorientation
    - **Neuromuscular abnormalities** can present as
      - diaphoresis, tachycardia, hyperthermia, hypertension, vomiting, and diarrhea.
    - **Hyperactivity of the autonomic** nervous system can present as
      - tremors, rigidity, clonus, hyperreflexia
    - **Clonus**
      - is a type of neurological condition that creates involuntary muscle contractions. Clonus often presents as uncontrollable, rhythmic, and shaking movements. In
      - In Serotonin Syndrome clonus can present as spontaneous, inducible, or ocular. This results in uncontrollable, rhythmic, shaking movements
        - Spontaneous- occurs without an outside prompt
        - Inducible- occurs when induced by an outside force
        - Ocular- occurs as roving eye movements.
  - **Discuss: What is SS?**
    - What is Serotonin?

- Serotonin is a neurotransmitter known to help regulate aggression, sleep, pain, anxiety, and depression.
- What is Serotonin Syndrome?
  - Serotonin Syndrome is an abundance of serotonin in the central nervous system.
  - Is a condition brought on by:
    - single dose serotonergic medication
    - overdose of a serotonergic medication
    - interaction between two or more serotonergic medications
    - SS is recognized by a combination of mental status changes, neuromuscular hyperactivity, and autonomic hyperactivity
- **Discuss risk and relevance**
  - **Risk**
  - Increased risk of serotonin syndrome if:
    - recently started taking or increased the dose of a medication known to increase serotonin levels.
    - Take more than one drug known to increase serotonin levels.
    - Take herbal supplements known to increase serotonin levels.
    - Use an illicit drug known to increase serotonin levels.
  - **Relevance**

- Many elderly residents are on multiple medications, some of which interact adversely with serotonergic drugs increasing the risk of developing SS (Fiske, Wetherell, & Gatz, 2009).
  - Since there are no diagnostic tests to diagnose serotonin syndrome, care providers must rely on their education, expertise and use of assessment tools for recognizing SS.
  - The geriatric population is especially at risk due to their potential for polypharmacy (Poeschla, Bartle, & Hansen, 2011).
  - The prevalence of major depressive disorder for adults aged 65 and older in long term care is 14% to 42% higher than community dwelling adults (1-5%) (Fiske, Wetherell, & Gatz, 2009), suggesting that older adults are likely to be prescribed serotonergic medications to treat depression and/or anxiety
- How to assess for SS
    - Serotonin Syndrome will present within the first 24 hours of starting, or increasing a serotonergic agent. Serotonin Syndrome presents as mild, moderate, or severe.
    - **Mild-**
      - presentation may include tremor, twitching, anxiety, hyperreflexia, tachycardia, diaphoresis, and gastrointestinal distress
    - **Moderate-**

- may present with increased agitation and restlessness.

Hyperreflexia intensifies and clonus of the lower extremities.

Diarrhea, nausea, vomiting, tachycardia, hypertension, and fever.

- **Severe-**

- Has progressed **to life-threatening** that can lead to multiorgan failure. Presentation includes muscle rigidity, fever, increased confusion or change in baseline, delirium and possible seizure.

- **Hunter Serotonin Toxicity Criteria**

- Hunter decision tree highlights the autonomous symptoms associated for predicting SS. These symptoms are
- clonus (spontaneous, inducible, or ocular), agitation (akathisia), diaphoresis, tremor, and hyperreflexia.
- With additional revision, the Hunter scale was reformatted to include high temperature and rigidity which is indicative of life-threatening Serotonin Syndrome

- **Monitoring**

- The purpose is to increase assessments on residents at risk of developing serotonin syndrome using the 24-hour dose monitoring form.

- **Case study**

- Mrs. MayBea is an 82-year-old woman with a history of depression. She is being treated with sertraline (Zoloft) 25 mg every morning. She has been taking sertraline for 10 years. She lives in a long-term-care facility and is progressing in dementia. She has a history of back pain and is



treated with Tramadol 50mg PRN q 6 hours. Staff members at the facility has noticed that she is more isolative than usual and tells the prescriber. Dr. Feelbetter increases her Zoloft to 25 mg bid and she received a Tramadol 50 mg for headache. Within 24 hours of increasing Zoloft, staff found Mrs. MayBea to be more confused and agitated than usual.

- **What do we do?**
  - Obtain vital signs –
    - pulse 115, blood pressure 134/88, respirations 14, temperature 102 degrees F.
  - -Use Hunter decision tree
    - -Check for clonus
      - No spontaneous clonus
      - No inducible clonus
      - No ocular clonus
  - -agitation and diaphoresis
    - yes
  - Tremor and hyperreflexia
    - yes
  - Does she have serotonin syndrome?
    - Yes, mild SS notify provider. Treatment includes stopping serotonergic medication, increased monitoring and benzodiazepines as needed. Discretion of provider for hospital referral.

- What if we didn't do anything?
  - Mrs. MayBea has unresponsive episodes. She is in bed, but her arms and legs are jerking, and she is having diarrhea on herself.
- What has happened?
  - Serotonin Syndrome has progressed from mild to moderate.
    - Moderate treatment often includes hospital placement. She gets admitted to the hospital all serotonergic medications discontinued, receives benzodiazepines for tremors and tachycardia, and IV fluids for to reduce the risk of renal failure. After 2 days in the hospital Mrs. MayBea was released.