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## **Observed incidence of linezolid-associated serotonin syndrome during concomitant serotonergic therapy**

### **Disciplines**

Pharmacy and Pharmaceutical Sciences

### **Comments**

Poster presented at Faculty Scholarship Celebration, St. John Fisher College, October 25, 2012.

# Observed incidence of linezolid-associated serotonin syndrome during concomitant serotonergic therapy

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## INTRODUCTION

- While confirmed cases of serotonin syndrome (SS) have been associated with linezolid, the incidence in patients receiving linezolid in combination with other serotonergic medications has not been well established
  - Incidence in published retrospective studies ranges from 0.54% to 4.17%<sup>1-4</sup>
- The Hunter Serotonin Toxicity Criteria (HSTC) are the most widely accepted criteria used to diagnosis SS

### Any of the following in the presence of a serotonergic agent

Spontaneous clonus

Inducible clonus AND agitation OR diaphoresis

Ocular clonus AND agitation OR diaphoresis

Tremor AND hyperreflexia

Hypertonicity AND temperature > 38 C AND ocular clonus

## OBJECTIVE

Prospectively determine the incidence of SS in hospitalized patients receiving linezolid and concomitant serotonergic therapy

## METHODS

- IRB-approved prospective analysis
- Inclusion criteria: ≥ 18 years of age, receipt of linezolid between March 1, 2012 and June 15, 2012
- Exclusion criteria: none
- Primary outcome: development of SS, by definitive diagnosis via the primary patient care team or by satisfying the HSTC
- Concomitant serotonergic therapy was defined as any agent known to affect serotonin activity
- A CPOE-based report of active linezolid orders was generated daily to capture patients for inclusion
  - Electronic health records (EHR) of included patients were assessed for signs and symptoms of SS daily until development of SS or hospital discharge
  - If documentation in the EHR suggested possible SS, the primary patient care team was contacted to confirm

## RESULTS

- 130 unique courses of linezolid were received by 121 unique patients
  - 37 (28.5%) were in patients who received concomitant serotonergic therapy

Table 1. Demographic Information

	n = 37
Median Age (IQR) [years]	64 (50-75)
Female (%)	25 (67.6%)
Median Length of Stay (IQR) [days]	13 (7-19)
Median Duration of Linezolid Therapy (IQR) [hours]	78 (44-167)
Pulmonary Disease	45.9%
Cardiovascular Disease	27.0%
Seizure Disorder	18.9%
Liver Disease	2.7%

Figure 1. # of Concomitant Serotonergic Agents

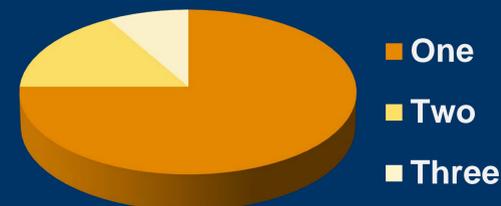


Figure 2. Linezolid Indication

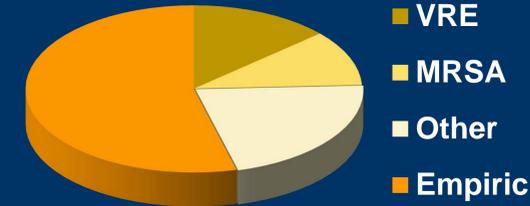
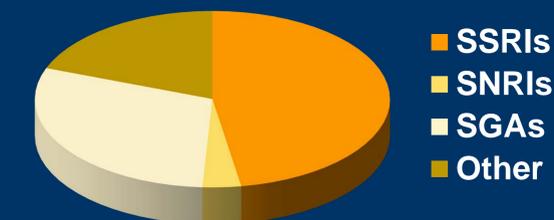
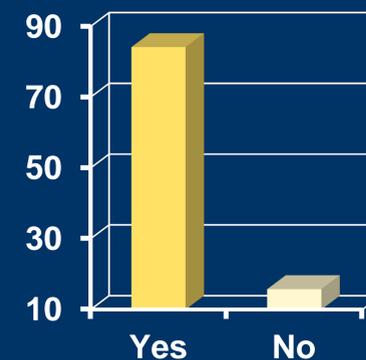


Figure 3. Concomitant Serotonergic Agents



SSRIs, selective serotonin reuptake inhibitors; SNRIs, serotonin norepinephrine reuptake inhibitors; SGAs, second generation antipsychotics

Figure 4. Agents Continued as Home Medication



## RESULTS

- No patients receiving linezolid in combination with other serotonergic therapy developed the primary outcome
- The following symptoms were observed
  - Six patients were agitated
    - Five during combination therapy
      - Two of the five were agitated throughout admission
      - The other was agitated 9 days after completion of linezolid
    - One patient was diaphoretic during combination therapy
- Although the primary team did not make a diagnosis of SS, the ID consult team listed SS on the differential for a patient hospitalized with traumatic brain injury and sympathetic storming who had persistent fever, tachycardia, and flushing

## DISCUSSION

- The incidence of linezolid-associated SS in 37 patients receiving linezolid in combination with other known serotonergic agents at a large academic medical center was zero
- To our knowledge this is the first prospective study investigating the incidence of linezolid-associated SS
- Limitations
  - Single center
  - Short study period
  - Patients were not physically assessed daily by investigators
- Linezolid-associated SS is rare despite use with serotonergic therapy at West Virginia University Hospitals
- Further observation is needed in order to describe the true incidence of this life-threatening reaction and related risk factors

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Disclosure: Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation. Questions or comments can be directed to mwoytowish@sffc.edu.