Background
Metaxalone has only recently been associated with serotonin syndrome. There are two previously reported cases in the peer reviewed literature, and 4 cases that have been presented in abstract form.

Hypothesis
The mechanism of action of this centrally acting muscle relaxant is unknown, however the observation of serotonin syndrome in patients with metaxalone overdose suggests a role in the serotonin pathway.

Case Report
(Case 1) A 29 year old female with intentional overdose of metaxalone presented to the emergency department with altered mental status, seizure-like activity, hyperthermia, rigidity in the lower extremities, myoclonus and hyperreflexia. Her medication list included paroxetine. She was intubated and sedated with benzodiazepines, and actively cooled. Serum paroxetine level was 23 ng/mL (therapeutic range 20-200 ng/mL), and serum metaxalone level was 31 mcg/mL (peak plasma concentrations average 0.9 mcg/mL at 3.3 hours following a single 400 mg oral dose). (Case 2) A 27-year-old male presented to the emergency department with altered mental status, rigidity in his lower extremities, myoclonus and hyperreflexia. He reported having taken extra metaxalone. His medication list also included escitalopram. He was managed aggressively with IV boluses of diazepam, in total 80 mg, in the emergency department. Serum escitalopram level was 24 ng/mL with a therapeutic range of 21-64ng/mL, and serum metaxalone level was 58 mcg/mL.

Discussion
The observation of serotonin syndrome with metaxalone overdose is growing in the literature. Previous authors have noted the structural similarity between metaxalone and linezolid. It is possible that this structural similarity results MAO inhibition by metaxalone. Direct MAOI activity by metaxalone has yet to be demonstrated. Of the 6 cases of metaxalone associated serotonin syndrome (2 published, 4 presented in abstract form), only two report metaxalone levels, and none report therapeutic serum SSRI levels associated with supratherapeutic metaxalone levels.

Conclusion
Two additional cases of serotonin syndrome associated with metaxalone overdose are added to the literature. These are the first cases to report therapeutic levels of SSRI in conjunction with supratherapeutic metaxalone levels.