Objective 3

Evaluate a pain patient's regimen to identify common medications used in pain management implicated in serotonin toxicity: analyze a drug-drug interaction report to determine utility of information provided



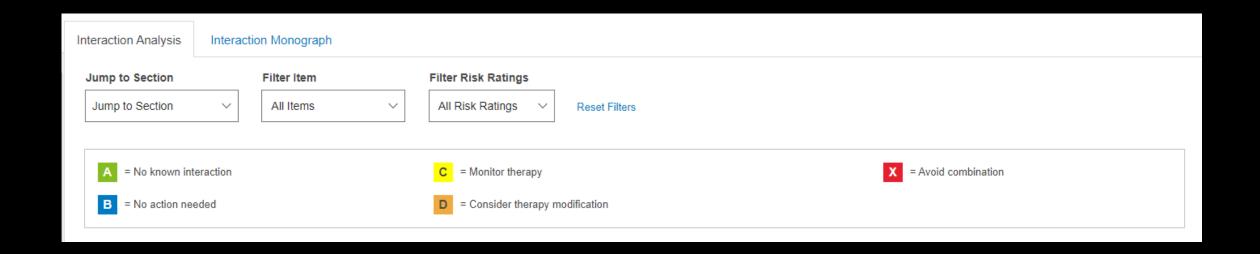
Drug Interaction Tool

- Can be used to evaluate the risk for drug interactions
- Data obtained from drug interaction tool must be analyzed carefully
- Drug reference databases such as LexiComp™ or Micromedex™ often have a drug interaction option
- Most interaction tools will give you a basic analysis with the option to click on a link for more information



Drug Interaction Tool

Most interaction tools will give you a key for the severity of the drug interaction



Lexicomp Online, Interactions Online, Hudson, Ohio: Up-to-date, Inc.; 2013; July, 2020. Available at https://online.lexi.com/lco/action/interact



Patient Case – EH: High Risk Medications

- EH, a 62 year old pt with metastatic breast cancer to the spine, is well known to your team. Her cancer has been relatively stable the past 3 years with treatment. EH is in the hospital for spinal fusion surgery for worsening back pain. After surgery she develop confusion, anxiety, myoclonus, increased heart rate, and increased blood pressure.
- PMH: CKD III, DM II (controlled w/diet & exercise), depression
- Meds:
 - Home Meds: Sertraline 100 mg daily, methadone 5 mg PO Q8 hrs., Senna 8.6 mg BID, gabapentin 800 mg BID – discontinued for elevated SCr
 - Hospital Meds: enoxaparin 60 units daily, morphine PCA 7mg every 15 mins. as needed (using 20 doses/day), desipramine 25 mg QHS, ondansetron 8 mg q8 hours as needed
- Labs: WNL except for elevated HR, BP, and SCr
- Possible causes for EH's symptoms?



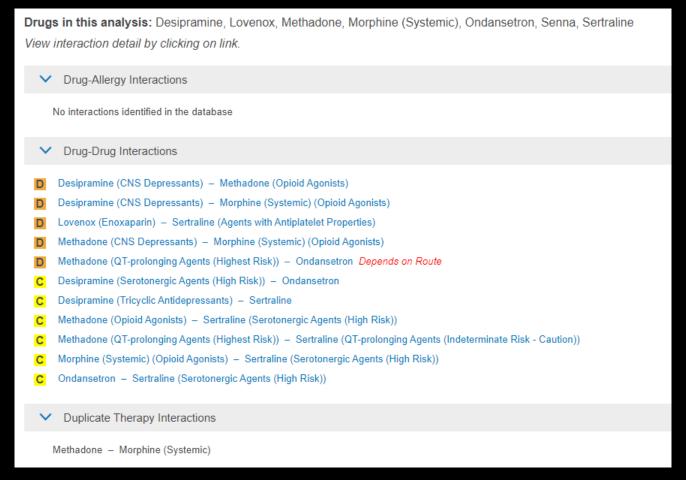
Patient Case – EH: Drug Interaction Report

Example of a drug interaction report



Patient Case – EH: Drug Interaction Report

Example of a drug interaction report





Patient Case - BP: High Risk Medications

- BP is a 52 year old male with a history of SCC of tonsil NED x 18 months. He reports to your pain clinic for management of his chronic pain caused by his cancer treatments mixed nociceptive & neuropathic pain
- BP presents with symptoms of insomnia, dizziness, mild tachycardia, N/V, cramping, and muscle twitching
 - PMH: FM, IBS, RA, GAD, hypothyroid, RLS

- Current Medications:
- Albuterol 2 puffs q6 prn
- Amlodipine 5 mg daily
- Simvastatin 40 mg daily
- Buprenorphine 15 mcg patch weekly
- Buspirone 10 mg twice daily
- Venlafaxine XR 150 mg daily
- Gabapentin 600 mg TID
- Hydrocodone 10/325 mg
- Hydroxyzine 25 mg TID prn
- Lactulose 15 mg TID
- Nortriptyline 75 mg daily
- Ondansetron 8 mg q8 PRN



Patient Case BP: Drug Interaction Report

Drug-Allergy Interactions Drug-Drug Interactions Buprenorphine (Opioids (Mixed Agonist / Antagonist)) - OxyCODONE (Opioid Agonists) AmLODIPine - Simvastatin Depends on Dose Buprenorphine - Gabapentin (CNS Depressants) Buprenorphine - HydrOXYzine (CNS Depressants) Buprenorphine - Nortriptyline (CNS Depressants) Gabapentin (CNS Depressants) - OxyCODONE HydrOXYzine (CNS Depressants) - OxyCODONE Nortriptyline (CNS Depressants) - OxyCODONE Albuterol (Beta2-Agonists) - Nortriptyline (Tricyclic Antidepressants) Buprenorphine (Opioid Agonists) - Venlafaxine (Serotonergic Agents (High Risk)) BusPIRone - Nortriptyline (Serotonergic Agents (High Risk)) BusPIRone - Venlafaxine (Serotonergic Agents (High Risk))

Gabapentin (CNS Depressants) - HydrOXYzine

Gabapentin (CNS Depressants) - Nortriptyline (CNS Depressants) HydrOXYzine - Nortriptyline (CNS Depressants) Nortriptyline (Serotonergic Agents (High Risk)) - Ondansetron Nortriptyline (Tricyclic Antidepressants) - Venlafaxine (Serotonin/Norepinephrine Reuptake Inhibitors) Ondansetron - Venlafaxine (Serotonergic Agents (High Risk)) OxyCODONE (Opioid Agonists) - Venlafaxine (Serotonergic Agents (High Risk)) Albuterol (QT-prolonging Agents (Indeterminate Risk - Caution)) - Ondansetron Depends on Route Buprenorphine (Opioid Agonists) - BusPIRone (Serotonergic Agents (Moderate Risk)) Buprenorphine (QT-prolonging Agents (Indeterminate Risk - Avoid)) - Ondansetron Depends on Route BusPIRone (Serotonergic Agents (Moderate Risk)) - Ondansetron (Antiemetics (5HT3 Antagonists)) BusPIRone (Serotonergic Agents (Moderate Risk)) - OxyCODONE (Opioid Agonists) HydrOXYzine (QT-prolonging Agents (Indeterminate Risk - Caution)) - Ondansetron Depends on Route **Duplicate Therapy Interactions** Buprenorphine - OxyCODONE

Opioids and Serotonin

- Fentanyl
- Tramadol
- Methadone
- Oxycodone

Baldo BA, Rose MA. The anaesthetist, opioid analgesic drugs, and serotonin toxicity: a mechanistic and clinical review. *Br J Anaesth.* 2020;124(1):44-62.



Objective 4

Provide a brief overview of available evidence for the treatment of serotonin toxicity with special attention to any gaps in knowledge and outcomes.



Management...

- Stop all serotonergic agents
- Supportive Care
 - -BP management
 - -Temp management
 - -Respiratory management
 - –ICU monitoring (severe)



...Management

Pharmacologic

- Benzodiazepines for severe agitation
 - Avoid medications with anticholinergic effects (eg haloperidol)
- Cyproheptadine
 - 5-HT1A and 5-HT2A antagonist
 - Monitor for hypotension
 - Initial dosing between 4-16mg
 - -2 mg every 2 hrs. until resolved
- Olanzapine
 - Theoretical

Gillman PK. The serotonin syndrome and its treatment. *J Psychopharmacol.* 1999;13(1):100-109. Graudins A, Stearman A, Chan B. Treatment of the serotonin syndrome with cyproheptadine. *J Emerg Med.* 1998;16(4):615-619. McDaniel WW. Serotonin syndrome: early management with cyproheptadine. *Ann Pharmacother.* 2001;35(7-8):870-873.



... Management for our Cases

EH

- Restart gabapentin at renal dosing
- -Consider stopping desipramine or rotating methadone

BP

- -Thorough history of why medications were started, length of therapy, benefit, side effects?
- Consider alternate anxiolytic
- Consider opioid rotation
- –Consider stopping TCA



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