Clinical Pharmacology & Toxicology Pearl of the Week

~ Restarting a medication post-overdose ~

Background

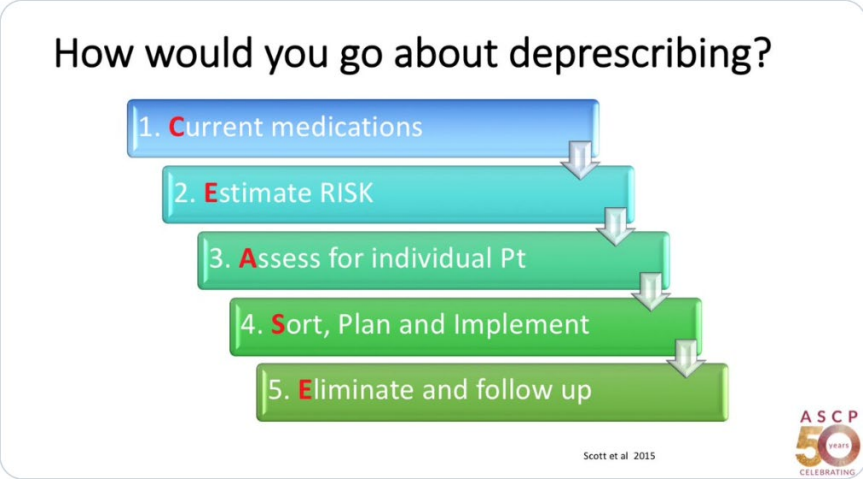
- ✓ There is currently a lack of guidance concerning the timing of reintroduction of medications after overdose, especially antidepressants or antipsychotics.
- ✓ This pearl of the week outlines some principles to consider regarding when or if to restart a medication post-overdose.

1. Do they need the medication?

- ✓ Now is a good time to reassess all of the patient's medications. You can't overdose on a medication you don't have.

2. Risk vs benefit of the medication

- ✓ What is the risk of the patient receiving the medication?
- ✓ What is the risk of them not receiving the medication?
- ✓ What's the worst possible thing you can think of happening if we decided to restart this medication right now?
- ✓ If a switch to a different medication is planned, has there been an appropriate washout period in-between medications?



3. What are the properties of the drug?

- ✓ Pharmacokinetics, Pharmacodynamics, Toxicokinetics, Toxicodynamics.
- ✓ The commonly cited "5 half-life rule" (100%, 50%, 25%, 12.5%, 6.25%, 3.125%) can be used. Starting from a steady state, 5 half-lives will remove 97% or a drug; whereas 10 half-lives will remove 99.9% of a drug.
- ✓ Accepting this rule blindly can be problematic. Need to consider active metabolites, saturation and genetic variations in CYP Enzymes, or a changes in physiologic milieu. Some active metabolites have longer half-lives than the parent drug. In some cases, the enzymes breaking these drugs down can be saturated, and changing a dose without respecting this can result in iatrogenic toxicity (e.g. phenytoin). Furthermore, half-lives can be prolonged in overdose.

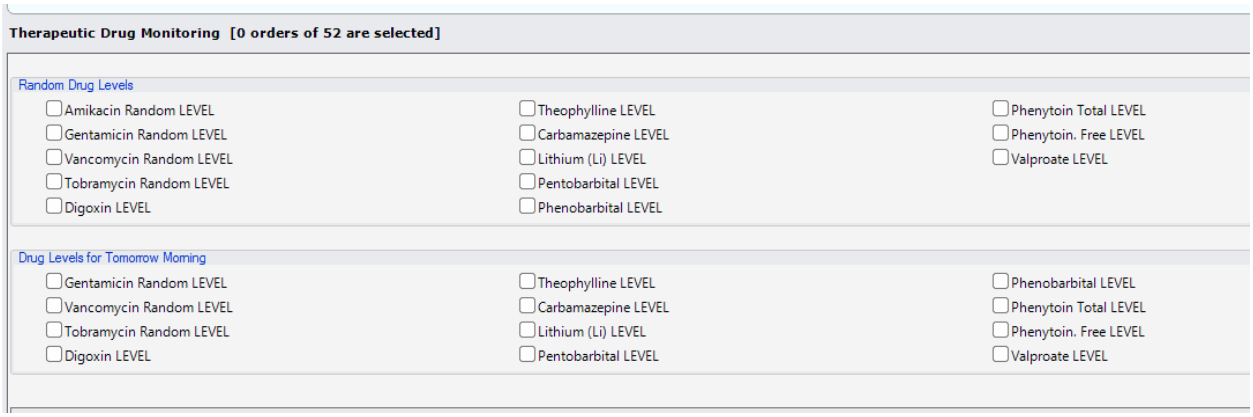
4. Is the patient showing signs of drug toxicity or withdrawal?

- ✓ Does the patient still look toxic? Have the patient's symptoms resolved?
- ✓ Is the patient still in hospital? If yes, are they still on a cardiac monitor?
- ✓ For drugs such as antidepressants, antipsychotics and cardiac drugs the biggest risks are going to be CNS depression, cardiotoxicity, or hypoglycemia.

- ✓ Not all drugs are associated with a withdrawal syndrome. The most likely culprits are SSRIs, SNRIs, baclofen, opiates, benzodiazepines and ethanol. Stopping beta blockers and clonidine cold turkey could result in rebound hypertension. Stopping a dopaminergic agent suddenly could result in NMS.
- ✓ Is your patient complaining of flu-like symptoms and the feeling of electroshock-like sensations flowing through them? Might be time to restart that venlafaxine.

5. Can we do blood concentrations / therapeutic drug monitoring? If we can, do the levels correlate with toxicity, therapeutic benefit or both?

- ✓ Usually if a patient's drug levels have fallen within a therapeutic range, they can be restarted on their medications.
- ✓ This is particularly true with drugs which have predictable linear elimination kinetics.
- ✓ This said, plasma concentrations associated with toxicity are poorly documented for most drugs and for some drugs, toxicity and benefit can occur below the therapeutic range.
- ✓ Also, unless the drug is listed in the hospital's Therapeutic Drug Monitoring order set, it will be a send out to a major lab in the USA and take about 3 weeks to come back. Here is an example of some of the medications which can be monitored in hospital:



6. If the medication is restarted, is a drug interaction possible?

- ✓ Have we administered something in the management of the poisoning that might result in a drug interaction if a medication is restarted? Some antidepressant drugs need massive washouts during switching to prevent problems.
- ✓ If this patient hadn't overdosed, are there guidelines around starting or switching a new psychotropic drugs? Consider reviewing the Psychotropic Handbook or these references: http://wiki.psychiatrienet.nl/index.php/SwitchAntidepressants or http://wiki.psychiatrienet.nl/index.php/SwitchAntipsychotics

7. If the decision has been made to restart the medication:

- ✓ Start low, go slow.
- ✓ Restart the most clinically important drug first.
- ✓ If multiple drugs are deemed clinically important, restart the drug with the shortest half-life first.

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click HERE for clinical issues the CP service can assist with.

ThePoison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.