CO's CURE Podcast
Ketamine

Provider: Hello, I'm Dr. Cathy O'Neil, a hospitalist practicing in Denver, and in this episode of CO's CURE podcast we will be talking about oral ketamine for the treatment of pain. Our goal is to decrease the use of opioids for pain in an effort to combat the opioid epidemic in our communities.

Ketamine has been around for a long time and the IV form has been used for years in anesthesia. There is also some data that IV Ketamine could be used for depression. It is also used orally in some chronic pain clinics. Here, to discuss Ketamine, with me is Pharmacist Rachel Duncan. Rachel, how does ketamine work?

Rachael: It is a noncompetitive reversible inhibitor of NMDA receptor. Ketamine also acts at mu opioid, GABA, and other receptors.

Cathy: It's usually used IV but we are trying it orally, what can you tell me about that?

Rachael: There is minimal data on oral dosing, but it has been used in by our colleagues in pain clinics for certain conditions. On the inpatient side, it has specifically been studied in patients with complex regional pain syndrome. The oral route allows for easier administration in certain situations, such as a patient without IV access and lasts longer than the IV formulation. Oral ketamine has a lower bioavailability due to significant first pass effect, which also means that the side effects we typically associate with IV administration are experienced at a much lower rate. The oral dose recommended in the guidelines should cause less dissociative side effects. The oral formulation is really just taking the IV formula and mixing it with a sweet drink due to bitter taste.

Cathy: When should we use it?

Rachael: The Colorados CURE Guidelines recommend oral ketamine as third-line therapy for musculoskeletal pain, specifically for those patients with complex regional pain syndrome. It should only be used after the patient has failed first and second line therapy, such as scheduled APAP and IBU, lidoderm patches, a muscle relaxant, gabapentin, topical agents, and nonpharmacologic therapies like heating pad, ice, mobility, and PT/OT. If the provider chooses to use oral ketamine, it should be IN ADDITION to the scheduled first and second line therapies, and should be the first agent removed from the plan once pain is controlled. The initial dosing recommendation is 25-50 mg po q 8 hr PRN. If the patient is finding significant relief, it is reasonable to schedule doses, and can be increased in frequency up to Q 4 hrs as well as an increase in dose. We recommend not to exceed 1000mg po in a 24 hr period. Oral ketamine is not commercially available, which means there needs to be a plan in place to taper it off completely before the patient can be discharged. Like opioids, ketamine should not be abruptly stopped if the patient has been on it for > 72 hours and has been getting scheduled, increasing

doses. A taper prior to discharge to avoid withdrawal effects is recommended. It's reasonable to cut the dose in half each day until it can be safely discontinued. (give example)

Cathy: What kind of monitoring do we need and what side-effects can occur?

Rachael: Initially, vitals should be checked 1 hour after the first oral dose, then every 4 hours. Although the risk of respiratory depression is INCREDIBLY low, the patient should be on pulse oximetry in order to monitor oxygenation. In patients that are on opioid therapy, the provider should consider lowering the opioid dose prior to starting oral ketamine to avoid respiratory depression. If the patient experiences an acute change in vitals or intolerable psycho-mimetic effects, stop ketamine and consider administering a low dose benzodiazepine, such as lorazepam or diazepam.

- psychomimetic SEs include hallucinations, anxiety, vivid dreams, dysphoria, CV SEs include tachycardia, HTN, myocardial depression, CNS SEs include tremors, tonic-clonic movements, sedation, ICP

Cathy: What patients are candidates for using ketamine for pain?

Rachael: Because of the side effects mentioned above, not all patients are appropriate for ketamine oral therapy. Remember, it's last line therapy for MSK pain. Contraindications and cautions: avoid use if seizures, psychosis, poorly controlled HTN, heart failure, arrhythmia, ICP, recent stroke, severe respiratory insufficiency or PTSD.

If you have a pain service in house, an order for ketamine oral therapy should be concomitant with a consult to your pain service.

Cathy: Due to the use of IV ketamine in the ED ALTO guidelines and for other indications on the inpatient side, is there anything you want to share about the use of IV ketamine?

Rachael: Sure, while the inpatient guidelines don't recommend IV ketamine, as there's a lack of literature to support it for the five specific pathways, we understand that there may be instances where providers may want to use it. If a patient is strict NPO or has a mixed bag of diagnoses, it may be appropriate for that patient. In that case, it's important to understand that IV use looks completely different than oral use. It's critical to start low – we recommend trying a "bolus" dose at 0.2 mg/kg, which should be given slow IVP, ie over 5-10 minutes. When I say slow, I mean SLOW to avoid the psychomimetic side effects we discussed earlier. If that seems to give significant relief, an infusion can be started at 0.1 mg/kg/hr. Due to the short half-life of ketamine, repeated boluses aren't typically optimal-an infusion is a better way to go. Again, if you decide to use IV ketamine, it is important to understand that the dosing for pain is completely different than the dosing for sedation. Sedation doses are typically between 1-2 mg/kg, almost 10x what we're using for pain. Keep boluses < 0.3 mg/kg and keep infusion doses low based on your hospital's protocols.

Cathy: Thank you for all that information Rachel. One last thing; because Ketamine is a schedule III drug, with potential for abuse, it should not be prescribed at discharge. If it has helped patients, then they should be referred to a chronic pain specialist.

Thank you for listening and I hope you found this educational. More information on dosing and citations on ketamine are found on our website.