On-Demand Clinical News

Use of Ketamine for Pain Management in Hospice Care

By Karen Bruestle-Wallace, Pharm. D., BCGP

Ketamine is an effective option for hospice patients who have pain that does not fully respond to opioids—even with increasing doses. It may be especially useful for neuropathic pain that does not respond fully to usual pain regimens that may include, opioids, NSAIDS, certain antidepressants, anticonvulsants, and gabapentinoids. Ketamine appears to be synergistic with opioids in patients who no longer have an analgesic response to high doses of opioids. It is also reported to be opioid-sparing and appears to play a role in opioid potentiation. Keep in mind the use of ketamine for pain is off-label and it can be very complex to dose.

Contraindications, side effects, and monitoring parameters are listed in Table 1. If needed, a ProCare pharmacist can help guide a decision about whether or not ketamine would be appropriate.

Table 1: Contraindications, Side Effects, and Monitoring

Contraindications	Uncontrolled psychosis; brain metastases with uncontrolled headaches and/or uncontrolled swelling; sepsis; and uncontrolled seizures; CAD*; glaucoma*; acute globe (eye) injuries*; porphyria*; and thyroid disorders*
Side Effects	Psychotomimetic**: hallucinations, delusions, delirium, vivid dreams, nightmares, dysphoria, dreamlike states, confusion and dissociative reactions Other: sedation, increased secretions, nausea, vomiting, hypertension, tachycardia, increased cerebrospinal fluid pressure, increased intraocular pressure, diplopia and nystagmus
Side Effect Management	Psychotomimetic side effects (treatment or prevention): Oral haloperidol 2-5mg at HS or 0.5-1mg TID; or diazepam 5mg at HS Increased salivation/secretions: hyoscyamine, other anti-secretory medications
Monitoring: Oral Administration	Monitor pain and side effects daily during dose titrations and at least 3-4 days after each dose increase
Monitoring: Low-Dose (analgesic) IV administration	Monitor pain every hour; and respiratory rate, blood pressure, and heart rate about every 2-4 hours, especially if receiving high-dose opioids***

*Relative contraindications (may not apply to hospice patients). Evaluate risks vs. benefits of using in a hospice patient.
**Less likely with oral administration of ketamine than with infusions.
*** Ketamine does not suppress respiration, but can cause a reversal of opioid tolerance and opioid potentiation, which may suppress respiration if the opioid dose has not been reduced appropriately.

Continued on Page 3

Diabetes Management at the End-of-Life

By Madeline Vallejo, Pharm. D.

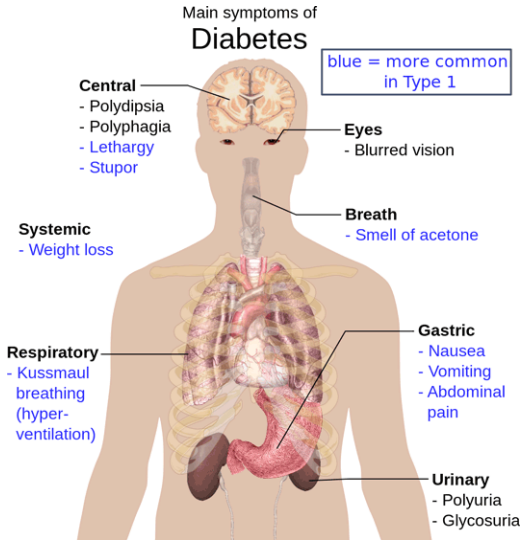
Diabetes is more common in older adults due to age-related physiological changes, such as increased abdominal fat, sarcopenia, and chronic low-grade inflammation that can lead to increased insulin resistance in peripheral tissues. In the elderly, the diabetes guidelines recommend less aggressive glycemic control. This is due to the fact that hyperglycemia generally does not cause any acute issues. Hyperglycemia is harmful *over time* for the kidneys, heart, arteries, nerves, and eyes. As patients get older and life expectancy decreases, those long-term risks are not as significant or applicable.

Typical goals for diabetes management at the end-of-life are to promote comfort, control symptoms (including pain, and symptoms caused by hypoglycemia and hyperglycemia), decrease complexity of treatment, relax target glucose levels, and reduce or discontinue monitoring.

Hypoglycemia is very low blood sugar, usually <72mg/dl. Some symptoms include shakiness, dizziness, sweating, and anxiety. Terminal patients have a higher risk of hypoglycemia with reduced oral intake. Hyperglycemia is very high blood sugar, defined by some sources as >270mg/dl. Some symptoms include increased thirst, fatigue, blurred vision, and weight loss. However, since symptoms are typically more prevalent with hypoglycemia, this is more of a concern while on hospice than hyperglycemia.

Continued on Page 2

Diabetes Management at the End-of-Life continued from page 1



The following are some general tips for management of diabetes in end-of-life.

Type 1 Diabetes: The body cannot make its own insulin. This is an autoimmune disorder typically with an early (often childhood) onset. Thus, this is also called "insulin-dependent" diabetes *(not to be confused with type 2 diabetes patients that are using insulin to manage their glucose)*.

- There is not enough evidence to support discontinuation of insulin
- Simplify current insulin regimen
- Sole use of sliding scale should be avoided

Type 2 Diabetes: The body either resists the effects of insulin, or does not make enough insulin to manage glucose levels appropriately. This used to be called "adult-onset diabetes", but today more children are being diagnosed with the disorder due to the rise in childhood obesity.

- If diet is controlled, no routine blood glucose checks required
- Reduce or stop oral diabetic medications and monitor for symptoms
- May use once daily long-acting insulin, or twice daily intermediate-acting (NPH) insulin – conservative dosing recommended, with goal to avoid unnecessarily high glucose levels
- Addition of sliding scale or post-prandial regimens using rapid-acting or short-acting insulins may be considered if tighter control desired
- Non-fasting levels of up to 300 mg/dL are often acceptable on hospice, as long as the patient remains asymptomatic

Steroid-Induced Diabetes

- Steroids will most likely be reduced or discontinued in terminal phase and blood sugars should normalize
- No need for routine blood glucose monitoring

References:

1. Diaz Rodriguez JJ. "Perspective and general approach of diabetes in palliative care" Hos Pal Med Int Jnl. 2018;2(3): 197-202.
2. SJ Lee, MA Jacobson, and CB Johnston. "Improving Diabetes Care for Hospice Patients" American Journal of Hospice and Palliative medicine. 2016;33(6): 517-519.
3. MN Munshi, H Florez, ES Huang, et al. "Management of Diabetes in Long-term Care and Skilled Nursing Facilities: A Position Statement of the American Diabetes Association" Diabetes Care. 2016;39:308-318.
4. K Quinn, P Hudson, and T Dunning. "Diabetes Management in Patients Receiving Palliative Care" J Pain Symptom Manage 2006;32:275-286.

Use of Ketamine for Pain Management in Hospice Care continued from Page 1

Ketamine is soluble in water and lipids and has many routes of administration. It can be given intravenous, subcutaneous, intramuscular, oral, sublingual, nasal, rectal, topical, and epidural. Dosing via the oral, sublingual, intravenous, and subcutaneous routes are most commonly used for pain and will be reviewed further.

Ketamine dosing is complex. Concurrent opioid adjustments are generally also needed. Oral or sublingual administration of ketamine is preferred. Ketamine infusions can be used, but are best reserved in an inpatient setting, and should not exceed a specified max, in order to avoid anesthesia. See table 2.

Table 2: Ketamine Dosing for Pain

Ketamine Route	Oral/Sublingual	Infusion (IV/Subcut)
Concurrent Opioid	Consider 25-50% dose reduction with ketamine initiation; continue to reduce by same percent as ketamine increased.	Consider 30-50% dose reduction with ketamine initiation; continue to reduce the opioid by the same percent as ketamine increased.
Starting Dose	10-25mg q8h	0.1 mg/kg/hour for analgesia
Titration	1/4 to 1/3 (25-33%) of the total daily dose every 3-4 days	1-2 mg every 2 hours for more aggressive pain management; 20-30% every 12-24 hours for more conservative management
Max Doses	2 mg/kg every 8 hours; usual maximum 50 mg every 6 hours	0.5 mg/kg/hour for analgesia; usual max 20-25 mg/hour
Comments	Some reports describe maximum doses of 200 mg po/sl every 6 hours (800 mg/day).	Recommended setting is in an IPU or skilled nursing facility. Higher doses than max may cause unwanted anesthesia. Dilute subcut ketamine with 0.9% sodium chloride to reduce irritation.

When able, patients on continuous infusions of ketamine can be converted to oral ketamine. The conversion range is 1-3:1 IV:PO. If the patient has only been on the ketamine infusion for a few days, use a conversion range of 1:1. Give the total daily oral dose in three divided doses. Generally, a taper off infusion while starting oral medication is recommended. For the first 24 hours, continue parenteral ketamine at 50% or original rate. If possible, reduce parenteral ketamine to 25% of original rate on day 2 before stopping the infusion. Titrate the oral dose by 10-25 mg/day every 3-4 days or by 20-30% every 3-4 days. If the patient experiences pain before next dose is due, consider shortening the dosing interval.

In summary, the advantages, disadvantages, and possible contraindications must be evaluated to determine if the patient is a candidate for ketamine. Some advantages of ketamine include that it is a non-opioid for pain, has no significant effect on pulmonary function, has many routes of administration and is cost-effective when compared to most other pain regimens. Disadvantages may include possible psychotomimetic effects (though not as likely with oral dosing), little data regarding long-term use, it must be compounded for oral or sublingual use, kept refrigerated, and is only good for seven days. Although not a first-line agent for pain, ketamine provides another good option for patients that fail to fully respond to increasing opioid doses and other adjuvants for pain management.

Continued on Page 4

Use of Ketamine for Pain Management in Hospice Care continued from Page 3

References:

1. Li, L. and Vlidides, P. (2016). Ketamine: 50 Years of Modulating the Mind. *Frontiers in Human Neuroscience, 10*(612), DOI: 10.3389/fnhum.2016.00612

2. Ketamine. (2019, March 1). Retrieved from http://www.cesar.umd.edu/cesar/drugs/ketamine.asp

3. Anderson, L. (2018, Nov. 5). *Ketamine Abuse*. Retrieved from https://www.drugs.com/illicit/ketamine.html

4. Lexi-Comp OnlineTM, Lexi-Drugs Online TM, Hudson, Ohio: Lexi-Comp, Inc.; Accessed: June 2018

5. Ingraham, P. (2018, Nov 21). *The 3 Basic Types of Pain Nociceptive, neuropathic and "other" (and then some more".* Retrieved from https://www.painscience.com/articles/pain-types.php

6. ProCare HospiceCare, (2016). *Ketamine Use-Quick Guide.* (brochure). Gainesville, GA: ProCare HospiceCare.

7. Clark, J. (1995). Effective Treatment of Severe Cancer Pain of the Head Using Low-Dose Ketamine in an Opioid-Tolerant Patient. *Journal of Pain and Symptom Management, 10*(4), 310-314.

8. Rigo, F. K., Trevisan, G., Godoy, M., Rossato, M., Dalmolin, G., Silva, M.,...Ferreira, J. (2017). Management of Neuropathic Chronic

Upcoming Lunch-and-Learn Presentations

July: Management of Insomnia in Hospice Care
Presenter: Joelle Potts, PharmD, CGP
Dates: Tuesday, July 9, 2019 at 3:00PM ET; Wednesday, July 10, 2019 at 12:00PM ET

August: Pharmacotherapy: A review of Benzodiazepines
Presenters: Shaun Gutstein, PharmD
Dates: Tuesday, August 13, 2019 at 3:00PM ET; Wednesday, August 14, 2019 at 12:00PM ET

RSVP by contacting Suzanne Stewart, Lunch-and-Learn Coordinator, at:
1-800-662-0586 ext. 3303 or sstewart@procarerx.com

Summer Clinical Seminar!
August 15, 2019
Stay tuned for more information!

ProCare HospiceCare welcomes all suggestions and comments. If you would like additional information about our services, have ideas for articles, or wish to submit a comment, email us at **resources@procarerx.com**.

ProCare HospiceCare

1267 Professional Pkwy., Gainesville, GA 30507

Executive Editor: Meri Madison, PharmD
Editor: Kristin Speer, PharmD, BCPS