

# PALLIATIVE PEARLS

BY ENCLARA PHARMACIA

## Acute Seizure Management Case August 2017

### PATIENT CASE

LT is a 65 year-old female with a primary diagnosis of breast cancer metastatic to the brain and bones. She has a history of HTN, depression and intolerance to morphine resulting in nausea and vomiting. LT is being admitted to hospice today after declining further treatment. She lives at home with her husband who is her primary caregiver. LT's cancer has been spreading aggressively and her goal is to remain as comfortable as possible.

### Current medications:

- Atenolol 25mg PO daily for HTN
- Citalopram 20mg PO daily for depression
- Dexamethasone 4mg PO twice daily for bone pain
- Gabapentin 200mg PO at bedtime for nerve pain
- Loratadine 10mg PO daily for seasonal allergies
- Lorazepam 0.5mg PO every 4 hours as needed for anxiety or agitation
- Methadone 5mg PO every 8 hours for pain
- Omeprazole 20mg PO daily for stomach upset
- Oxybutynin 5mg PO daily for bladder control
- Oxycodone 10mg PO every 2 hours needed for breakthrough pain or shortness of breath
- Oxycodone 20mg/ml: 0.5ml (10mg) PO every 2 hours as needed for pain or shortness of breath
- Polyethylene glycol 17grams PO daily as needed for constipation
- Prochlorperazine 10mg PO every 6 hours as needed for nausea and/or vomiting

Prior to admission, LT has been taking all of the above medications and tolerating them well, including the oxycodone despite her history of morphine intolerance. Due to the presence of brain metastasis, the hospice nurse is requesting an order for lorazepam suppositories to be in the home in the case of an acute seizure. The pharmacist recommends diazepam suppositories instead of lorazepam. The nurse asks the pharmacist to explain the difference between lorazepam and diazepam for acute seizure management.

### HOW COMMON ARE SEIZURES AT END OF LIFE?

Seizures are a rare but serious complication at end of life. The incidence of seizure occurrence in hospice patients is not known. Patients at an increased risk for seizures are those with brain cancer, cerebrovascular disease, metabolic abnormalities, certain genetic disorders and/or pre-existing seizure disorders.<sup>1</sup> Most acute seizures are short-lived and terminate spontaneously. The exception is status epilepticus (SE), defined as a crisis in which seizure activity is abnormal, prolonged and refractory to

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management. SE presents as continuous seizures lasting at least 5 minutes or two or more distinct seizures without complete recovery of consciousness in between. Guidelines for managing SE recommend the use of intravenous medications and suggest that neurological, respiratory and cardiovascular monitoring be available. Considering that many hospice patients reside at home, these resources may not always be available or easily accessible. The ability to administer medication through alternate routes is important to avoid hospital or hospice IPU admission for acute seizure management.<sup>2</sup>

### WHAT ARE THE STAGES OF STATUS EPILEPTICUS (SE)?<sup>3</sup>

- Stage I-Early Phase: Ongoing convulsions for more than 5 minutes, which are most commonly managed in the home with early preparation of medication and supplies
- Stage II-Established: Prolonged seizure activity with convulsions or recurrent seizures without regaining consciousness in between, lasting from 10 to 30 minutes
- Stage III-Refractory: Seizure continues despite stage I/II treatment, lasting 30 to 60 minutes
- Stage IV-Super-Refractory: Continuous seizures despite treatment lasting more than 24 hours

### WHAT MEDICATIONS ARE USED TO MANAGE SE?

- Stage I: Early Phase
  - Intravenous (IV): Lorazepam, diazepam, midazolam
  - Intramuscular (IM): Midazolam
    - IV lorazepam or IM midazolam are effective in initial treatment of early SE
    - IV lorazepam is preferred as first-line treatment over diazepam.
  - Rectal: Diazepam
  - Intranasal (IN): Lorazepam, midazolam
  - Buccal: Midazolam
    - Alternative when IV or IM routes are not feasible.
- Stage II: Established SE
  - IV: Phenytoin, fosphenytoin, valproic acid, levetirecetam, phenobarbital
    - Similar evidence of efficacy among these agents
  - IM: Phenobarbital
- Stage III: Refractory SE
  - IV continuous infusion: Midazolam, propofol
    - Management with anesthetics is associated with high morbidity and mortality and low success rates.
- Stage IV: Super-Refractory SE
  - Ketamine (IV infusion), Magnesium (IV), Topiramate (Enteral), Immunotherapy

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### HOW DO LORAZEPAM AND DIAZEPAM COMPARE AND WHEN ARE THEY RECOMMENDED?<sup>3,4,5</sup>

Intravenous lorazepam has a longer initial duration of action than diazepam, however it is less lipid-soluble and does not undergo rapid redistribution into peripheral tissues as seen with diazepam. For these reasons, lorazepam is considered first-line treatment in status epilepticus. In addition, IV lorazepam has a lower incidence of adverse effects and a more rapid antiepileptic effect compared to IV diazepam. However, peak concentrations of sublingual lorazepam may not occur for an hour and rectal absorption is erratic. Therefore, sublingual and rectal administration of lorazepam is not recommended for the treatment of SE.

Rectally administered diazepam is rapidly absorbed with peak serum concentrations reached within 6 minutes. Diazepam is highly lipophilic, allowing it to readily cross the blood-brain barrier, improving its anticonvulsant effect. However, intramuscular and oral diazepam administration is slow and variable. Although adverse effects following rectal diazepam are rare, the most serious adverse effect is respiratory difficulty.

### PHARMACIST ASSESSMENT:

Rectal diazepam is the drug of choice for acute seizures lasting more than 2 minutes and for the management of status epilepticus. Rectal diazepam should be initiated at 0.2mg/kg or 10 to 20mg at the onset of seizure. It can be repeated hourly until the seizure ends. A maintenance dose of 20mg rectally nightly has been suggested to reduce future seizures.<sup>1</sup>

### RECOMMENDATION:

The pharmacist explains the difference in rectal absorption between lorazepam and diazepam and recommends the use of diazepam suppositories due to its bioavailability, ease of administration and rapid time to peak serum concentration. The nurse agrees and will request an order from the physician for diazepam 10mg rectal suppositories.

### For additional information on this topic, please review these references:

Enclara Pharmacia's On Demand Educational Webinar, "Seizure Management in Adults and Children on Hospice Care" and resource "Quick Facts on Seizures at End-of-Life". Click [here](#) to log in

1. Connelly J, Weissman De. Fast Facts and Concepts #229. Seizure management in the dying patient. 2015 Aug. Available from:
2. Droney J, Hall E. Status epilepticus in a hospice inpatient setting. *J Pain Symptom Manage*. 2008; 36(1): 97-105.
3. Trinka E, Hofler J, Litinger M, Brigo F. Pharmacotherapy for status epilepticus. *Drugs*. 2015; 75:1499-1521.
4. Lee J, Huh L, Korn P, Farrell K. Guideline for the management of convulsive status epilepticus in infants and children. *BCM J*. 2011 Jul/Aug;53(6):279-285.

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5. Dooley JM. Rectal use of benzodiazepines. *Epilepsia*.1998;39:S24-S27.
6. Clinical Pharmacology [database online]. Tampa, FL: Elsevier/Gold Standard, Inc.; 2017. Access 2017 Jun. Available from: <http://www.clinicalpharmacology.com>