On-Demand Clinical News

Diabetes Management at End of Life

Kristin Braschler, Pharm.D., BCPS

Health care providers often encounter diabetes and associated complications in patients at end of life. In these patients, tight glycemic control may be nearly impossible to achieve. Furthermore, an accumulation of evidence is demonstrating that, in patients with advanced age, long-standing diabetes and/or significant comorbidities, tight glycemic control can be harmful. Unfortunately, there is very little data and guidance on how to manage diabetes in end-of-life. Based on the best available published literature, ProCare will provide some guidance on the approach to caring for this patient population at end of life, particularly as it involves the use of costly diabetes medications and monitoring.

First, in general, it is important to keep in mind each individual's goals of care as they pertain to palliation and hospice care. How advanced is the patient's diabetes? Severity of the diabetes or length of time the patient has had the illness can influence how tightly serum glucose levels should be managed. In general, hospice patients with diabetes will require less strict glycemic control. Regardless of whether or not diabetes is considered to be contributing to the reason for hospice admission, it is important to keep in mind that the patient with diabetes may become symptomatic during hospice care due to hyper- or hypoglycemia, and it is the expectation that hospice will provide and/or prevent such symptoms. Finally, renal and liver function tests are useful for guiding potential discontinuation (or continuation at a reduced dose) of most diabetes medications; renal and liver tests within 6 months prior to (or upon) hospice admission are valuable.

Patients with diabetes in end of life have been categorized into 3 different groups or severities[1] (the majority of hospice patients with diabetes can be expected to fall within the first two groups):

1. Active Disease but Relatively Stable:
   Prognosis is several months to more than a year; enteral intake is fair with sporadic improvements or worsening

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FDA Drug Approval News: Cymbalta (duloxetine) Generic Approval

Cody Midlam, PharmD, CGP

On December 11, 2013 the U.S. Food and Drug Administration approved the first generic versions of Cymbalta (duloxetine delayed-release capsules), a prescription medicine used to treat a number of conditions; acute and maintenance treatment of major depressive disorder (MDD); treatment of generalized anxiety disorder (GAD); management of diabetic peripheral neuropathic pain (DPNP); management of fibromyalgia (FM); chronic musculoskeletal pain (eg, chronic low back pain, and osteoarthritis).

As with many prescription medications it is always important to check a patient's renal and hepatic status prior to initiating any new therapies. Note, duloxetine is not recommended for patients with hepatic impairment or renal impairment with a creatinine clearance (CrCl) below 30mL/min or ESRD. Dosage adjustment may be required with mild to moderate renal impairment.

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2. Impending Death or Organ or System Failure:
   Prognosis is days to weeks; declining calorie intake with anorexia
3. Actively Dying:
   Patient is actively dying; no enteral intake

Differing approaches to the care of each patient category has been suggested, and are summarized here[1]:

Active but Stable (eg: Dementia, Cardiomyopathy)[1]:

- Begin a dialogue with patients/caregivers about reducing glycemic control intensity
- Focus on acute prevention of HYPOglycemia
- Maintain reasonable prevention of HYPERglycemia (less than 180mg/dl)
- Continue insulin at this stage if type 1 DM
- (Re)educate patient/caregivers of the symptoms of hypoglycemia (sweating, dizziness, confusion, shakiness, weakness, tachycardia, increased appetite), but note that hypoglycemia unawareness occurs more often in the elderly and those with multiple comorbidities
- Caution use of NPH insulins due to peaks/risk of hypoglycemia; may need to adjust dose
- Rapid acting insulin may be preferred since it can be given even after a meal has begun – doses may be reduced if patient did not finish meal
- Adjust dose of long acting insulin based on fasting BGs, not post-prandial BGs
- Provide instruction to patient/caregiver on how to manage diabetes medications if not eating or if n/v occurs (see table 2 for general dosing recommendations)
- Consider renal/hepatic impairment (see table 2 for general dosing recommendations)
- Maintain pleasure-based diet with limit on highly concentrated carbohydrates
- Finger sticks: consider goals of care, tailor to individual (DM1 may require more often than DM2)

Impending Death, Advancing Disease or Organ (eg; Liver Failure)[1]:

- Greater focus on prevention of HYPOglycemia vs hyperglycemia control
- Education of patient/caregivers about signs/symptoms of hypoglycemia and plan of action
- Decrease insulin at this stage if type 1 DM, especially if renal/hepatic impairment (insulin is renally cleared, and hepatic gluconeogenesis reduced)
- Decrease insulin and/or oral diabetes medications if type II DM, especially if renal/hepatic impairment (see table 2)
- Generally recommend to D/C nauseagenic meds (DPP4 inhibitors, GLP1 agonists, alpha-glucosidase inhibitors, amylin analogues) at this time
- Be flexible with patient diets – consider what patient is able to tolerate
- Finger sticks: consider d/c in type II DM, and only when needed to guide therapy decisions in type I DM
- Consider patient/caregiver preferences (often feelings of loss of control, stress about severity of disease/life expectancy; use as catalyst for discussion about goals of care)

Actively Dying (eg; massive intracerebral hemorrhage, obtundation, or agonal respirations)[1]:

- Consider withdrawal of all diabetes medications for both DM I and II in most cases
- Focus care on comfort only

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Analgesic Pain Medications and Coverage Under the Hospice Benefit: Recent Directives from the Centers for Medicare and Medicaid Services

Cody Midlam, PharmD, CGP

In June and August of 2013, the Centers for Medicare and Medicaid Services (CMS) communicated with Medicare Part D prescription providers, informing them of a change in policy; in which Medicare Part D providers should no longer be paying for analgesic medications when a patient is enrolled in hospice. Due to questions stemming from the previous memoranda, CMS addressed these questions in a memorandum dated October 30, 2013 and titled, *Clarification of Recovery of Part D Payment for Pain Medications for Beneficiaries Enrolled in Hospice.*

The most recent memorandum aims to provide regulatory guidance for Part D providers to prevent duplicate payments for drugs covered under the hospice benefit; guidance on how to prevent payment for analgesics going forward, and guidance on how to recoup payments for analgesics going back to 2011. A few notable excerpts from the CMS regulations are highlighted below:

- "…this guidance augments the prior CPI [Center for Program Integrity] guidance by outlining a consistent approach to financial reimbursement requests by Part D sponsors to hospice providers."
- "…for the purposes of this recovery effort only, we presume that all the drugs were used for the palliation and management of the terminal illness and/or related conditions. **They are, therefore, considered to be related to hospice care and thus a case-by-case analysis to determine relatedness is not required."**
- "Since the drugs were the payment responsibility of the Medicare hospice, the PDE [prescription drug event (a claim for analgesics)] reflects an overpayment that should be recovered from the hospice. The specific hospices that need to be contacted for payment recoupment were identified by CPI in earlier guidance."

In summary, CMS has provided guidance for Medicare Part D drug plans to recoup payment for analgesic medications dated through the beginning of 2011. Their directive applies to patients who were enrolled in a hospice program, and had analgesic medications billed to the Part D plan during the hospice enrollment period. This recoupment effort has begun, and Part D plans have been actively sending letters to certain hospices to recoup payments for analgesics going back to 2011. Going forward; per CMS, all prescription analgesics will be hospice covered, regardless of diagnosis and 'relatedness'. A list of common analgesic examples seen in the hospice setting is provided below:

Commonly Used Analgesics in the Hospice Setting

I. OPIOID

1. Morphine (IV/SC/IM/PO/SL), Oral Morphine; Short-Acting, and Long-Acting ER Tablet (MS Contin), ER Capsule (Brand Avinza, Kadian)
2. Oxycodone (PO/SL), Oral Oxycodone; Short-Acting, and Long-Acting ER Tablet (Brand Oxycontin),
3. Methadone (PO/SL/IV/SC/IM)
4. Hydromorphone (PO/SL/IV/SC/IM/PR), Oral Hydromorphone; Short-Acting, and Long-Acting Tablet (Brand Exalgo),
5. Codeine (PO/IV)
6. Tramadol (PO)
7. Fentanyl (IV, SL, Transdermal)
8. Meperidine (PO, IM, SC)

Commonly Used Analgesics in the Hospice Setting

II. NSAID

1. Meloxicam (PO)
2. Naproxen (PO)
3. Ibuprofen (PO/IV)
4. Indomethacin (PO)
5. Celecoxib (PO) Capsule (Brand Celebrex)

III. OTHER

1. Acetaminophen (PO/PR)
2. Aspirin (PO, PR)
3. Lidocaine patches (TD)
4. Ketamine (PO, IV)

IV. COMBINATION ANALGESICS:

1. Hydrocodone/ Acetaminophen (PO)
2. Oxycodone/ Acetaminophen (PO)
3. Codeine/ Acetaminophen (PO)
4. Tramadol/ Acetaminophen (PO)

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Special dosing precautions and recommendations for diabetes medications are summarized in Table 2[1]. In general, most medications need dosage reductions due to renal and/or hepatic impairment, which is common to the hospice and diabetes patient populations. Oral intake and side effects of medications should also be considered.

TABLE 2. COMMONLY PRESCRIBED DIABETES MEDICATIONS

Drug class	*Examples*	*Comments*	*Dose considerations*
Insulin *Rapid-acting* *Long-acting*	glulisine, NPH insulin, glargine	Rapid-acting insulin may benefit patients who have erratic appetites or miss meals due to unforeseen nausea or vomiting. Long-acting insulin (glargine) may cause less hypoglycemia, due to "peakless" pharmacodynamics.	Dosage should be adjusted in patients with renal and/or liver dysfunction and stopped altogether in the presence of organ failure. Dose adjustments should be made based on food intake.
Sulfonylureas	glipizide, glimepiride, glyburide	Caution should be taken with agents with long half-lives and active metabolites. Patients may benefit from a shorter-acting agent (glipizide) with inactive metabolites.	Dose should be adjusted in patients with renal and/or liver dysfunction and stopped altogether in the presence of organ failure. Dose adjustments should be made based on food intake.
Meglitinides	repaglinide, nateglinide	May benefit patients who have erratic appetites or unexpectedly may miss meals due to rapid onset and preprandial dosing.	Dose should be adjusted in patients with renal and/or liver dysfunction and stopped altogether if organ failure. Dose adjustments should be made based on food intake but a lower risk of hypoglycemia exists in this class.
Biguanides	metformin	Very low risk of hypoglycemia, but patients may exhibit undesirable weight loss and GI distress. Caution must be taken in patients with compromised renal or liver function due to the risk of lactic acidosis.	Discontinue in patients with hepatic or renal failure. There is a high level of GI intolerability especially at higher doses.
Thiazolidinediones	pioglitazone, rosiglitazone (restricted access)	Very low risk of hypoglycemia, but undesirable fluid retention and edema may occur. Severe caution must be taken in patients with compromised cardiac function, as this class may worsen heart failure. Close monitoring is required.	Discontinue in patients with liver failure and significant cardiac compromise.
Alpha glucosidase inhibitors	acarbose, miglitol	May benefit patients who have erratic appetites or miss meals due to quick onset and dosed with meal. There is an undesirable incidence of GI distress.	Should not be given to patients who are not currently eating.
GLP-1 receptor agonist **Amylin analog**	exenatide, liraglutide, pramlintide,	Long-term data is lacking. Prescribed mostly for post-prandial hyperglycemia Nausea is a commonly encountered side effect. *Warning: Acute pancreatitis and renal failure*	Dose adjust GLP-1 drugs and possibly Amylin analog for renal failure
DPP-IV inhibitor	sitagliptin, saxagliptin	Long-term data is lacking. Prescribed mostly for postprandial hyperglycemia. Nausea is a commonly encountered side effect. *Warning: Acute pancreatitis and renal failure*	Dose must be adjusted for renal and liver failure

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The use of oral steroids poses a special concern in hospice patients with diabetes because the risks of steroid-induced hyperglycemia and associated symptoms must be balanced against the benefits of palliating other symptoms. The onset of hyperglycemia can vary from as soon as a few hours to as late as several months or years after start of administering oral steroids, and the effect is considered dose-dependent[1]. Providers should anticipate the need to increase/add anti-hyperglycemic agents, but also consider goals of care for each patient[1]. Consider a finger stick prior to start of oral steroids, and periodically thereafter to guide diabetes medication therapy/dose adjustments and continued oral steroid use. Providers should consider the risks of hyperglycemia (and how it might be managed) vs benefits of control over other symptoms, many of which oral steroids help manage.

In summary, hospice and palliative care providers should expect to encounter diabetes and associated complications in patients at end-of-life, and appreciate that very little literature and guidance is available to assist with management of care. Formulating an appropriate therapeutic plan involves a thorough understanding of the patient's/caregiver's goals of care. It also requires in-depth knowledge of diabetes pathophysiology and medications used to manage this condition and associated symptoms and complications. ProCare pharmacists are available 24/7 to help guide your team in the appropriate use of diabetes medications, and to recommend safer and less costly alternatives where appropriate.

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1. Angelo M, Ruchalski C, Sproge BJ. An approach to diabetes mellitus in hospice and palliative medicine. J Palliat Med. 2011 Jan;14(1):83-7. doi: 10.1089/jpm.2010.0191. Epub 2010 Dec 31.

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The example list above includes many common analgesic medications, however, it is prudent for each hospice to determine which medications they feel are most clearly represented by the term 'analgesics' in their own unique setting. A one-size-fits-all approach may not be appropriate due to the various settings and cultures each hospice embodies.

A number of medications that are commonly used in end of life care to manage pain are not included above. For example, steroids such as dexamethasone or prednisone are often used for bone pain. Antiepileptic medications such as gabapentin, or pregabalin, and antidepressants such as amitriptyline, nortriptyline, or duloxetine are often used for treating neuropathic pain. These medications may be used to treat pain, or they may be used for other indications.

It is also important to note, that CMS has provided guidance on how hospices can create and utilize a formulary. Hospices typically have a formulary that lists drugs most commonly used for pain and symptom management. Hospices are able to create a formulary for analgesic medications, in which the hospice determines which analgesics are on the hospice formulary and which are not. Per the CMS document, *Part D Payment for Drugs for Beneficiaries Enrolled in Hospice—Request for Comments*,

"…sometimes a patient requests a specific drug which is not on the hospice formulary. The hospice does not have to provide that specific drug if the hospice interdisciplinary group determines that a medication on its formulary would work as well."

If a non-formulary analgesic is not covered by the hospice, it cannot be covered under the Part D benefit either (as described previously), and is thus the responsibility of the patient. The formulary must be able to provide pain and symptom relief for the beneficiary. If the drugs on the formulary are not providing adequate pain and symptom relief, it is expected that the hospice will use off-formulary drugs to do so.

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ProCare HospiceCare Assists Clients in Meeting CR8358 Reporting Requirements

New CMS reporting requirements for pharmacy claims incorporated into ProCare HospiceCare's product offering

Change Request 8358 issued by the Department of Health & Human Services (DHHS) and the Centers for Medicare & Medicaid Services (CMS) created additional reporting requirements for hospices on certain pharmacy items.

Voluntary reporting of these additional elements commenced January 1, 2014. Mandatory submission goes into effect April 1, 2014. To support both the voluntary and mandatory reporting, ProCare HospiceCare includes the additional CMS required data elements and line item details as part of its standard reporting package provided to clients.

"At ProCare HospiceCare, our mandate is to meet the needs of our client base. Accordingly, we are pleased to be able to help our clients meet the new CMS reporting requirements as part of our standard pharmacy spend management product offering," states Raeanna Lewarne, RPh, PharmD, BCPS, Vice President of Clinical Operations and Hospice Sales.

ProCare HospiceCare helps you put patients and families first by providing customized pharmacy solutions based on a local pharmacy network. Our easy-to-use program will reduce medication costs while allowing you to maintain your current providers. We are driven by a passion for patient care along with online, real-time prescription claims processing expertise and user-friendly reporting that hospices want and need for CMS auditing.

If you are currently contracted with your pharmacy benefit manager under a per diem model, you should contact ProCare HospiceCare immediately to see how the upcoming Medicare changes may affect you.

Contact us at: 800-377-1037 or www.ProCareHospiceCare.com

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**.

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