The Diabetic Hospice Patient
Incorporating Evidence and Medications Into Goals of Care
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Whether the primary illness or a comorbidity, diabetes mellitus is a common and often quite complex disease state needing thorough assessment and treatment by the hospice clinician. Translatable evidence, national consensus guidelines, and patient-specific goals of care should guide the clinician in the liberalization of glycemic control, individualization of blood glucose monitoring, and prevention of hypoglycemia while enhancing quality of life for the hospice patient. This article will highlight the various pharmaceutical modalities available that are critical to understand and appropriately use as well as provide the hospice clinician with “bedside pearls” to capture key and relevant practice considerations.

KEY WORDS
diabetes, glycemic control, goals of care, hospice, hypoglycemia

The management of diabetes mellitus in a hospice patient involves many potential challenges. Few directly applicable references are available to guide the clinician in the care of a diabetic patient in hospice or palliative care. Quinn et al\(^1\) developed focus groups and performed a survey to address questions regarding anecdotal diabetes management in palliative care patients. More recently, Angelo et al\(^2\) published an approach to guide clinicians in diabetes care for a palliative care patient by delineating three patient categories (active disease but relatively stable, impending death or organ or system failure, and actively dying) with accompanying suggestions for a palliative plan of care. Likewise, Tice\(^3\) described suggested management of diabetes at end of life. In addition, several recent pivotal studies and ongoing analyses, as well as national consensus guidelines, help give context to discussions specific for glycemic control in a hospice patient. Of central concern, though, is the need to be proactive in developing an appropriate and continually evolving plan of care that focuses on quality of care and patient-identified goals of care. Nutritional and physiological changes as end of life approaches mandate a need to be vigilant in recognizing signs and symptoms of hypoglycemia, as well as in making medication adjustments in anticipation of need. There have been significant additions to the medication arsenal in the last few years, and a thorough understanding of the various therapeutic modalities is essential to ensure optimal glycemic control in the hospice patient.

PREVALENCE
According to the American Diabetes Association (ADA), 8.3% of the US population or 25.8 million have diabetes\(^4\). Another 7 million people are believed to be undiagnosed. Diabetes is currently the seventh leading cause of death\(^5\) with 231,404 deaths in 2007 and is the leading cause of kidney failure\(^4\) accounting for 44% of the new cases in 2008. The incidence of diabetes, most notably Type II diabetes, is increasing at epidemic rates because of, in large part, the social factor of obesity. Oncology patients have a sixfold higher incidence of diabetes than the general population\(^1\)—most likely secondary to insulin resistance, glucose intolerance, and steroid-induced abnormalities. With the increasing prevalence of diabetes seen in the general population coupled with a large percentage (40%) of hospice patients admitted with cancer as a primary diagnosis,\(^6\) the hospice clinician should be prepared to encounter patients with both disease states and be knowledgeable about the complexities involved in such care.

PIVOTAL STUDIES
Two landmark studies published in the 1990s, the Diabetes Control and Complications Trial\(^7\) and UK Prospective Diabetes Study,\(^8\) revolutionized diabetic medical care. These studies provided statistical evidence that aggressive glycemic control promoted a reduction in the long-term microvascular complications of retinopathy, nephropathy,
and neuropathy, as well as a decrease in morbidity and mortality. In addition to these benefits, macrovascular complications (cardiovascular, stroke, amputations), metabolic syndrome, and insulin resistance were reduced.

Three more recent studies, Action to Control Cardiovascular Risk in Diabetes (ACCORD),9 The Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE),10 and Veterans Affairs Diabetes Trial (VADT),11 have attempted to further define specific cardiovascular outcomes with intensive glycemic control in Type II diabetic patients with high cardiovascular risks. The ACCORD study, a large North American study with 10,251 patients, involved two arms—an intensive therapy arm with a target hemoglobin A1C below 6% and a standard therapy arm with a targeted hemoglobin A1C from 7% to 7.9%. The intensive arm was prematurely stopped 17 months before the anticipated end of the study because of an increase in mortality (hazard ratio, 1.22; 95% confidence interval [CI], 1.01-1.46; \( P = .04 \)) and a nonstatistical reduction in major cardiovascular events (hazard ratio, 0.90; 95% CI, 0.78-1.04; \( P = .16 \)). The Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation study was an equally large study with 11,140 patients enrolled from Europe and Asia. Average hemoglobin A1C was 6.5% in the intensive arm and 7.3% in the standard treatment arm for a period of 5 years. Although there was a 10% relative reduction (hazard ratio, 0.90; 95% CI, 0.82-0.98; \( P = .01 \)) in macrovascular and microvascular events, most of this effect was secondary to the 21% reduction in nephropathy alone (hazard ratio, 0.79; 95% CI, 0.66-0.93; \( P = .006 \)). There was no statistical difference seen in cardiovascular events, cardiovascular mortality, or all-cause mortality (\( P = .32 \), \( P = .12 \), \( P = .28 \), respectively). The VADT study evaluated 1791 patients in the Veteran’s Administration system for the primary outcome of a first occurrence of a major cardiovascular event (myocardial infarction, stroke, heart failure, inoperable coronary disease, cardiovascular death, vascular surgery, and amputation for ischemic gangrene). After 5.6 years of follow-up data, this study ended with nonstatistical significance (hazard ratio, 0.89; 95% CI, 0.74-1.05; \( P = .14 \)) for the composite of cardiovascular events in the intensive arm with a median hemoglobin A1C 6.9% as compared with the normal treatment arm with a median hemoglobin A1C 8.4%.

Individually, ACCORD, The Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation, and VADT showed no significant reduction in cardiovascular outcomes with intensive glycemic control; however, a recent meta-analysis of these studies showed a statistically significant reduction in major cardiovascular outcomes especially nonfatal myocardial infarction.12 No effect was seen on mortality, and the major cardiovascular outcome was seen in patients without baseline cardiovascular disease.

Controversy still exists regarding the effect of intensive blood glucose lowering on the rate of cardiovascular events despite these studies. Further analysis is ongoing, but evidence seems to suggest that the key to cardiovascular benefit (prevention of myocardial infarction, stroke, or death) in diabetes treatment may be with the initiation of intensive therapy early in the treatment course.13,14 According to the ADA, intensive glycemic control (A1C < 7%) is appropriate to reduce microvascular and neuropathic complications, and if this intensive control is implemented at the time of diagnosis, there is the potential for long-term reduction in macrovascular complications as well.15 What does that mean for a hospice patient who has been a diabetic for 25 years? Is cardiovascular health a patient-identified goal of care? What primary cardiovascular prevention can be actualized and is of value in the short period (weeks to months) that remains for the hospice patient?

### GOALS OF CARE

These pivotal studies, in addition to numerous others, have provided the framework for the recommendations of nationally recognized diabetes care. The general medical treatment of diabetes is guided by the ADA Standards of Medical Care and 2011 Clinical Practice Recommendations (Tables 1 and 2). It is important to note that continued emphasis of these standards and practice recommendations focuses on long-term complications and control of concomitant comorbidities. The ADA Position Statement emphasizes salient discussion points to address for a diabetic hospice plan of care—“less stringent A1C goals may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, and extensive comorbid conditions” and “for patients with advanced diabetes complications, life-limiting comorbid illness, or substantial cognitive or functional impairment, it is reasonable to set less-intensive glycemic target goals.”13 The American Geriatric Society has also acknowledged that if life expectancy

<table>
<thead>
<tr>
<th>TABLE 1 American Diabetes Association Standards of Medical Care13</th>
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<tbody>
<tr>
<td><strong>Prevent acute complications</strong></td>
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<tr>
<td><strong>Decrease risk of long-term complications</strong></td>
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<tr>
<td><em>Every 1% decrease in HgA1C reduces microvascular complications by 40%</em></td>
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<tr>
<td><strong>Control other comorbid states</strong></td>
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<tr>
<td><em>Every 10 mm Hg decrease in systolic blood pressure reduces related complications by 12%</em></td>
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</table>
is prognosticated as less than 5 years, a nonintensive HgA1C goal of 8% (equates to mean blood glucose of 187 mg/dL) is acceptable.15 These national consensus guidelines lend support that less intensive glycemic control in a hospice patient does not equate to substandard care but rather follows the lack of specifically defined outcomes relevant to this population in the pivotal studies, as well as patient-specific goals. Conversations between the hospice clinician and the patient may further define these patient-specific goals to include the following:

(1) **Liberalize glycemic control.** What is an acceptable blood glucose in a hospice patient? Ranges such as 110 to 270 mg/dL, 150 to 250 mg/dL, and 90 to 360 mg/dL have been published by several authors.1,3,16,17 Optimally, the range should allow for the patient to enjoy a quality of life that does not include symptoms of hypoglycemia or hyperglycemia. A range of 80 to 300 mg/dL will generally be well tolerated by most patients without incurring any symptoms of hypoglycemia or hyperglycemia.

(2) **Individualize blood glucose monitoring.** Quinn et al1 believe that there should be a purpose behind testing blood glucose, and if physicians and nurses do not implement care based on the results, they should not be testing at all. Although there can be wide variation in the desire and need to perform blood glucose monitoring by both patients and clinicians, blood glucose monitoring remains an important element of a diabetic plan of care as a means to verify the cause of symptoms and to make medication adjustments.

(3) **Prevent hypoglycemic symptoms.** Turnbull et al12 suggested that clinicians should make every effort to prevent hypoglycemia in patients with advanced disease. Comfort-oriented, quality hospice care should attempt to prevent this complication through patient/family education, suggesting raising glycemic targets and facilitating dietary or medication adjustments as appropriate. Although prevention is the goal, the hospice clinician must also be cognizant of the treatment options available in case symptomatic hypoglycemia occurs.

### HYPOGLYCEMIA

Because hypoglycemia can increase morbidity, diminish quality of life, and possibly contribute to mortality, a major goal in the diabetic hospice patient’s plan of care is the prevention of hypoglycemia. Hypoglycemic symptoms such as shakiness, tachycardia, sweating, anxiety, nervousness, dizziness, weakness, headache, irritability, confusion, and/or lowered consciousness can be very distressing. These symptoms may be misinterpreted as other concomitant issues or simply labeled as disease progression and thus cause an ineffective or inaccurate plan of care to be implemented. In fact, there has been some discussion that a percentage of the unexpected deaths in the ACCORD trial may have been related to or precipitated from hypoglycemia.18 The hospice clinician must also assess the potential cause of hypoglycemia, so an estimate of the expected duration of the hypoglycemic episode can be hypothesized. This involves a thorough understanding of the pharmacokinetics (especially onset, peak, and half-life) of the type of insulin or oral hypoglycemic agent administered. For example, an inadvertent overdose of regular insulin will not cause the same degree and duration of hypoglycemia as would an inadvertent overdose of glargine insulin.

There may be a time when despite a plan of care aimed at preventing hypoglycemia, an episode occurs nonetheless. The following options and case study offer clinical guidance for the treatment of hypoglycemia in a hospice patient.

### Reducing, Adjusting, or Eliminating Hypoglycemic-Producing Medications

The degree of hypoglycemia, objectively from an actual blood glucose result or subjectively from significant symptom burden, determines whether a simple reduction in dosage of insulin or oral hypoglycemics or a total discontinuation is necessary. Another option may be to adjust medications to those less prone to cause prolonged hypoglycemia such as rapid or shorter acting insulin formulations or oral hypoglycemics with more favorable pharmacokinetics (shorter half-life or duration of action) or medications that do not lower glucose levels when used as sole agents (Tables 3 and 4).

### Oral Glucose-Elevating Nutritionals/Medications

In a conscious patient with swallowing abilities, the administration of one cup of skim milk, a half cup of orange juice, or the consumption of several pieces of hard candy is often enough to raise glucose levels to eliminate symptomatic
hypoglycemia. Fifteen to twenty grams of commercially available glucose tablets or gels can also be used. A second administration can be given within 15 minutes if the blood glucose level is still below normal and/or the patient is still symptomatic. Once stabilization of the symptoms has occurred, the patient should be instructed to consume a snack or meal if able to avoid another hypoglycemic event.

**Injectable Glucose-Elevating Medications**

D50W (25 g dextrose in 50 mL) is the most widely used medication to quickly elevate blood glucose especially in an unconscious patient or a patient in a healthcare environment. Because intravenous access is required for administration, this becomes a potential barrier in a hospice patient. Repeat administrations of D50W may be necessary for a single hypoglycemic reaction. Glucagon is a standard hospital medication used to treat hypoglycemia in acute situations especially with unconscious patients. It is a hormone normally produced in the \( \alpha \)-cells of the islet of Langerhans, and its mechanism of action involves promoting glycogenolysis in the liver. Although it can be administered subcutaneously, intramuscularly, or intravenously, glucagon is less likely to be effective in a hospice patient.

<table>
<thead>
<tr>
<th>TABLE 3 Antidiabetic Agents (Except Insulin)(^{19,20})</th>
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<tbody>
<tr>
<td><strong>Category</strong></td>
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<tr>
<td>Sulfonylurea: first generation</td>
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<td></td>
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<tr>
<td></td>
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<tr>
<td>Second generation</td>
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<tr>
<td>Biguanide</td>
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<tr>
<td>Thiazolidinediones</td>
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<td></td>
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<tr>
<td>( \alpha )-Glucosidase inhibitors</td>
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<td></td>
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<tr>
<td>Meglitinides</td>
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<td></td>
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<tr>
<td>Incretin-mimetic</td>
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<td></td>
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<tr>
<td>DPP-4 Inhibitor</td>
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<td></td>
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<td>Amylin analog</td>
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\(^a\)Hypoglycemia was possible under certain conditions (deficient caloric intake, strenuous activity, use with concomitant insulin/sulfonylureas or alcohol).

\(^b\)Not administered as a sole agent (hypoglycemia producing with insulin/sulfonylureas but not with metformin).
whose glycogen stores or liver function may be impaired, thus promoting suboptimal glycogenolysis.

**Continuous Infusions of Glucose Solutions**

Patients who continue to have repeated hypoglycemic episodes or a prolonged reaction despite the above interventions may require a continuous infusion of dextrose solution. Hypodermoclysis with 5% dextrose in water may be considered if intravenous access is not readily available. In severe cases, intravenous access will need to be obtained for a more concentrated dextrose solution to be administered with the rate titrated to maintain a symptom-free blood glucose level.

**Bedside Pearl.** A homecare diabetic hospice patient should be encouraged to have a supply of commercially available glucose gel available at all times. Even in a semiconscious state, the patient can tolerate the gel being administered buccally with oral stimulation to illicit a swallowing reflex. Should an oral glucose-elevating attempt fail, the hospice plan of care should delineate the patient’s goals regarding emergency dispatch (911) and/or hospitalization. Most often, having more aggressive interventions such as D50W or glucagon in a home environment is not practical and is not standard practice.

**HYPOGLYCEMIC CASE REPORT**

AJ is a 46-year-old white woman with a hospice diagnosis of liver cancer and diabetes mellitus as a comorbidity. She was recently discharged from the hospital to her home after treatment of ascites and dyspnea. During her hospitalization, she battled intermittent episodes of hypoglycemia. Prednisone was added to her medication regimen for symptom control of her dyspnea, as well as to potentially promote a drug-induced increase in her glucose level. Her hospice homecare team received a telephone call from her daughter 48 hours after being discharged from the hospital. She stated that her mother was barely arousable and breathing “funny.” The daughter measured her blood glucose level, and it was 46 mg/dL. While the hospice homecare nurse was on route, the daughter was able to administer a sugar paste buccally. Upon arrival at the home, a repeat blood glucose level measurement was 60 mg/dL, and the patient was transferred to an inpatient hospice unit for further evaluation and treatment. During the first 24 hours at the inpatient hospice unit, the patient continued to have severe episodes of hypoglycemia despite repeated oral and intermittent intravenous D50W administrations. A continuous subcutaneous dextrose solution was started as the only means to keep her blood glucose above 80 mg/dL and afford her an acceptable level of symptom relief, but it became clear that the rate needed to maintain her blood glucose was not conducive to subcutaneous administration. A peripherally inserted central catheter was placed, and the patient was discharged on D40W at 25 mL/hour continuously with a portable ambulatory pump. She remained at home and was able to maintain a symptom-free glucose level for 10 weeks until her death. The cause of her hyperinsulinemia was never fully elucidated.

**ADDITONIAL COMPLEXITIES FOR THE DIABETIC HOSPICE PATIENT**

The diabetic hospice patient has a potential myriad of changes or clinical factors occurring, often concurrently, and each requires thorough assessment, critical thinking, discussion, monitoring, and potential adjustments to the overall plan of care. Further discussion will include pathophysiological changes, nutritional changes, infection, decreased activity levels, and drug-induced hyperglycemia.

**Pathophysiological Changes.** Changes in renal or hepatic function can greatly influence glycemic control in a hospice patient by altering the pharmacokinetics of medications. As renal function declines and the patient remains on his/her “usual, unaltered” antidiabetic regimen, an enhanced blood glucose-lowering effect may be realized.

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**TABLE 4 Insulin Formulations and Pharmacokinetics**

<table>
<thead>
<tr>
<th>Category</th>
<th>Type of Insulin</th>
<th>Onset, h</th>
<th>Peak, h</th>
<th>Duration, h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid</td>
<td>Lispro (Humalog®)</td>
<td>0.25-0.5</td>
<td>0.5-1.5</td>
<td>3-6</td>
</tr>
<tr>
<td></td>
<td>Aspart (NovoLog®)</td>
<td>0.17-0.33</td>
<td>1-3</td>
<td>3-5</td>
</tr>
<tr>
<td></td>
<td>Glulisine (Apidra®)</td>
<td>0.25</td>
<td>0.5-1.5</td>
<td>3-5</td>
</tr>
<tr>
<td>Short acting</td>
<td>Regular (R®)</td>
<td>0.5-1</td>
<td>1-5</td>
<td>4-10</td>
</tr>
<tr>
<td>Intermediate</td>
<td>NPH</td>
<td>1-4</td>
<td>6-14</td>
<td>12-24</td>
</tr>
<tr>
<td>Long acting</td>
<td>Detemir (Levemir®)</td>
<td>3-4</td>
<td>No true peak</td>
<td>6-23</td>
</tr>
<tr>
<td></td>
<td>Glargine (Lantus®)</td>
<td>1-2</td>
<td>No true peak</td>
<td>24</td>
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leading to potential negative outcomes. Likewise in the liver, impaired glycogenolysis can quickly change the homeostasis of diabetic control. Medications such as metformin or a thiazolidinedione whose mechanism of action involves a hepatic process should be carefully evaluated for use in a diabetic hospice patient with liver impairment. A hospice patient with significant nausea and vomiting who is having difficulty taking his/her oral antidiabetic medication might need to have adjustments in his/her medication regimen, including the initiation of insulin therapy with increased blood glucose monitoring. Goals of care discussions should occur throughout the course of care but especially during medication adjustment periods.

**Bedside Pearl.** Knowledge, either known or suspected, of the patient’s renal function and its potential impact on the current choice of medications should be incorporated proactively and continually in the overall goals of care discussion. It is not acceptable to wait for a negative patient event to trigger a medication change if the clinician critically analyzed the potential ahead of time and should have acted in the patient’s best interest.

**Nutritional Changes.** Anorexia, unrelieved symptoms, alterations in the gastrointestinal system, and psychological factors play a significant role in a patient’s nutritional status. Common issues seen in hospice patients such as thrush, xerostomia, or gastroparesis can impact the patient’s ability to maintain their nutritional baseline. Food preferences and aversions, as well as the ability to prepare foods, need to be assessed. Altered timing of meals or missing entire meals can also impact the pharmacological plan of care.

**Bedside Pearl.** The hospice clinician should verify the appropriate coordination of the insulin administration with meal availability in long-term care environments. The plan of care should also address what action should be taken if the patient fails to consume most of his/her meal after having received his/her full ordered dosage of insulin.

**Infection.** The correlation between infection and negative glycemic control is well known. Infection is commonly cited as the number 1 precipitating cause of diabetic ketoacidosis—a serious complication of diabetes. Physiologically, stress-induced hyperglycemia occurs secondary to enhanced glycogenolysis, enhanced gluconeogenesis, increased release of counterregulatory hormones, and increased release of proinflammatory cytokines, which contribute to insulin resistance.

**Bedside Pearl.** The hospice plan of care should be adjusted during periods of infection to maintain glycemic control aligned with patient-directed goals of care. This may include increased insulin requirements and/or increased blood glucose monitoring for a finite period.

**Decreased Activity Levels.** Upon admission to hospice, some diabetic patients are very active with a high functional status. As disease progresses and functional status declines, keen assessment is warranted to determine when activity levels change to a point where an adjustment in the overall diabetic plan of care is required to account for the decrease in exercise/activity.

**Bedside Pearl.** The hospice clinician should assess and monitor activity levels over time that differ significantly from the patient’s baseline and correlate this change with the patient’s blood glucose monitoring to determine when the plan of care needs to be adjusted.

**Drug-Induced Hyperglycemia.** Several well-known palliative care symptom management medications are diabetogenic and thus can cause an increase in blood glucose levels. These include glucocorticoids (prednisone, dexamethasone), atypical antipsychotics (olanzapine, risperidone, quetiapine), diuretics (furosemide, torsemide, bumetanide), and octreotide. Should the hospice nurse check a random blood glucose level after initiating these medications to see if a drug-induced hyperglycemia state exists or wait until there are symptoms suggestive of hyperglycemia? Symptoms such as dry skin, drowsiness, blurred vision, nausea, polydipsia, and polyphagia can often be missed or interpreted as general decline (except for polyphagia, which is seen as a benefit in most hospice patients because of the increased appetite side effect of glucocorticoids) so hyperglycemia would probably be missed.

**Bedside Pearl.** The hospice clinician should evaluate any medication change—a newly ordered or discontinued medication—to ascertain whether glycemic control will potentially be impacted from a physiological effect or a drug interaction.

**PHARMACOLOGICAL CHOICES**

The pharmaceutical plan of care for a diabetic hospice patient needs to be a dynamic, ever-evolving process to achieve the necessary balance of glycemic control and optimal patient outcomes. In the last 10 years, many additional pharmacological choices have been added to the antidiabetic arsenal. To optimize a diabetic hospice patient’s pharmaceutical plan of care, the clinician must have knowledge of the medication choices available (Table 3).

**INSULIN**

Within the past decade, we have seen quite a revolution in insulin products. To ensure proper utilization and dosing, the hospice clinician must understand the unique pharmacokinetic profiles of the newer insulins (Table 4; Figure 1). Insulins are designated as rapid, short acting, intermediate, or long acting based on their duration of action. The rapid analogs and short-acting insulins are appropriate for bolus, postprandial, or sliding scale orders because their onset and peak action correspond to the time course needed to manage the expected glucose load. Anecdotally, some controversy exists regarding sliding scale insulin in a hospice plan.
Clinicians are often faced with making decisions about glucose monitoring in a hospice patient without empirical evidence to support how to appropriately order sliding scale insulin. When the end of life is imminent, maintenance of strict glycemic control can be detrimental to the quality of life. Unnecessary tests such as frequent blood glucose monitoring and complex insulin regimens are burdensome, especially in a homecare environment. Because patients and families may have spent years striving for tight glycemic control, they will require sensitive and goal-directed conversations as the plan of care shifts and benefit versus burden is weighed.

The rapid acting insulin analogs have the advantage of inducing less hypoglycemia than regular insulin because of their more favorable pharmacokinetic profiles. Hirsch reported up to 25% less hypoglycemia with lispro than regular insulin. Because of their more rapid onset of action, rapid acting insulin analogs may also be more appropriate in patients with erratic consumption of meals because they can be administered closer to the actual start of a meal (aspart 10-15 minutes prior, glulisine or lispro 15-20 minutes prior, regular 30-60 minutes prior). Although regular insulin is still widely used, its pharmacokinetic parameters have wider ranges, which confer greater interpatient and intrapatient variability. Hospice patients may also experience this greater variability because of altered absorption, bioavailability, and renal function changes. The major disadvantage seen with rapid acting insulin analogs is cost, as they are roughly twice the cost of regular insulin.

The intermediate and long-acting insulins are designed to manage the basal insulin requirements, which account for the normal physiological processes of lipolysis and glycogenolysis. Although NPH and detemir insulins have a duration range up to 23 to 24 hours, they are both more commonly administered twice daily whereas glargine insulin is almost always administered once daily. Furthermore, detemir and glargine insulins are “peakless” (Figure 1), and this uniformity and avoidance of peaks and valleys allow for a lower potential for hypoglycemia episodes.

Clinicians may have two more insulin options to consider in the near future, as a new inhaled formulation (Afresa®) and a new buccal spray formulation (Oral-Lyn®) are currently under investigation.

Bedside Pearl. The hospice clinician must assess and educate the patient/caregiver regarding the possibility of insulin name confusion. This look-alike, sound-alike confusion can lead to dangerous errors such as when Lantus is used instead of Lispro or Levemir or Humalog is thought to be the same as Novolog. All insulin formulations are unique, and there is no direct interchangeability.

SULFONYLUREAS

Sulfonylureas comprise the “workhorse” category of antidiabetic agents. The first-generation sulfonylureas have been around for years and should rarely be used in a hospice patient, as the second-generation agents have a more reliable pharmacokinetic profile. Chlorpropamide, for example, should be avoided in a hospice patient as the risks of severe hypoglycemia (related to a prolonged half-life) and hyponatremia outweigh any benefit. Their mechanism of action involves the stimulation of insulin release from the pancreas. Although occasionally seen concurrently with insulin in a hospice pharmaceutical plan of care, this combination may have more risks (additive hypoglycemic potential) than benefits. Even as a sole agent, sulfonylureas are hypoglycemic producing, and as such, the American Academy of Clinical Endocrinologists has suggested a less pronounced role for sulfonylureas in the geriatric population. Sulfonylureas need to be adjusted as dietary and physiological factors change. Caution should be exercised when nonsteroidal anti-inflammatory agents (NSAIDs) or salicylates are added to a patient stabilized on a sulfonylurea, as displacement from protein binding can occur causing an enhanced sulfonylurea effect, which may manifest as a hypoglycemic reaction.

Bedside Pearl. Glipizide or glimepiride is the preferred sulfonylurea for patients with renal dysfunction, especially older adults, as either has a lower relative likelihood of inducing hypoglycemia compared with glyburide.

BIGUANIDE

A revolution in diabetic medication management occurred when metformin entered the US market. Since its arrival, it has become a very popular agent—both as a single agent and in combination with other medications.
Mechanistically, metformin is labeled as a “sensitizer” because it improves the peripheral uptake and utilization of glucose. Because of this sensitizer role, metformin is often seen in patients classified with insulin resistance (on high doses of insulin with suboptimal outcomes). It also decreases hepatic glucose production and output. Unlike sulfonylureas, it does not directly stimulate insulin release, and thus, it is not hypoglycemia producing when used as a single agent. Metformin is relatively contraindicated in patients with liver or renal dysfunction. Patients with creatinine greater than 1.5 mg/dL (men) or 1.4 mg/dL (women) have an increased risk of lactic acidosis. It may be difficult to differentiate lactic acidosis symptoms from general decline or disease progression because of the nonspecific nature of the symptom complex including myalgia, malaise, abdominal pain, hypotension, somnolence, and respiratory impairment. Using metformin without knowledge of a patient’s renal function may result in symptoms being mistakenly attributed to decline or disease progression.

**Bedside Pearl.** Metformin may be a good first choice if glycemic control is needed in a hospice patient with adequate liver and renal function, as it can be used as a sole agent, and there would be no concern for drug-induced hypoglycemia.

**THIAZOLIDINEDIONES**

Like metformin, thiazolidinediones are also sensitizers, as they decrease insulin resistance in skeletal muscle and fat tissue. They also decrease hepatic glucose output and may help to preserve β-cell function in the pancreas. Originally thought to be a novel addition to the choices for glycemic control, thiazolidinediones have now been relegated to a minor role because of unacceptable adverse effects. Increased cardiovascular risk, most notably myocardial infarction and heart failure, have been identified with thiazolidinediones. Although there are some conflicting data regarding cardiovascular events and mortality between the two thiazolidinediones on the US market, the Food and Drug Administration placed restrictions on the prescribing of rosiglitazone in September 2010. Rosiglitazone and pioglitazone have also been proven to have an increased upper arm fracture risk, particularly seen in women. Although there are some conflicting data regarding cardiovascular events and mortality between the two thiazolidinediones on the US market, the Food and Drug Administration placed restrictions on the prescribing of rosiglitazone in September 2010. Rosiglitazone and pioglitazone have also been proven to have an increased upper arm fracture risk, particularly seen in women. Thiazolidinediones is peripheral edema. The hospice clinician should evaluate risks versus benefits of continued use and avoid the vicious cycle of thiazolidinedione-induced edema triggering the prescribing of furosemide, which may lead to a diuretic-induced increase in blood glucose levels and the need for further glycemic control adjustments.

**α-GLUCOSIDASE INHIBITORS**

Many hospice patients have significant changes in their dietary habits and often skip meals. For this reason, α-glucosidase inhibitors are a good option for the hospice patient because they are administered only at the time of a meal. If a patient chooses to skip a meal or is not able to eat because of disease progression or other symptoms, the medication should not be administered. Labeled as “starch blockers,” α-glucosidase inhibitors delay the intestinal absorption of glucose. Because they do not stimulate insulin release, they cannot produce hypoglycemia when used as a single agent.

**Bedside Pearl.** The major drawback of α-glucosidase inhibitors is gastrointestinal intolerance. The hospice clinician should assess for diarrhea, abdominal pain, and flatulence.

**MEGLITINIDES**

These short-acting secretagogues stimulate insulin release from the pancreas and thus can be hypoglycemic producing. Like α-glucosidase inhibitors, they are administered at the time of a meal and are not administered if a meal is skipped.

**Bedside Pearl.** Caution should be exercised when fluconazole is administered concurrently with repaglinide as there can be a drug interaction causing a prolonged blood glucose-lowering effect.

**INCRETIN MIMETICS**

As mentioned earlier, there are many counterregulatory and feedback mechanisms in the body responsible for the intricate regulation of insulin. One of these is a chemical known as glucagon-like peptide (GLP-1), which is secreted by the gastrointestinal tract in response to food that stimulates insulin release. Incretin mimetics enhance glucose-dependent insulin secretion and suppresses elevated glucagon secretion similar to GLP-1. Although a novel mechanism, the use of these agents is inhibited because they have to be administered subcutaneously and they cause a significant degree of gastrointestinal symptoms, specifically nausea and vomiting. Recently published reports of renal problems, including renal failure, have surfaced with the use of exenatide. Although recently approved, liraglutide has an increased risk of pancreatitis and thyroid gland tumors.

**DIPEPTIDYLPEPTIDASE IV INHIBITORS**

Dipeptidylpeptidase IV (DPP-4) is the enzyme responsible for the degradation of glucoregulatory hormones like GLP-1. By inhibiting this enzyme, DPP-4 inhibitors allow GLP-1 to continue to work to increase postprandial insulin release and decrease glucagon levels. Dipeptidylpeptidase IV inhibitors are not hypoglycemic producing when used as sole agents. Some published reports have shown concern over potential immunologic effects seen, but
more data and long-term use are needed to fully support this concern.34,35

**Bedside Pearl.** This oral antidiabetic drug category has been associated with increased prescribing in the last couple years because of ease of administration (once daily) and its lack of producing hypoglycemia. Renal function determines appropriate dosing.

**AMYLIN ANALOG**

Amylin is a neuroendocrine hormone cosynthesized from the β-cells of the pancreas to control postprandial glucose. Pramlintide, a synthetic analog of amylin, also slows gastric emptying, suppresses glucagon secretion, and modulates appetite. Unfortunately, it is administered as a subcutaneous injection and has not seemed to find its niche in diabetic plans of care.

**CONCLUSION**

Although challenging, the diabetic hospice patient offers opportunities for the clinician to critically think through many facets of care to ensure that an optimal plan of care is implemented and continually monitored and adjusted. Translatable evidence and patient-specific goals of care should guide the clinician in the liberalization of glycemic control and individualization of blood glucose monitoring while enhancing quality of life. Instead of intensive glycemic control, the hospice clinician should focus on the prevention of hypoglycemia in the diabetic hospice patient’s plan of care. Additional clinical and behavioral studies with diabetic hospice patients, such as outcomes and quality of life analyses, would afford clinicians specific evidence to define or reinforce best nursing practice. Clinicians will be required to be well educated on pharmacological options, as antidiabetic medications should be based on patient-specific and drug-specific factors to maximize goal attainment while minimizing inherent medication adverse effects and the risk of medication-induced hypoglycemia.

**References**


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