

End of the Road: Diabetes Care When Insulin May Not Be an Option

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PRESENTATION

J.U. is a 53-year-old man with uncomplicated type 2 diabetes who requires a commercial driver's license (CDL) for his occupation as a truck driver and mechanic. His diabetes was controlled with increasing doses of metformin and glipizide during the first 4 years after his diagnosis. Despite nutrition counseling, diabetes education classes, and physician visits every 3–6 months, nonadherence with therapeutic lifestyle changes contributed to his A1C fluctuating between 7.2 and 10.2% over 3 years. His health care provider recommended insulin therapy numerous times, but J.U.'s needle fear, lifestyle preferences, and fear of losing his job led to patient refusal and clinical inertia.

He is seen for an urgent appointment after his Department of Transportation (DOT) physical was failed for hyperglycemia (glucose > 200 mg/dl) and significant levels of glucose in the urine. He reports fatigue, polyphagia, polydipsia, and polyuria. He has not been compliant with self-monitoring of blood glucose (SMBG) or recommended therapeutic lifestyle changes.

At the time of this visit, his diabetes medication regimen consists of metformin 1,000 mg twice daily and glipizide 10 mg twice daily with meals. His A1C is 8.1%, weight is 207 lb (BMI 32.5 kg/m²), blood pressure is 110/72 mmHg, pulse is 80 bpm, serum creatinine is 0.9 mg/dl, total cholesterol is 116 mg/dl, triglyceride level is 207 mg/dl, LDL cholesterol

is 46 mg/dl, and HDL cholesterol is 29 mg/dl.

He has a known history of hyperlipidemia treated with a statin, hypertension treated with an ACE inhibitor, and gastroesophageal reflux disease treated with a proton pump inhibitor. He has smoked two packs of cigarettes per day for 32 years, with multiple failed quit attempts, and denies alcohol or illicit drug use.

J.U. provides the primary source of income for his family and has financial difficulties. Having to stop work, even for a brief period, would be financially devastating to his family. His physician signs a medical examination form certifying that his diabetes will be closely monitored and managed, which will allow the patient 6 months to control his diabetes and pass the DOT physical. The patient is referred to the clinical pharmacist to provide diabetes disease state management as part of a collaborative practice agreement within a patient-centered medical home.

Progress After Pharmacist Referral

During frequent visits, the pharmacist reinforces diabetes education, including lifestyle modifications, diabetes symptoms, complications, goals of care, SMBG, and medications. Each session concludes with patient goal-setting.

Diabetes testing supplies are obtained through the patient's insurance with low out-of-pocket

costs. The pharmacist switches his glipizide prescription to the extended-release formulation to optimize therapy and initiates sitagliptin 100 mg daily. Manufacturer rebates allow J.U. to obtain sitagliptin at a low cost.

In a period of 8 weeks, J.U.'s average fasting blood glucose level improves to 154 mg/dl, and his A1C improves to 7.9%. A shared decision is made among the patient, his provider, and the pharmacist to initiate pioglitazone 15 mg daily. After 3 months of quadruple oral therapy, his A1C is 6.8%, and weight gain has been limited to 3.5 lb with strict diet and exercise.

QUESTIONS

1. What regulatory barriers exist for CDL holders with diabetes?
2. What therapy options exist for the treatment of type 2 diabetes when insulin therapy is refused or not plausible?
3. How can physicians rely on other members of the health care team to assist in treating patients with diabetes?

COMMENTARY

The use of CDLs for interstate commerce (defined as trade, traffic, or transportation between a place in a state and a place outside such state, between two places in a state through another state or place outside of the United States, or between two places in a state as part of trade, traffic, or transportation originating or terminating outside the state or United

States) is controlled under federal regulations issued by the Federal Motor Carrier Safety Administration (FMCSA).¹ CDL holders who require insulin to control diabetes are currently disqualified from operating a motor vehicle in interstate commerce until they obtain a medical exemption.^{2,3} The FMCSA has 180 days to grant or deny an exemption after the patient obtains clearance from a medical examination, an endocrinologist, and an optometrist.³ Medical examination by a licensed practitioner typically requires documentation of a patient's adequate individual disease management skills while on insulin for 1 month for patients with type 2 diabetes or 2 months for those with type 1 diabetes.^{4,5}

Private driving and use of a CDL for intrastate commerce (defined as any trade, traffic, or transportation in any state that is not interstate commerce) are regulated by individual states, with most requiring medical clearance to drive if the patient has diabetes or other conditions that may lead to altered consciousness while driving.¹ The federal exemption rules for insulin-treated patients with diabetes do not extend to intrastate commerce.³ Given the differences in regulations based on how a CDL is used, it is important for clinicians to have good relationships with their patients and to be familiar with both federal restrictions regarding interstate commerce and state-specific requirements for intrastate commerce.

Oral antihyperglycemic agents and noninsulin injectables are not listed as therapies disqualifying individuals from driving in interstate commerce or requiring a medical exemption. Effective oral and noninsulin injectable options are increasing. Complementary mechanisms of action and nonadditive side-effect profiles allow clinicians and patients to personalize treat-

ment plans when insulin is not a preferred option.

In this case, an oral dipeptidyl peptidase 4 (DPP-4) inhibitor was added after the patient reached maximum doses of metformin and a sulfonylurea. DPP-4 inhibitors provide modest reductions in A1C, carry a low risk of hypoglycemia, and do not promote weight gain.

Glucagon-like peptide 1 (GLP-1) receptor agonists share these benefits with DPP-4 inhibitors and may also promote weight loss and provide greater reductions in A1C. Dosing flexibility is another benefit of GLP-1 receptor agonists, with a once-weekly exenatide option now available.

GLP-1 receptor agonists are only available in injectable dosage forms, and nausea is a common—although generally transient—side effect. However, given the patient's needle aversion, this option was reserved. Pioglitazone, a thiazolidinedione (TZD), was chosen as a fourth oral agent after triple therapy failed to reduce his A1C to goal.

TZDs are associated with an increased risk of edema, weight gain, and hypoglycemia. The patient received education about the possible associations between pioglitazone and bladder cancer, bone fractures, and cardiovascular side effects and decided with his providers that the benefits of its ability to lower fasting and postprandial hyperglycemia outweighed these risks.

Many other oral treatment options are approved for treatment of type 2 diabetes, including α -glucosidase inhibitors, bile acid sequestrants, bromocriptine, and sodium-glucose cotransporter 2 (SGLT-2) inhibitors. Canagliflozin was the first SGLT-2 inhibitor available in the United States and is a novel oral antihyperglycemic for the treatment of type 2 diabetes, but it

was not available while managing this patient. It works by inhibiting glucose reabsorption of glucose in the renal tubules and lowers the renal glucose threshold, resulting in increased urinary excretion of glucose. It provides average A1C lowering of about 0.7 and 1% for the 100- and 300-mg doses as monotherapy, respectively. It is associated with a low incidence of hypoglycemia and modest weight loss. When studied as monotherapy, 1 patient for every 10 treated with canagliflozin experienced mycotic or bacterial urinary tract infections. It also was associated with mild and transient increases in serum creatinine, hypotension, and hyperkalemia.⁶

Insulin should be considered in cases of severe hyperglycemia (as indicated by an A1C > 9%), regardless of treatment status or when patients fail to achieve glycemic targets despite treatment with oral antihyperglycemics and lifestyle changes.⁷ Initiating therapy should be a shared decision. Beginning insulin therapy must take into account patient perceptions, preferences, risks, and professional regulations that are often overlooked or about which providers and patients were previously unaware.

When insulin is not an option, it is not the end of the road. Personalized, intensive, and frequent disease state management of diabetes is an effective strategy. Many noninsulin treatment options exist and can be combined to achieve blood glucose targets.

Clinicians treating patients with type 2 diabetes should be aware of the risks, benefits, dosing recommendations, and costs of all oral and injectable treatment options. Incorporation of patient-specific preferences and clinical information should be made to make treatment decisions shared and personalized.

The burden of diabetes is often overwhelming. Social, cultural, and financial issues often become barriers to optimal care. Regulatory restrictions add another level of complexity to the adequate treatment of patients with diabetes. Clinicians need to be aware of federal and state regulations regarding their patients' occupation and disease state before making treatment decisions. Alternative employment opportunities are not always an option, and taking time from work to obtain necessary exemptions may prove costly to such patients. Relying on other members of the health care team, including pharmacists, diabetes educators, and dietitians, can help with the complexity of treating and educating patients with diabetes.

CLINICAL PEARLS

- Commercial truck drivers face complex regulatory requirements that make the use of insulin products to control diabetes difficult or impossible for some. Interstate and

intrastate commerce are regulated differently. Exemptions for insulin use are allowed but may take several months to acquire.

- Many noninsulin therapies exist for the treatment of type 2 diabetes. Many possible combinations of medications can help patients achieve glycemic control. Knowledge of each medication's benefits, safety profile, cautions, and costs is important when making treatment decisions.
- Involving other members of the health care team, including pharmacists, diabetes educators, dietitians, social workers, and nurses, can help patients with diabetes achieve their health care goals.

REFERENCES

- ¹Sheenan RJ: Federal motor carrier safety regulations: general applicability and definitions. *Federal Register* 5:350, 2011
- ²Sheenan RJ: Federal motor carrier safety regulations: physical qualifications and examinations. *Federal Register* 5:372, 2011

- ³Federal Motor Carrier Safety Administration: Driver exemption programs [article online]. Available from <http://www.fmcsa.dot.gov/rules-regulations/topics/medical/exemptions.htm>. Accessed 10 June 2013

- ⁴Sandberg AM: Qualifications of drivers: eligibility criteria and applications: diabetes exemption. *Federal Register* 70:67777–67781, 2005

- ⁵Sandberg AM: Qualifications of drivers: exemption: applications: diabetes. *Federal Register* 68:52441–52452, 2003

- ⁶Stenlöf K, Cefalu WT, Kim KA, Alba M, Usiskin K: Efficacy and safety of canagliflozin monotherapy in subjects with type 2 diabetes mellitus inadequately controlled with diet and exercise. *Diabetes Obes Metab* 15:372–382, 2013

- ⁷American Diabetes Association: Standards of medical care in diabetes—2013. *Diabetes Care* 36 (Suppl. 1):S11–S66, 2013

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