

RETHINKING FIRST LINE THERAPY IN SEVERE TYPE 2 DIABETES

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ABSTRACT

A 52 year old woman presented with symptomatic severe hyperglycemia and a diagnosis of diabetes mellitus was made. The clinical question was how to best start treatment in this patient given an unusually high hemoglobin A1C level of 12.6 percent. She was also symptomatic with a recent weight loss of 23 pounds. A literature search revealed that a common pharmacological treatment for diabetes mellitus were oral hypoglycemics, but given such high A1C levels, insulin is a first line therapy. This patient saw an A1C improvement from 12.6 to 5.4 percent over a few months on Metformin and Gliclazide. It would be beneficial if newly diagnosed diabetics with such severe hyperglycemia could improve their sugar levels and symptoms without starting an insulin regime.

CASE HISTORY

A 52 year old menopausal woman with a family history of diabetes mellitus, hypertension, and cancer presented to her family doctor with a 23 pound weight loss over the last two and a half months. She reported no change in appetite. The patient is a smoker and had a blood pressure of 130/70 and a BMI of 27.8 after the weight loss. Blood work was arranged to be reviewed at the next visit. The blood work revealed vitamin B12 deficiency, dyslipidemia, a fasting blood sugar level of 18.5 and an A1C of 12.2. The blood sugars were tested a second time to confirm a diagnosis of diabetes mellitus. The second test revealed a fasting blood sugar level of 18.8 and a severe hemoglobin A1C level of 12.6 which led to a diagnosis of diabetes mellitus. The patient was started on a monotherapy of 1 tablet of metformin 500 mg TID for 30 days on December 1st, 2016. The patient was also referred to a dietician and started on ASA 81mg OD and Crestor. After the 30 days, the patient reported average fasting blood sugar levels of 16-26 and her metformin was increased to 1 mg BID. Gliclazide 60mg Xtended release OD was also added. The patient reported fasting blood sugar levels of 5-6 during a March 2nd visit. The hemoglobin A1C was 8.4 at this visit and the medications remained unchanged. The patient reported fasting blood sugar levels of 5.6-7.4 at a visit in May and the most recent bloodwork in June revealed a fasting blood sugar level of 5.9 and an A1C of 5.4. The patient was able to lower her hemoglobin A1C level from a severe 12.6 to a normal 5.4 with Metformin and Gliclazide.

LITERATURE REVIEW

The clinical question in this case was how to initiate pharmacological therapy in a patient with new onset diabetes mellitus and a high hemoglobin A1C. To help answer this question, "Diabetes mellitus treatment" was searched on UpToDate. This produced an article entitled "Initial management of blood glucose in adults with type 2 diabetes mellitus" which suggested that for symptomatic or severe hyperglycemia patients, insulin therapy is indicated for initial treatment.¹ Metformin monotherapy is not recommended as the initial dose is too low to improve symptoms.¹ A link on this article lead to another article on UpToDate entitled "Insulin therapy in type 2 diabetes mellitus". According to this article, insulin should be considered for patients presenting with an A1C greater than 9.5 percent, fasting plasma glucose

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>250mg/dL, random glucose consistently >300mg/dL, ketonuria, or unplanned weight loss with hyperglycemia.² “Insulin therapy type 2 diabetes” was searched for in the University of Manitoba library database. The search produced an article review from JAMA about insulin therapy for type 2 diabetes mellitus which states that insulin therapy can reverse glucose toxicity in patients with severe hyperglycemia (HbA1C >10%).³ The terms “Oral hypoglycaemic diabetes mellitus” were searched in the University of Manitoba library database to find an article which looks at the use of oral hypoglycaemics in type 2 diabetes mellitus. This small study reviewed 156 type 2 diabetes mellitus patients using oral hypoglycaemic agents (OHAs) and found that the most commonly prescribed regimen was Metformin plus Gliclazide.⁴ This finding is consistent with other studies.⁴

DISCUSSION

The challenge in this case was how to best treat new onset diabetes in a patient with severe hemoglobin A1C levels and who is symptomatic. Along with focusing on diet and exercise, it was important to initiate a pharmacological regimen since this 52 year old patient had a hemoglobin A1C of 12.6 percent on recent blood work. With such a high A1C level, the literature suggests that insulin would be an appropriate choice as first line therapy. However, this patient was started initially on 500 mg Metformin monotherapy TID for a month. One month later, her reported fasting blood sugar levels were in the range of 16-26 so the Metformin was increased to 1000 mg BID and 1 tablet once daily of 60mg extended release Gliclazide was added. The patient reported normal average fasting blood sugar levels a month later during a February visit and again during a March visit. Her HbA1C levels were 8.4 at in March, a sharp drop from her initial levels of 12.6 in December. The same treatment regimen was continued and her HbA1C levels were measured at 5.4 in June. The patient’s hemoglobin A1C level dropped from 12.6 in December to 5.4 the following June with oral hypoglycemic agents as the only pharmacological treatment.

The significance of these findings is that the patient was able to get her severe hemoglobin A1C levels under control with just lifestyle modification and oral hypoglycemics. She did not have to use insulin for sugar control even with her severe levels. While insulin therapy offers great glycemic control, it is not without its challenges. Insulin requires extensive patient and family education and is more invasive than oral agents. Patients may be reluctant to start taking insulin because of these factors and it may be more difficult to follow the treatment plan. The possible side effect of weight gain on insulin may also deter patients from taking their doses appropriately.² For patients with severe, symptomatic hyperglycemia who are hesitant about starting insulin, it may be beneficial to offer oral hypoglycemics as first line therapy to control their diabetes.

CONCLUSION

Although insulin is considered first line therapy for patients with severe and symptomatic type 2 diabetes mellitus, oral hypoglycemics may be more appropriate to trial first and observe the progress. This is especially true for patients who are hesitant about starting

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insulin. The patient in this case responded well to a combination treatment of Metformin and Gliclazide, although it is not yet known if these normal hemoglobin A1C levels can be maintained long term. More research regarding other pharmacological options for newly diagnosed severe type two diabetes is needed.

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