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Choosing GLP-1RA Over Insulin for Patients with Type 2 Diabetes and Severe Hyperglycemia

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Introduction: Although insulin remains the recommended treatment in type 2 diabetes for hyperglycemia with catabolic symptoms, it is also the generally recommended treatment for persistent hyperglycemia or hemoglobin A1c (HbA1c) values above 10% [1]. Recent data has suggested that glucagon-like peptide 1 receptor agonists (GLP-1RAs) are also powerful at glucose lowering while additionally offering extra-glycemic benefits such as weight loss with minimal risk of hypoglycemia. Unfortunately, data on initial use of GLP-1RA is limited in patients with very high hemoglobin A1cs. Our objective was to evaluate outcomes in patients with type 2 diabetes and a baseline HbA1c of 10% or greater treated with GLP-1RAs instead of insulin. **Methods:** This study is a small retrospective case series of insulin-naïve patients with uncontrolled type 2 diabetes who were prescribed an injectable GLP-1RA. Patients included had a baseline hemoglobin A1c $\geq 10\%$ without signs of catabolism (weight loss, ketosis, significant polyuria), a minimum of one follow-up visit after initiating GLP-1RA, and at least one HbA1c measurement within six months of initiating treatment. Patients were excluded if they had previously been on insulin or a GLP-1RA in the past 1 year. The primary endpoint was change in HbA1c after 3-6 months of GLP-1RA use. **Results:** Of the patients initially screened, 7 patients fulfilled criteria and were included in the final analysis. The age range was 45-73 with 4 female patients and 3 male patients. The number of years patients had been diagnosed with type 2 diabetes ranged from 0 to 13 with 1 patient having newly diagnosed diabetes not previously on medications. Of the 6 patients who were on medical treatment at

baseline, 3 patients were on monotherapy with either metformin or a sulfonylurea and 3 patients were on 2-4 oral hypoglycemic agents. Patients were continued on their initial medication regimen with the exception of DPP-4 inhibitors which were stopped at the time of GLP-1RA initiation. Mean baseline HbA1c prior to initiation of GLP-1RA was 11.9%. Following 3-6 months of GLP-1RA use, mean HbA1c significantly improved to 7.5% (p value= 0. 0005). All patients showed improvement of HbA1c in response to GLP-1RA initiation (mean HbA1c reduction = 4.4, minimum = 1.9, maximum = 7.5). All patients remained on GLP-1RA without significant side effects. **Conclusion:** In this limited case series of patients with HbA1c \geq 10%, GLP-1RAs were well tolerated and resulted in significant improvement in HbA1c. Our results suggest that GLP-1RAs should be considered as an alternative treatment option to insulin in non-catabolic patients with very high hemoglobin A1cs. References: 1. Committee ADAPP. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2022. *Diabetes Care*. 2021;45(Supplement_1): S125-S143. doi: 10.2337/dc22-S009

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