COMMENT ON KOMÉ ET AL.

One Size Does Not Fit All: Understanding Microdosing Semaglutide for Diabetes in Multidose Pens

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I read the letter by Komé et al. (1), regarding the microdosing of semaglutide, with great interest. Physicians who work daily with individuals living with diabetes and obesity appreciate your sharing of this strategy and your encouragement to report our experiences. It has been the patients—particularly those living with obesity—who first adopted this technique, learning about it from social media and sharing their experiences with us. A simple internet search for "semaglutide clicks or microdosing" yields thousands of results, yet only your letter appears in PubMed. The same outcomes are observed when searching for the microdosing of tirzepatide.

The introduction of semaglutide and tirzepatide has been a turning point in diabetes and obesity. However, their success has led to recurrent market shortages. The American Diabetes Association has described the potential use of a microdosing strategy as an alternative during shortages (2). Recently, a study using a mathematical model on semaglutide and tirzepatide indicated that extending the dosing interval to every 2 weeks once the weight loss goal is achieved could help maintain the weight loss (3).

From a practical point of view, I agree with the importance of carefully selecting appropriate candidates. In addition to the mentioned profiles (1), other patient groups and situations may be considered. *1*) In patients undergoing multiple simultaneous treatment changes, microdosing may improve tolerability, reduce adverse effects, and allow for better monitoring of the drug's efficacy. *2*) Microdosing could be used during shortages when temporarily switching to oral semaglutide is not feasible or requires using a superior equivalent dose proportionated by 14 mg semaglutide. *3*) Microdosing can be used during temporary medication suspensions, such as during planned surgery or therapeutic vacations, where dose reintroduction must be gradual. *4*) Microdosing can be used as adjunctive treatment at the first phase of ketogenic or very-low-calorie diets to enhance adherence.

This practice is not currently included in clinical guidelines, and no randomized controlled trials support microdosing. According to the prescribing information, the shelf life of an opened semaglutide pen is 60 days (4), while that for tirzepatide is 30 days (5). For effective and safe use, structured diabetes education is crucial. Key aspects include properly storing pens, using a new needle with each injection, having a contingency plan, and maintaining communication with the health care team. Written materials should always be provided.

Can we be more sustainable in managing diabetes and obesity? Disposable pens are more convenient and hygienic but generate significant waste, directly contributing to landfill accumulation. This presents an opportunity to develop techniques for reusing and recycling these pens.

The limitation due to the cost of these therapies has driven the development of a parallel low-cost black market for GLP-1–related peptides online—one only needs to look at social media. The primary concern is that these substances have not undergone rigorous manufacturing process controls, posing a serious safety risk for users. It is crucial to emphasize the importance of obtaining medications through official channels.

In conclusion, semaglutide and tirzepatide microdosing has emerged as a potentially useful strategy in the treatment of type 2 diabetes and obesity despite not being supported by clinical trials or official guidelines.

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