Editorial

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Asymptomatic Hypoglycemia after Metabolic Surgery: New Insights from Perioperative Continuous Glucose Monitoring

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Continuous glucose monitoring (CGM) has revolutionized the management of diabetes requiring intensive insulin therapy. In the last decade, the indications of CGM have expanded to various areas, including but not limited to non-intensive insulin therapy [1], behavioral modification in type 2 diabetes mellitus [2], and in-hospital glucose monitoring during the coronavirus disease 2019 (COVID-19) pandemic [3].

The role of CGM in perioperative management of metabolic surgery, which has a profound and immediate impact on glucose metabolism even before weight loss occurs, has been extensively investigated. After metabolic surgery, particularly Roux-en-Y gastric bypass (RYGB), accelerated absorption of nutrients with increased secretion of incretin and insulin are believed to result in postbariatric hypoglycemia (PBH) [4,5]. Recently, it has been reported that asymptomatic hypoglycemia, which predominantly occurs during the nighttime, is relatively common after sleeve gastrectomy (SG). Greater glycemic variability and symptomatic hypoglycemia, which are often post-prandial, characterize glycemic patterns after RYGB [6]. In addition to the post-prandial changes, patients with PBH after RYGB also showed higher glycemic variability and increased time below range (TBR, <70 mg/dL) compared to healthy controls at night, indicating additional pathophysiologic mechanisms beyond prandial changes [7].

In this issue of *Diabetes and Metabolism Journal*, Kim et al. [8] reported the standardized core CGM metrics obtained by intermittently scanned CGM (isCGM) during the perioperative period of metabolic surgery. The study identified improvements of mean glucose and glycemic variability and increase of hypoglycemia after metabolic surgery [8]. In this study [8], standardized core CGM metrics of three days before and three days after surgery were analyzed. The majority of participants underwent laparoscopic SG with duodenojejunal bypass (50%) or laparoscopic SG alone (30%). Improvement of mean glucose and glycemic variability appeared immediately after the surgery, reaching steady state at 3 days after the metabolic surgery. The TBR (<70 or 54 mg/dL) was significantly increased and time above range (>250 or 180 mg/dL) was significantly decreased after surgery. This resulted in a non-significant decrease in time in range (TIR, 70 to 180 mg/dL) in those with baseline glycosylated hemoglobin (HbA1c) <8.0% (85.0% to 78.7%, $n=13$) and a significantly increased TIR in those with baseline HbA1c ≥8.0% (50.9% to 90.4%, $n=7$). It should be noted that the participants in this study would not have had a profoundly increased risk of severe hypoglycemia such as that in people with type 1 diabetes mellitus or long-standing type 2 diabetes mellitus at baseline. Although only one individual experienced symptomatic hypoglycemia, the authors were able to detect rapid glycemic changes by isCGM during the perioperative period and discontinued insulin and oral glucose lowering drugs proactively.

Importantly, an overall increase in TBR <54 mg/dL from 0.4%±1.1% to 3.9%±8.1%, which further increased during the night (0.1%±0.5% to 10.2%±21.0%), highlights the impor-

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tance of proactive management to prevent hypoglycemia in the postoperative period of metabolic surgery, even when the patients do not complain of symptoms of hypoglycemia. Increase in TBR <54 mg/dL was more prominent when baseline HbA1c was <8.0%, reaching 6.5% after metabolic surgery, indicating the need for a high index of suspicion for PBH in such cases.

Lack of symptomatic hypoglycemia in all but one study participant in this study despite the marked increase in TBR <54 mg/dL is an interesting finding. Given the baseline clinical characteristics, it is unlikely that the study participants had impaired awareness of hypoglycemia at baseline. A recent meta-analysis on the rate of PBH concluded that it is more prevalent than currently believed and is comparable after RYGB and SG, although glucose variability is higher after RYGB [9]. Given that majority of the participants in Kim et al.'s study underwent SG [8], it could be expected that the asymptomatic nocturnal pattern of PBH, which is less symptomatic than the postprandial PBH frequently observed after RYGB [6], would be the dominant type of PBH in the study population. With a lower amplitude of glucose excursions, the nocturnal patterned PBH in SG would cause less symptomatic hypoglycemia.

An alternative explanation for the lack of symptomatic hypoglycemia in the vast majority of participants in Kim et al. [8] is the use of the first generation of isCGM devices, which could have been less accurate than the latest devices. However, the reported accuracy of the device based on Clarke error grid analysis, in which 99.4% of glucose values were in zones A and B, indicates that the accuracy of the device was not a major influence on the study results.

Therefore, the substantial increase in nocturnal TBR <54 mg/dL despite the lack of symptoms of hypoglycemia in Kim et al.'s study is consistent with a recent study revealing differential patterns of PBH according to type of metabolic surgery [6]. Given the increased all-cause mortality and major adverse cardiovascular events with clinically significant (level 2) hypoglycemia [10], the results of Kim et al. [8] highlight the importance of early detection of clinically significant but asymptomatic PBH by CGM, especially in patients who undergo SG.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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