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SYMPOSIUM

Safe Glycemic Management during Closed-Loop Treatment of Type 1 Diabetes: The Role of Glucagon, Use of Multiple Sensors, and Compensation for Stress Hyperglycemia

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Abstract

Patients with type 1 diabetes mellitus (T1DM) must make frequent decisions and lifestyle adjustments in order to manage their disorder. Automated treatment would reduce the need for these self-management decisions and reduce the risk for long-term complications. Investigators in the field of closed-loop glycemic control systems are now moving from inpatient to outpatient testing of such systems.

As outpatient systems are developed, the element of safety increases in importance. One such concern is the risk for hypoglycemia, due in part to the delayed onset and prolonged action duration of currently available subcutaneous insulin preparations. We found that, as compared to an insulin-only closed-loop system, a system that also delivers glucagon when needed led to substantially less hypoglycemia. Though the capability of glucagon delivery would mandate the need for a second hormone chamber, glucagon in small doses is tolerated very well.

People with T1DM often develop hyperglycemia from emotional stress or medical stress. Automated closed-loop systems should be able to detect such changes in insulin sensitivity and adapt insulin delivery accordingly. We recently verified the adaptability of a model-based closed-loop system in which the gain factors that govern a proportional-integral-derivative-like system are adjusted according to frequently measured insulin sensitivity. Automated systems can be tested by physical exercise to increase glucose uptake and insulin sensitivity or by administering corticosteroids to reduce insulin sensitivity.

Another source of risk in closed-loop systems is suboptimal performance of amperometric glucose sensors. Inaccuracy can result from calibration error, biofouling, and current drift. We found that concurrent use of more than one sensor typically leads to better sensor accuracy than use of a single sensor. For example, using the average of two sensors substantially reduces the proportion of large sensor errors. The use of more than two allows the use of voting algorithms, which can temporarily exclude a sensor whose signal is outlying.

Elements such as the use of glucagon to minimize hypoglycemia, adaptation to changes in insulin sensitivity, and sensor redundancy will likely increase safety during outpatient use of closed-loop glycemic control systems.

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Abbreviations: (ARD) absolute relative difference, (IOB) insulin on board, (MRS) magnetic resonance spectroscopy, (SD) standard deviation, (T1DM) type 1 diabetes mellitus, (TDIR) total daily insulin requirement, (TEM) transmission electron microscopy

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