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SYMPOSIUM

Factors Influencing the Effectiveness of Glucagon for Preventing Hypoglycemia

Jessica R. Castle, M.D.,[1] Julia M. Engle, B.A.,[2] Joseph El Youssef, M.B.B.S.,[1] Ryan G. Massoud, B.S.,[2] and W. Kenneth Ward, M.D.[1,2]

Abstract

Background:

Administration of small, intermittent doses of glucagon during closed-loop insulin delivery markedly reduces the frequency of hypoglycemia. However, in some cases, hypoglycemia occurs despite administration of glucagon in this setting.

Methods:

Fourteen adult subjects with type 1 diabetes participated in 22 closed-loop studies, duration 21.5 ± 2.0 h. The majority of subjects completed two studies, one with insulin + glucagon, given subcutaneously by algorithm during impending hypoglycemia, and one with insulin + placebo. The more accurate of two subcutaneous glucose sensors was used as the controller input. To better understand reasons for success or failure of glucagon to prevent hypoglycemia, each response to a glucagon dose over 0.5 μg/kg was analyzed (n = 19 episodes).

Results:

Hypoglycemia occurred in the hour after glucagon delivery in 37% of these episodes. In the failures, estimated insulin on board was significantly higher versus successes (5.8 ± 0.5 versus 2.9 ± 0.5 U, $p < .001$). Glucose at the time of glucagon delivery was significantly lower in failures versus successes (86 ± 3 versus 95 ± 3 mg/dl, $p = .04$). Sensor bias (glucose overestimation) was highly correlated with starting glucose ($r = 0.65$, $p = .002$). Prior cumulative glucagon dose was not associated with success or failure.

Conclusion:

Glucagon may fail to prevent hypoglycemia when insulin on board is high or when glucagon delivery is delayed due to overestimation of glucose by the sensor. Improvements in sensor accuracy and delivery of larger or earlier glucagon doses when insulin on board is high may further reduce the frequency of hypoglycemia.

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Author Affiliations: [1]Oregon Health and Science University, Portland, Oregon; and [2]Legacy Health, Portland, Oregon

Abbreviations: (CBG) capillary blood glucose, (FMPD) fading memory proportional derivative, (VBG) venous blood glucose

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Corresponding Author: Jessica R. Castle, M.D., Oregon Health and Science University, 3181 SW Sam Jackson Park Rd., Portland, OR 97239; email address castleje@ohsu.edu