Competing interests

None declared.

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DOI: 10.1111/dme.14116

The importance of prandial insulin bolus timing with hybrid closed-loop systems

Diabet. Med. 36, 1716–1717 (2019)

Attainment of glycaemic targets for people with type 1 diabetes is challenging and management of postprandial hyperglycaemia is one key contributing factor. Because of delays in subcutaneous insulin absorption, administering rapid-acting insulin boluses 15–20 min before a meal leads to ~ 30% reduction in postprandial glucose compared with boluses delivered immediately before the meal [1–3]. There is also a greater risk of postprandial hypoglycaemia when people administer insulin boluses post meal. People with type 1 diabetes who routinely bolus rapid-acting insulin pre-meal have better HbA_{1c} values, according to large registry data [4].

Despite this evidence, in practice, many people with type 1 diabetes inject/bolus rapid-acting insulin during or after meals. Some people feel more confident in the amount of carbohydrate to bolus for after they have eaten it, and others find waiting 15–20 min after administering the insulin bolus inconvenient.

Introduction of closed-loop systems into routine clinical practice for people with type 1 diabetes has the potential for improved glucose control compared with conventional intensive insulin therapy [5]. Currently available closed-loop systems use a hybrid approach, requiring manual user input for meal boluses, whereas basal rates are automatically adjusted by an algorithm in response to sensor glucose concentrations. There are important differences between standard pump therapy or sensor-augmented pump therapy, and closed-loop systems with regards to the impact of timing of prandial insulin boluses.

Ingestion of carbohydrate without bolus insulin delivery leads to a rise in glucose levels. Closed-loop systems detect the rise in sensor glucose concentration and automatically deliver increased insulin infusion rates to manage the prandial glucose excursion. Delayed administration of the mealtime insulin bolus may cause over-delivery of insulin and subsequent hypoglycaemia if the additional closed-loop directed insulin is not taken into consideration (Fig. 1). The greater the time interval between meal commencement and the insulin bolus being delivered, the greater the risk of hypoglycaemia. Bolus calculators used during closed-loop may account only for the insulin on board from a previous bolus, not from additional closed-loop delivered insulin and the active insulin displayed on closed-loop screens includes only the bolus insulin received.

It is important that closed-loop users are aware of the potential safety implications of post-meal bolusing before using closed-loop systems, and are advised to either reduce the delayed meal bolus or miss the bolus completely and allow the closed-loop to manage the postprandial glucose excursion with the consequence of higher postprandial glucose excursion.

There are some safety restrictions in place in the commercially available Medtronic 670G hybrid closed-loop system to mitigate this risk. The closed-loop system will not allow an additional bolus to be given once the maximum hourly delivery limit has been reached while in Auto Mode; however, this may result in postprandial hyperglycaemia. This safety feature is also associated with increased alarm burden and more frequent exits from Auto Mode, and could potentially lead to more hyperglycaemia if insulin settings are

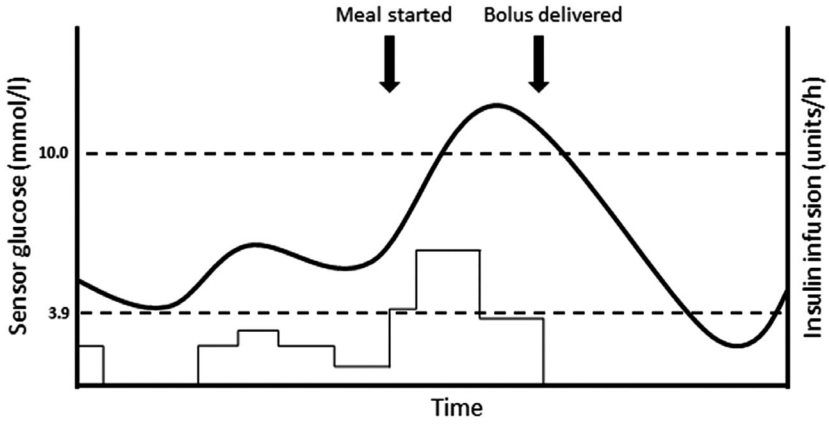

FIGURE 1 Impact of post-meal bolusing on sensor glucose concentration during hybrid closed-loop insulin delivery. Thick black line represents sensor glucose. Thin black line represents algorithm driven insulin delivery. Horizontal dashed lines reflect target glucose range.

not adjusted appropriately. Future, more aggressive closed-loop systems, which have more flexibility to target tighter glucose control, are likely to have fewer restrictions and are unlikely to impose such tight constraints on insulin delivery rates.

This is an important safety issue, unique to hybrid closed-loop systems, which users and healthcare providers need to be aware of and should form a key part of training on closed-loop systems. Wider recognition of the importance of pre-meal bolusing, including within informal educational environments, such as online diabetes forums, will help to optimize safety and efficacy of closed-loop system use.

Funding sources

Support for closed-loop studies by National Institute for Health Research Cambridge Biomedical Research Centre, JDRF, European Union Horizon 2020 research and innovation program (grant agreement no 731560), The Leona M. and Harry B. Helmsley Charitable Trust, Efficacy and Mechanism Evaluation Programme National Institute for Health Research (14/23/09), and Wellcome Trust Strategic Award (100574/Z/12/Z).

Competing interests

RH reports having received speaker honoraria from Eli Lilly and Novo Nordisk, serving on advisory panel for Eli Lilly and Novo Nordisk, receiving license fees from B. Braun and Medtronic; having served as a consultant to B. Braun, and patents and patent applications related to closed-loop. SH serves as a member of Sigma (Dexcom) advisory board, and reports having received training honoraria from Medtronic and Sanofi. CB and JMA declare no duality of interest associated with this manuscript.

Acknowledgements

Support for closed-loop studies by National Institute for Health Research Cambridge Biomedical Research Centre, JDRF, European Union Horizon 2020 research and innovation program (grant agreement no 731560), The Leona M. and Harry B. Helmsley Charitable Trust, Efficacy and Mechanism Evaluation Programme National Institute for Health Research (14/23/09), and Wellcome Trust Strategic Award (100574/Z/12/Z).

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