Journal club: Ready-to-use glucagon as a treatment for hypoglycaemia

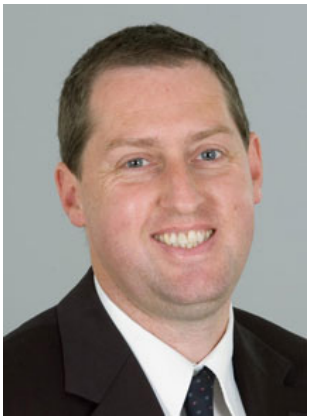
Fasting can pose a particular risk to people with type 1 diabetes, conferring a significantly increased risk of hypoglycaemia. Fasting is part of the observance of a number of religions, and the Islamic holy month of Ramadan is perhaps the most obvious of these. A significant proportion of people with type 1 diabetes wish to observe the practice of fasting during Ramadan. This can be quite challenging both for the individual and for the healthcare professionals charged with their care.

The study by Metab Algefarri and colleagues is helpful as it describes the challenges of living with hypoglycaemia during Ramadan and suggests a novel approach using low-dose glucagon as a management strategy for dealing with the problem. Glucagon is currently reserved for the treatment of severe hypoglycaemia where the individual is unable to consume fast-acting carbohydrate.

Glucagon has a role alongside insulin in the normal physiology of glucose control. The beta-cells sense rising glucose and release insulin, with an overall effect to lower blood glucose. Conversely, the alpha-cells sense falling glucose and release glucagon, which has the effect of raising blood glucose, primarily via the breakdown of glycogen (stored carbohydrate) but also via breakdown of amino acids and fat. The two hormones act synchronously and maintain blood glucose levels within the normal range.

In normal life, glucagon is not primarily involved in the response to severe hypoglycaemia, although this has been the main, and very limited, therapeutic use for many years. The limited use has partly been due to the lack of a stable, usable formulation; in turn, pharmaceutical companies have not developed a ready-to-use formulation because of the limited clinical use – the problem has been circular.

To date, the response to the issue of hypoglycaemia has been to teach people to eat more carbohydrate. That is not always acceptable, as we see in the current paper, but more generally it may also lead to unwanted weight gain, the consequences of which I discussed in the previous issue. There is a growing understanding that perhaps glucagon could have a wider clinical use, and it is no coincidence that we are starting to see licensed formulations of ready-to-use glucagon with a long shelf life coming to market. We can perhaps look forward to the time when we will have to learn to balance two hormones for the management of type 1 diabetes rather than one! ■



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Citation: Flanagan D (2022) Journal club: Journal club: Ready-to-use glucagon as a treatment for hypoglycaemia. *Journal of Diabetes Nursing* **26**: JDN241

Mini-dose glucagon to treat hypoglycaemia during Ramadan fasting

Many Muslim people with type 1 diabetes observe Ramadan fasting, despite the risk of hypoglycaemia that this can confer. Unlike oral medications, subcutaneous injections do not invalidate Ramadan fasts. This study sought to determine whether mini-dose glucagon injections were a safe and effective intervention to prevent and treat mild-to-moderate hypoglycaemia during Ramadan fasting.

In a 4-week crossover trial, 17 adults with type 1 diabetes who were fasting for Ramadan (daily fasting window around 15 hours) were assigned to use either glucagon or oral glucose tablets to treat hypoglycaemia, both for a 2-week period. Participants were trained to reconstitute and inject the glucagon (GlucaGen HypoKit, Novo Nordisk) at a dose of 150 µg for glucose levels 2.8–3.8 mmol/L and at 300 µg for levels 2.2–2.7 mmol/L. Corresponding oral glucose doses were 15 g and 30 g.

A total of 80 hypoglycaemia events that met the criteria for analysis occurred. The primary endpoint of blood glucose levels at 30 minutes after the hypoglycaemic event was significantly higher in the glucagon arm than the oral glucose arm (3.6 vs 2.5 mmol/L; $P<0.001$). Subanalysis showed that this difference was sustained in participants who had been fasting for more than 8 hours. Participants in the glucagon arm had a significantly greater time in target range (61.0% vs 55.1%), and significantly less time below range (5.8% vs 12.8%). No participant in the glucagon arm had to abandon their fasts, whereas 12% in the glucose arm had to stop.

No serious adverse events were reported. Nausea and injection site discomfort occurred in six of 17 participants; the nausea was intolerable in one individual.

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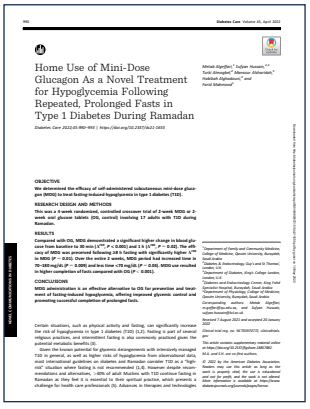
Home Use of Mini-Dose Glucagon As a Novel Treatment for Hypoglycemia Following Repeated, Prolonged Fasts in Type 1 Diabetes During Ramadan