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LETTER

Protein 'pre-loads' in type 2 diabetes: what do we know and what do we need to find out?

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Abbreviations
CCK Cholecystokinin
GLP-1 Glucagon-like peptide-1

To the Editor: We read with interest the Short Communication from Jakubowicz et al, published recently in *Diabetologia* [1]. The authors reported that acute administration of 50 g whey protein, in liquid form, 30 min before a high carbohydrate breakfast, substantially reduced postprandial glycaemia as compared with placebo in patients with type 2 diabetes, and there were concomitant increases in both glucagon-like peptide-1 (GLP-1) and insulin.

These outcomes are consistent with our study, published in 2009, involving a 55 g whey pre-load in type 2 diabetic patients, which adopted a very similar study design [2], and was cited by Jakubowicz and Froy in a previous review [3], but to our surprise, not in their paper [1]. Moreover, we showed that the whey pre-load also slowed the emptying of the subsequent meal from the stomach, and stimulated glucose-dependent insulinotropic polypeptide (GIP) and cholecystokinin (CCK), in addition to GLP-1 and insulin. It is now appreciated that slowing gastric emptying represents an important mechanism by which dietary or pharmacological strategies can attenuate postprandial glycaemia [4]; this includes the 'short-acting' GLP-1 receptor agonists [5]. Stimulation of both GLP-1 and CCK are likely to contribute to the slowing of gastric emptying induced by whey protein.

While the impressive effects of such a 'pre-load' strategy in the acute setting are now clear, it is important to refine this approach for practical long-term use. Whey protein is relatively expensive, and the cost of such a large dose taken on a regular basis would be prohibitive for many patients. Whey supplements would also incur a substantial burden in energy consumption, unless it were shown that patients compensate by adjusting their overall energy intake. Whey also has the capacity to increase glucagon [6], which would be counterproductive to glycaemic control. Accordingly, future studies should examine how the dose of whey could be minimised (for example, by combining a pre-load with an inhibitor of dipeptidyl peptidase 4 [7]) and whether the effects of whey on glycaemia are sustained with long-term use. It would also be important to refine which type 2 diabetic patients should be selected for this therapeutic strategy; probably those with a relatively low HbA_{1c} (~7.5% [58 mmol/mol] or less) would be ideal, given that this is the group in whom postprandial glycaemia, as opposed to preprandial blood glucose, makes the predominant contribution to overall glycaemic control [8].

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