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Original research

Protein and fat meal content increase insulin requirement in children with type 1 diabetes – Role of duration of diabetes

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ABSTRACT

Background and objective: Hyperglycaemia remains a challenge in type 1 diabetes since current regimes used to determine meal insulin requirements prove to be ineffective. This is particularly problematic for meals containing high amounts of protein and fat. We aimed to determine the post-prandial glycaemic response and total insulin need for mixed meals, using sensor-augmented insulin pumps in children with type 1 diabetes.

Methods: Twenty-two children with type 1 diabetes, aged 4–17 years on insulin pump therapy completed this home-based, cross-over, randomised controlled trial. Two meals with identical carbohydrate content – one with low fat and protein (LFLP) and one with high fat and protein (HFHP) contents – were consumed using normal insulin boluses. Blood glucose monitoring was done for 10 h post-meal, with correction bolus insulin given two-hourly if required.

Results: The HFHP meal required significantly more total insulin (3.48 *vs.* 2.7 units) as a result of increased post-meal correction insulin requirement (1.2 *vs.* 0.15 units) spread over a longer duration (6 *vs.* 3 h). The HFHP meals significantly increased the time spent above target glucose level. Duration of diabetes and total daily insulin use significantly influenced the post-prandial blood glucose response to the two meals.

Conclusion: When consuming carbohydrate-based mixed meals, children with type 1 diabetes on insulin pump therapy, required significantly more insulin over a longer period of time than the insulin requirement calculated using current regimes. This additional amount required is influenced by the duration of diabetes and total daily insulin use.

Introduction

For many people with type 1 diabetes, post-prandial hyperglycaemia remains one of the major challenges in diabetes care and contributes greatly to glucose variability and overall glycaemic control [1]. Even in the presence of a near normal glycosylated haemoglobin (HbA1c), diabetes complications can still develop [1]. Therapy includes lifetime management of exogenous insulin delivery either by injection or by subcutaneous insulin infusion, also known as insulin pump therapy, dietary and exercise management, as well as blood glucose monitoring with finger pricks and, for some, continuous glucose monitoring (CGM) systems [2].

Current practices for determining meal-time bolus insulin whether on multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII) (insulin pump therapy) involve carbohydrate counting, usually advanced (Level 3) carbohydrate counting where individualised insulin-to-carbohydrate ratios are used [2]. This and other methods of carbohydrate counting assume that only carbohydrates affect the post-prandial glucose rise in children with type 1 diabetes. However, many studies have indicated that factors such as the type of carbohydrate, the glycaemic index of the meal, and the fat, fibre and protein content of the meal play an important role in delaying post-prandial hyperglycaemia, and these factors should be considered when trying to optimise post-prandial glucose levels [3–5].

When using CSII, most pumps offer three modes to deliver bolus or meal-time insulin: the normal or standard bolus, the dual-wave or multi-wave bolus, and the square-wave or extended bolus. The use of only normal or standard boluses and carbohydrate counting alone, where all bolus insulin is delivered immediately and the

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dose is determined by the current blood glucose reading and carbohydrate content of the meal, can be ineffective in optimising post-prandial blood glucose levels for mixed meals as fat and protein have shown independent effects on post-prandial hyperglycaemia [3–5]. Consequently, Pańkowska et al. [6] developed a method of quantifying meal insulin based on all macronutrients of the meal (carbohydrate, fat and protein (CFP) counting). However, CFP counting may pose a risk for increased post-prandial hypoglycaemic events in the early hours post meal [3,6] and may be challenging to implement in the paediatric diabetes population. In 2014, the *Guide for nutritional management in children and adolescents with diabetes*, developed by the International Society for Paediatric and Adolescent Diabetes (ISPAD), indicated that randomised controlled trials, aimed at developing methods to better manage post-prandial hyperglycaemia after fat and protein rich meals, are needed [2].

The aim of this study was to determine the post-prandial glycaemic response and total insulin need for mixed meals with known, constant carbohydrate content but different fat and protein contents, using insulin pump therapy and CGM in children with type 1 diabetes.

Subjects

In total, 32 children with type 1 diabetes aged 4–17 years were recruited. The inclusion criteria were: use of sensor-augmented pump therapy for longer than one month; HbA1c $\leq$ 9.6% (81 mmol/mol) for the last three months; World Health Organization BMI/age z-score of -1 to below 3, thus not including wasted or obese individuals; and total daily insulin use of $\geq$0.5 u/kg to avoid inclusion of participants in the remission phase of diabetes.

The exclusion criteria were: smoking; coeliac disease; cystic fibrosis; concurrent conditions that can be associated with delayed gastric emptying or altered digestion; and the use of any medication or supplements that could influence gastric emptying, digestion or glucose levels, such as glucocorticoids or oral antidiabetic drugs. Participants had to be free of any acute illnesses at the start of the study.

The study was conducted in accordance with the Helsinki Declaration. Ethical approval was obtained from the Health Research Ethics Council of North-West University, South Africa (NWU-00042-15-S1).

Materials and methods

Study design

A home-based, cross-over, randomised controlled trial was performed. For all participants, optimal basal insulin rates, carbohydrate ratios and sensitivity factors were revised and adjusted by a paediatric endocrinologist before enrolment. Participants were randomised to treatment. The two meals were consumed at dinner time (18:00) under parental supervision, at least a day apart and within a month of one another, to ensure that factors which could potentially change HbA1c values such as illness, radical changes in diet or activity, or stress did not interfere with the results. Participants maintained their normal, habitual activity levels during the two study days. Pump settings, including basal rates and bolus wizard settings, had to remain unchanged from enrolment until after data collection was completed. Upon enrolment, participants received detailed study instructions, a cooler bag with their two individual study meals, three Enlite sensors (Medtronic, Inc., MN, USA), a blood glucose meter (Bayer Contour 2.4 Next Link 2.4 blood glucose meter; Bayer Indianapolis, IN, USA) and 30 strips for the meter.

Sensor-compatible insulin pumps used in the study included the 554 Veo, 754 Veo, 722 Paradigm and 640G from Medtronic (Medtronic, Inc., MN, USA). For CGM, Medtronic Enlite Sensors were used with two different transmitters, the Gaurdian Link and Gaurdian Connect, as different pump models were used. Study meals could only be taken on days 2–5 of the sensor lifespan as a sensor is least accurate on day 1 and day 6 [7]. All participants used rapid-acting insulin Novorapid (Novo Nordisk, Copenhagen, Denmark) in their pumps.

Test meals

Each participant received two different meals with the same carbohydrate content. One meal was high in fat and protein (HFHP) and the other low in fat and protein (LFLP). Meals consisted of smoked, skinless and boneless chicken breast, pre-prepared plain, white long-grain rice, ready prepared chicken gravy, and olive oil. The meals only required pre-heating in the microwave; no cooking was allowed. The fat and protein content was manipulated by the portion sizes of the chicken breast and the amount of gravy and olive oil. The rice was a low glycaemic index (GI) food.

The macronutrient content of the meals was calculated as follows: the total daily energy requirement for each participant was individually calculated using an age, weight and gender specific World Health Organization energy expenditure recommendation [8]. The total carbohydrate per day was then calculated at 50% of total energy, since 50–55% is recommended for children with type 1 diabetes [6]. Of the total daily carbohydrates, 25% was allocated to each study meal. The amount of carbohydrates for both meals was kept constant in order for the LFLP meal to be used as the control for the HFHP meal. The fat and protein content per meal, calculated as percentage energy, were as follows: LFLP meal carbohydrates 60%, fat 25%, and protein 15%; HFHP meal carbohydrates 40%, fat 35% and protein 25%.

Meal consumption procedures and capillary blood glucose testing

A pre-prandial blood glucose level of 4–11 mmol/L was required before the study meal could be taken. If the level was not in the specified range, the participant was allowed to give a correction bolus and then have the study meal 30–60 min later, if the capillary test then fell within the recommended range. The blood glucose level and indicated carbohydrate content of the meal were entered into the bolus wizard feature of the pump and a normal insulin bolus was then delivered 10 min prior to eating each meal. To limit variability of gastro intestinal clearance affected by fluid intake, participants were not allowed to have more than two to three glasses of water 30 min pre-meal to two hours post-meal. Meals had to be consumed within 20 min. Consuming the study meal was not permitted on an evening where the participant experienced a hypoglycaemic event (<4 mmol/L) during that day. Participants were allowed a breakfast and a low fat, light lunch meal of their choice but were not allowed to have any food two hours prior to the study. The entire process was repeated for the second meal on a different night.

After consumption of the study meal, in addition to CGM, capillary blood testing was performed by a parent at 30 min post-meal and then every two hours after the start of the meal for 10 h. Each blood glucose value was entered into the pump and a correction bolus (calculated by the pump) was delivered when required (also at 2-h intervals). All hypoglycaemic events and carbohydrate treatments were entered into the pump. In the case of a blood glucose value dropping below 4 mmol/L, the study was terminated as additional food had to be given, but the time of the hypoglycaemic events was still recorded and used for data analysis.