Body mass index and the efficacy of needle-free jet injection for the administration of rapid-acting insulin analogs, a post hoc analysis

We recently showed in a euglycaemic glucose clamp study among 18 healthy volunteers that using jet injectors rather than conventional pens significantly improved the time-action profiles of rapid-acting insulin analogs. Here, we investigated whether such profiles were modified by body mass index (BMI) and related weight parameters by comparing insulin administration by jet injection to that by conventional pen in subgroups defined by BMI, waist-to-hip ratio, waist circumference and insulin dose. After conventional administration, times to peak insulin levels (T-INsmax) occurred 3.1 ± 1.1 (95% confidence interval (CI) 3.1–3.2) min later and time to maximum glucose requirement (T-GRmax) 56.9 (95%CI 26.6–87.3) min later in more obese (BMI > 23.6 kg/m²) than in lean subjects (BMI < 23.6 kg/m²). In contrast, T-INsmax and T-GRmax were similar in subjects with high and low BMI, when insulin was administered by jet injection. We conclude that using jet injection for insulin administration may especially benefit subjects with higher body weight.

Keywords: body mass index/obesity indices, euglycaemic glucose clamp, insulin administration, insulin analogs, insulin aspart, jet injector, pharmacodynamics, pharmacokinetics

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Introduction

Most studies investigating the pharmacology of rapid-acting insulin analogs have been conducted in lean subjects, whereas many patients with type 1 and the majority of patients with insulin-requiring type 2 diabetes are overweight or obese. A high body mass index (BMI) may considerably delay the absorption rate and onset of action of regular insulin [1–3] and possibly also of rapid-acting insulin analogs. Such delays may be due to greater thickness of the subcutaneous tissue at the (abdominal) injection site or because higher insulin doses are required [4]. A delay in insulin absorption rate may exacerbate postprandial hyperglycaemia and, because the proportional contribution of postprandial glucose to the HbA1c increases with lower HbA1c values, interfere with the aim for tight glycaemic control [5].

In a recent study, we showed that jet injectors, which deliver insulin by means of air pressure instead of a needle, significantly advanced the time-action profile of the rapid-acting insulin analog aspart [6]. Jet injection results in a distinct spray-like dispersion pattern that ensures a larger absorptive area and faster penetration through the subcutaneous tissue compared to conventional administration by syringes or pens [7]. We hypothesized that the impact of adiposity on insulin absorption may be less when insulin is administered by jet injection. To test this hypothesis, we performed a post hoc analysis to assess whether BMI and other body weight parameters modified the pharmacology of insulin injected by jet injection.

Materials and Methods

Participants

Non-smoking healthy adults, aged 18–50 years and with a BMI of 18–28 kg/m² were enrolled and asked to provide written informed consent. The study was approved by the institutional review board of the Radboud University Nijmegen Medical Centre.

Experimental Study Design

The research protocol has been described in detail previously [6]. Briefly, all participants underwent two 8-h euglycaemic glucose clamps, using a randomized, controlled, double-blind, double-dummy, cross-over study design. Venous catheters were placed for administration of dextrose 20% and frequent blood sampling. Insulin aspart (Novo Nordisk, Bagsvaerd, Denmark) at a dose of 0.2 UI/kg body weight and a comparable volume of placebo solution (Test Medium Penfill®; Novo Nordisk) were then simultaneously injected subcutaneously on both sides of the lower abdomen. On one occasion, insulin was administered by the jet injector (InsuJet™; European Pharma Group, Schiphol Rijk, the Netherlands) and placebo by conventional pen (NovoPen III; Novo Nordisk). On the other occasion, the order was reversed.