Time-action profile of the long-acting insulin analogue insulin glargine in comparison to NPH insulin in Japanese volunteers

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In a previous euglycaemic glucose clamp study involving 15 healthy Caucasian men, we demonstrated that subcutaneous injections of insulin glargine resulted in a smooth time-action profile of 24 hours’ duration, i.e. no pronounced peak [1]. The aim of the present study, which employed the same experimental procedure as our previous trial, was specifically to determine the time-action profile of 0.4 IU/kg subcutaneously injected insulin glargine and human NPH insulin in healthy Japanese volunteers.

The study was conducted in a double-blind, placebo-controlled, three-way crossover, single-dose, randomized manner in accordance with the ethical principles of the Declaration of Helsinki. A low dose infusion of regular insulin (0.15 mIU/kg/min) was applied for the entire duration of this Biostator based glucose clamp study to suppress endogenous insulin secretion. Glucose infusion rates (GIR) necessary to maintain blood glucose at the target level of 5 mmol/L (90 mg/dL) were registered for 30 hours after injection of the study drug. A polynomial function of 6th order was fitted to individual GIR profiles to yield the peak metabolic effect (GIRmax) and the time to peak metabolic activity (tmaxGIR).

Fifteen healthy Japanese men were enrolled. Demographical parameters of the volunteers were similar in the present and previous study for age (29 ± 5 vs. 27 ± 4 years) and body mass index (21.1 ± 1.9 vs. 22.2 ± 1.8 kg/m²) [1]. However, Japanese volunteers in this study were significantly shorter (1.75 ± 0.09 vs. 1.82 ± 0.05 m, p<0.03) and had a lower weight (65.3 ± 11.2 vs. 73.5 ± 8.3 kg, p = 0.04) compared with the Caucasian volunteers.

The maximal metabolic activity observed with insulin glargine was lower compared with NPH insulin (GIRmax 3.0 ± 0.9 vs. 4.3 ± 1.8 mg/kg/min; p = 0.02) and was attained later (tmaxGIR 14.1 ± 8.8 vs. 6.8 ± 5.6 h; p = 0.03). After an initial onset of metabolic action following the subcutaneous administration of insulin glargine, metabolic activity remained constant for the remainder of the study; in contrast, a pronounced peak was detected 4-6 hours following NPH insulin administration (Fig 1). The lack of a pronounced peak with insulin glargine was indicated by a lower consumption of glucose in the first 4 hours post-injection compared with NPH insulin (AUC0-4 h 0.19 ± 0.35 vs 0.69 ± 0.42 g/kg; p < 0.01). Although the metabolic effect measured over 30 hours tended to be lower with insulin glargine compared with NPH insulin, the difference was not significant (AUC0-30 h 2.82 ± 1.61 vs. 3.63 ± 1.41 g/kg; p = 0.09). Both insulin glargine and NPH insulin were well tolerated. Two adverse events occurring in one subject in the NPH insulin group were considered unrelated to the study medication.

Comparison of the pharmacodynamic summary parameters of insulin glargine obtained with Japanese volunteers in this study with those obtained in our previous study in Caucasian volunteers revealed no differences. We conclude from these results that: (a) in Japanese volunteers, subcutaneous injection of insulin glargine leads to a smooth time-action profile with no pronounced peak, unlike NPH insulin, which gave rise to a distinct peak; (b) insulin glargine showed a similar time-action profile in Japanese and Caucasian volunteers; (c) insulin glargine, which has been shown to be effective at achieving and maintaining good glycaemic control in patients with both Type 1 and Type 2 diabetes [2-5], is also expected to be appropriate in the pharmacological treatment of Japanese patients with diabetes.

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References


