

## Explorative Study of Pharmacokinetics and Pharmacodynamics after Change in Basal Insulin Infusion Rate

Charlotte A. Ihlo, M.D.,<sup>1</sup> Torsten Lauritzen, M.D., Dr.Med.Sci.,<sup>2</sup> Jeppe Sturis, Ph.D.,<sup>3</sup>  
Ole Skyggebjerg, M.Sc., Ph.D.,<sup>4</sup> Jens S. Christiansen, M.D., FRCPI, Dr.Med.Sci.,<sup>1</sup>  
and Torben Laursen, M.D., Ph.D., Dr.Med.Sci.<sup>5</sup>

### Abstract

#### Background:

The use of insulin pumps is rapidly increasing and new, technologically more advanced pumps are continuously being developed. It is of interest to assess the clinical relevance of the many technical features of these pumps, e.g., the effect on pharmacokinetics and pharmacodynamics with change in infusion rate.

#### Method:

The aim of this study was to explore the sequence of pharmacokinetic and pharmacodynamic changes after dose doubling of the basal insulin infusion rate with subcutaneous bolus insulin injections once an hour, continuous subcutaneous insulin infusion, and continuous intravenous insulin infusion. Ten type 1 diabetes mellitus patients were included. The insulin doses were calculated based on the habitual insulin doses. The study was designed as an open-labeled, single-center, randomized, crossover exploratory trial.

#### Results:

Dose doubling of the basal insulin infusion rate with the three different administration protocols did not result in any clinically relevant differences in the time courses of the pharmacokinetic and pharmacodynamic parameters. With all three administration protocols, we observed a time interval of more than 6 hours before a new steady state of insulin was achieved.

#### Conclusions:

Our results indicate that frequent changes in basal subcutaneous insulin infusion rates are not of significant clinical relevance on a 24-hour basis. Regarding technological features of subcutaneous insulin pumps, no discernable advantages of increasing pump stroke frequency were found. This indicates that pump stroke frequency sophistication might not be of clinical relevance in pumps used for basal subcutaneous insulin infusion.

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**Author Affiliations:** <sup>1</sup>Department of Endocrinology M, Aarhus University Hospital, Aarhus C, Denmark; <sup>2</sup>Department of General Medicine, Institute of Public Health, Aarhus University, Aarhus C, Denmark; <sup>3</sup>Department of Insulin, Pharmacology, Histology and Delivery, Novo Nordisk A/S, Maelov, Denmark; <sup>4</sup>Insulin Pharmacology, Histology and Delivery, Novo Nordisk A/S, Maelov, Denmark and <sup>5</sup>Department of Pharmacology, Aarhus University, Aarhus C, Denmark

**Abbreviations:** (ANOVA) analysis of variance, (AUC) area under the curve, (CIII) continuous intravenous insulin infusion, (cl) clearance, (CSII) continuous subcutaneous insulin infusion, (CV) coefficient of variation, (GIR) glucose infusion rate, (HbA1c) hemoglobin A1c, (IAsp) insulin aspart, (IU) international unit, (IV) intravenous, (PG) plasma glucose, (s) serum, (SBII) subcutaneous bolus insulin injection, (SC) subcutaneous, (SD) standard deviation, (SE) standard error (ss) steady state, ( $t_{1/2}$ ) terminal half life in blood, ( $t_{50\%}$ ) terminal half life of insulin absorption, (T1DM) type 1 diabetes mellitus, (U-HCG) urinary human chorionic gonadotropin

**Keywords:** insulin aspart, insulin pump therapy, steady state

**Corresponding Author:** Charlotte A. Ihlo, M.D., Department of Endocrinology M, Aarhus Sygehus, NBG, Aarhus University Hospital, Noerrebrogade 44, Building 2, DK-8000 Aarhus C, Denmark; email address [charlotte.ihlo@dadlnet.dk](mailto:charlotte.ihlo@dadlnet.dk)