# Journal of Diabetes Science and Technology

Volume 7, Issue 6, November 2013 © Diabetes Technology Society



# Stability and Performance of Rapid-Acting Insulin Analogs Used for Continuous Subcutaneous Insulin Infusion: A Systematic Review

David Kerr, M.D.,<sup>1</sup> Erik Wizemann, M.D.,<sup>2</sup> Jakob Senstius, M.Sc.Pharm.,<sup>3</sup> Mette Zacho, M.D., Ph.D.,<sup>3</sup> and Francisco Javier Ampudia-Blasco, M.D.<sup>4</sup>

## **Abstract**

#### Aim:

We review and summarize the literature on the safety and stability of rapid-acting insulin analogs used for continuous subcutaneous insulin infusion (CSII) in patients with diabetes.

#### Methods:

Two predefined search strategies were systematically implemented to search Medline and the Cochrane Register of Clinical Trials for publications between 1996 and 2012.

#### Results:

Twenty studies were included in the review: 13 *in vitro* studies and 7 clinical studies. *In vitro* studies investigated the effects of extreme CSII conditions (high temperature and mechanical agitation) on the risk of catheter occlusions and insulin stability factors, such as potency, purity, high molecular weight protein content, pH stability, and preservative content (m-cresol, phenol). Under these conditions, the overall stability of rapidacting insulin analogs was similar for insulin lispro, insulin aspart, and insulin glulisine, although insulin glulisine showed greater susceptibility to insulin precipitation and catheter occlusions. A limited number of clinical trials were identified; this evidence-based information suggests that the rate of catheter occlusions in patients with type 1 diabetes using CSII treatment may vary depending on the rapid-acting analog used.

### **Conclusions:**

Based on a limited amount of available data, the safety, stability, and performance of the three available rapidacting insulin analogs available for use with CSII were similar. However, there is limited evidence suggesting that the risk of occlusion may vary with the insulin preparation under certain circumstances.

J Diabetes Sci Technol 2013;7(6):1595-1606

Author Affiliations: <sup>1</sup>Bournemouth Diabetes and Endocrine Centre, Royal Bournemouth Hospital NHS Foundation Trust, Dorset, United Kingdom; <sup>2</sup>Diabetes Schwerpunktpraxis, Herrenberg, Germany; <sup>3</sup>Novo Nordisk A/S, Bagsvaerd, Denmark; and <sup>4</sup>Department of Endocrinology and Nutrition, Clinic University Hospital of Valencia, Valencia, Spain

Abbreviations: (CI) confidence interval, (CSII) continuous subcutaneous insulin infusion, (HbA1c) glycosylated hemoglobin

Keywords: diabetes mellitus, insulin pump, protein stability, rapid-acting insulin

Corresponding Author: David Kerr, M.D., Bournemouth Diabetes and Endocrine Centre, Royal Bournemouth Hospital NHS Foundation Trust, Dorset, UK; email address <a href="mailto:david.kerr@rbch.nhs.uk">david.kerr@rbch.nhs.uk</a>