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SYMPOSIUM

Ultrafast-Acting Insulins: State of the Art

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Abstract

Optimal coverage of prandial insulin requirements remains an elusive goal. The invention of rapid-acting insulin analogs (RAIAs) was a big step forward in reducing postprandial glycemic excursions in patients with diabetes in comparison with using regular human insulin; however, even with these, the physiological situation cannot be adequately mimicked. Developing ultrafast-acting insulins (UFIs)—showing an even more rapid onset of action and a shorter duration of action after subcutaneous (SC) administration—is another step forward in achieving this goal. The need for UFIs has been gradually recognized over the years, and subsequently, a number of different approaches to cover this need are in clinical development. A rapid increase in circulating insulin levels can be achieved by different measures: modification of the primary structure of insulin molecule (as we know from RAIAs), addition of excipients that enhance the appearance in the monomeric state post-injection, or addition of enzymes that enable more free spreading of the insulin molecules in the SC tissue. Other measures to increase the insulin absorption rate increase the local blood flow nearby the insulin depot in the SC tissue, injecting the insulin intradermally or applying via another route, e.g., the lung. The development of these approaches is in different stages, from quite early stages to nearing market authorization. In time, daily practice will show if the introduction of UFIs will fulfill their clinical promise. In this review, the basic idea for UFIs will be presented and the different approaches will be briefly characterized.

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Abbreviations: (AP) artificial pancreas, (ARIA) alternative routes of insulin administration, (CGM) continuous glucose monitoring, (CSII) continuous subcutaneous insulin infusion, (FDA) Food and Drug Administration, (GIR) glucose infusion rate, (GV) glycemic variability, (HbA1c) hemoglobin A1c, (HGP) hepatic glucose production, (ID) intradermal, (IMI) injection-meal interval, (NDA) new drug application, (PD) pharmacodynamic, (PK) pharmacokinetic, (PPG) postprandial glycemic excursion, (RAIA) rapid-acting insulin analog, (RHI) regular human insulin, (rHuPH20) recombinant human hyaluronidase, (SC) subcutaneous, (T1DM) type 1 diabetes mellitus, (T2DM) type 2 diabetes mellitus, (TI) Technosphere insulin, (UFI) ultrafast-acting insulin

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