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Effects of Pulsatile Subcutaneous Injections of Insulin Lispro on Plasma Insulin Concentration Levels

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Abstract

Background:
Most insulin pumps used for the treatment of diabetes perform subcutaneous insulin injections by pulses. The purpose of this work is to analyze the effects of pulsatile injections of modern insulins on plasma insulin levels compared with a continuous insulin infusion.

Method:
We simulate pulsatile implementations of a basal rate profile over a day on a type 1 diabetes mellitus patient using insulin lispro. Pulse periods were varied between 1 and 60 min, and random pump errors were included, modeled as white noise, 1/f noise, or $1/f^2$ noise with relative standard deviations up to 10% of the pump output.

Results:
Oscillations in plasma insulin caused by the pulsatile injections were not significant with respect to the global variations for pulse periods below 15 min. This cutoff period was found to be robust to random pump errors with standard deviations up to 10% of the pump output and hence solely determined by the insulin kinetics. Additionally, we showed that the pulse period achieving the best implementation of a continuous profile is an increasing function of the error variance for a given type of noise.

Conclusions:
Our findings support that continuous insulin infusion can be implemented by a pulsatile injection of insulin as infrequent as a pulse every 15 min without significant effects on plasma insulin levels. If clinically confirmed, this result would have important consequences on the design and *in silico* testing of automated insulin treatment strategies, as increased delivery intervals imply higher accuracy of insulin delivery and facilitated implementations of closed-loop control algorithms.

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Abbreviations: (CSII) continuous subcutaneous insulin infusion, (MDI) multiple daily injections, (T1DM) type 1 diabetes mellitus

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