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2222 Insulin Lispro versus human regular insulin in continuous subcutaneous insulin infusion: a systematic review of comparative efficacy and safety

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Background and Aims: The present systematic review aims at comparing both the efficacy and safety of fast-acting insulin lispro analogue (Lispro) and human regular insulin (Regular) in type 1 diabetic patients treated with continuous subcutaneous insulin infusion (CSII).

Materials and Methods: Randomised clinical trials (RCTs) comparing Lispro vs Regular in CSII-treated type 1 diabetic patients were extensively searched in the literature, and the following efficacy and safety aspects were studied: 1) 1-h or 2-h postprandial hyperglycaemia; 2) HbA1c level; 3) the incidence of severe hypoglycaemia; and 4) the risk of ketoacidosis.

Results: Lispro was compared with Regular during CSII in one double-blind crossover RCT ($n = 30$) and in 5 open-label crossover RCTs (total: $n = 262$), each of 2 × 2- to 4-month duration. All these RCTs demonstrated significant reduction in postprandial hyperglycaemia (weighted mean difference or WMD: -1.66 mmol/l; $p < 0.001$; $n = 292$) and diminution in HbA1c level (WMD: -0.24% ; $p < 0.001$), without any significant difference in the incidence of severe hypoglycaemia (WMD: -0.17 hypos/patient/30 days; NS). In contrast, in an open-label parallel 4-month study, no significant differences in postprandial hyperglycaemia, HbA1c level and incidence of hypoglycaemia could be evidenced between Lispro ($n = 59$) and Regular ($n = 28$). In a trial testing the switch from Regular to Lispro in 62 diabetic patients, a 0.50% reduction in HbA1c level ($p < 0.001$) was maintained after 20 months of CSII with Lispro. None of these RCTs pointed out a higher risk of ketoacidotic episodes when using Lispro instead of Regular. Interestingly, two experimental crossover trials ($n = 7$ and 10) demonstrated an earlier and higher rise in blood glucose and ketone bodies, up to 3-5 hours after acute CSII interruption, when using Lispro instead of Regular. However, such early differences were not observed in one parallel trial comparing CSII interruption with Lispro ($n = 9$) vs Regular ($n = 9$), and quite similar late metabolic deteriorations were reported after 8-9 hours with both types of insulin in the two studies testing such a prolonged CSII interruption. Finally, despite the common use of CSII during pregnancy, it is noteworthy that the safety of Lispro has not been validated in large RCTs in CSII-treated pregnant women.

Conclusion: As compared with human regular insulin, insulin lispro resulted in significantly lower postprandial hyperglycaemia and HbA1c levels in CSII-treated type 1 diabetic patients, without significant differences in hypoglycaemic episodes. The earlier metabolic deterioration in case of acute interruption of insulin lispro infusion was not associated with a higher rate of ketoacidosis, at least in patients participating to clinical trials.