Two Randomized Crossover Glucose Clamp Studies of Nasulin™ and Lispro Subcutaneously

Robert M. Stote, MD; Sherwyn L. Schwartz, MD; Clayton A. Dehn, MS; Poul Strange, MD, PhD

CPEX Pharmaceuticals, Inc.
Exeter, New Hampshire, USA
rstote@cpexpharm.com

Objective:
Two glucose clamp studies compared the pharmacokinetic and pharmacodynamic results of CPEX Pharmaceuticals' intranasal insulin formulation, Nasulin,™ to lispro subcutaneously, one in healthy volunteers and one in subjects with type 1 diabetes mellitus (T1DM).

Methods:
After stabilization of glucose values (90–100 mg/dl in healthy volunteers and 90–110 mg/dl subjects with T1DM), 17 normal volunteers received 25 IU Nasulin, 25 IU at 0 and 60 minutes, or 5 IU lispro and six type 1 diabetes subjects received 50 IU Nasulin or 10 IU lispro followed by a 4-hour glucose clamp procedure.

Results:
In normal volunteers, Nasulin regimens resulted in higher peak values and earlier peaks in mean baseline-adjusted plasma insulin compared to lispro [C_{max} 62.1 (68) vs 36.9 (10.2) μIU/ml][T_{max} 18 (6) vs 54 (18) minutes]. The geometric mean ratio (GMR) peaked earlier and declined more rapidly with both Nasulin treatments compared to lispro. Mean area under curve–GMRs in the first hour were higher for the Nasulin arms [136.9 (78.7) and 134.8 (70.8 mg/kg)] vs lispro [111.7 (64.1) mg/kg] but were higher for lispro vs the 25 IU Nasulin arm over 240 minutes. In subjects with T1DM, the same results and trends were noted with the exception that C_{max} values were similar for Nasulin and lispro [42.3 (29.9) and 43.7 (17.3)], respectively. The maximum metabolism rate was highest in the lispro arm in both studies. The C_{max} of Nasulin showed more variability.

Conclusion:
These data support the ultrarapid-acting time-action profile of Nasulin and the consequent rapid onset of maximum glucose utilization. These features suggest that Nasulin would be valuable as prandial insulin with the advantage of a more rapid and effective postprandial glucose reduction than lispro in the first hour after dosing.