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ORIGINAL ARTICLES

Enhanced Absorption of Nasulin™, an Ultrarapid-Acting Intranasal Insulin Formulation, Using Single Nostril Administration in Normal Subjects

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Abstract

Background:

This pharmacokinetic (PK) study was designed to investigate the maximum intranasal insulin dose that could be achieved by repeated doses in a single nostril of a nasal spray of recombinant regular human insulin 1% in combination with cyclopentadecalactone (CPE-215) 2%, a compound that enhances absorption of molecules across mucous membranes (Nasulin™, CPEX Pharmaceuticals, Inc.).

Method:

A nine-period crossover study of 8 healthy, nonsmoking subjects (ages 18–50, body mass index <33 kg/m^2, weight >70 kg) were studied. In a fasted state, subjects were randomly given 25, 50, and 75 U in a single nostril on the first day and randomly given 50, 75, and 100 U doses utilizing both nostrils on two subsequent days. After a 45-minute PK assessment, subjects were given a meal. To determine the mechanism of enhanced absorption in a single nostril, a second study utilizing 24 subjects under similar conditions received 25 U, placebo (P) that included CPE-215 plus 25 U, and 50 U in a single nostril.

Results:

Single nostril administration revealed enhanced absorption with maximum concentrations (C_{max}) of 13, 65, and 96 μU/ml for the 25, 50, and 75 U doses, respectively. Dual nostril administration in two cohorts resulted in C_{max} of 31/42, 65/52, and 88/79 μU/ml for the 50, 75, and 100 U, respectively. In the second cohort, C_{max} was 23, 19, 56 μU/ml for the 25, P + 25, and 50 U doses, respectively.

Conclusions:

Repeated dosing in a single nostril resulted in enhanced absorption; this was not due to the increased CPE-215 but to the increased insulin administered.

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Abbreviations: (AUC) area under the curve, (BMI) body mass index, (C_{max}) maximum concentration, (CPE-215) cyclopentadecalactone, (ORMC) Orlando Regional Medical Center, (P) placebo, (PK) pharmacokinetic, (SE) standard error of the mean, (T_{max}) time to maximum concentration, (U) unit

Keywords: CPE-215, cyclopentadecalactone, intranasal insulin, Nasulin, ultrarapid time-action profile

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