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ORIGINAL ARTICLES

Pharmacokinetics and Pharmacodynamics of Intranasal Insulin Spray (Nasulin™) Administered to Healthy Male Volunteers: Influence of the Nasal Cycle

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Abstract

Background:

The pharmacokinetics and pharmacodynamics of a Bentley Pharmaceuticals proprietary intranasal (IN) insulin formulation (Nasulin™) were studied in healthy volunteers.

Methods:

Thirteen fasting healthy male volunteers received five doses of medication (one dose of 4 international units [IU] subcutaneous (SC) regular insulin and four doses of 25 IU IN insulin) at least 48 h apart. Serum insulin, serum C-peptide, and plasma glucose were measured in the 4 h after dosing. Profiles were compared for IN insulin spray following administration into the dominant nostril (more open at time of dosing) and into the nondominant nostril (less open at time of dosing).

Results:

The formulation was generally well tolerated. A rise in serum insulin levels accompanied by a decrease in plasma glucose was seen following all doses. For IN doses, peak insulin levels were generally attained in 10–20 min and remained elevated for approximately 40–50 min; the resultant effect on glucose peaked at 40 min and waned approximately 2 h postdosing. As reported in other studies, the interindividual response to insulin was variable. The comparative absorption of IN insulin relative to SC insulin was 12.0% (dominant nostril) or 15.4% (nondominant nostril) over 2 h. This increased somewhat if sneezers and volunteers with moderately blocked nostrils were removed from the analysis.

Conclusions:

This IN formulation was generally well tolerated and relatively well absorbed. While both insulin data (maximal plasma concentration and area under the plasma concentration time curve) and glucose data (% fall) support a trend toward better absorption from the nondominant nostril, this did not reach statistical significance. Nasulin can be administered without reference to the nasal cycle.

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Abbreviations: (AUC) area under the plasma concentration time curve, (BMI) body mass index, (Cmax) maximal plasma concentration, (CPE-215) cyclopentadecalactone, (IN) intranasal, (SC) subcutaneous, (IU) international units

Keywords: insulin kinetics, intranasal insulin, nasal cycle, plasma glucose

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