The Effect of Nasal Congestion on the Bioavailability of Intranasally Administered Epinephrine in Healthy Adult Subjects with Seasonal Allergies

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BACKGROUND
Intramuscular (IM) administration of epinephrine (EPI) is a first-line treatment of anaphylaxis. Intranasal (IN) EPI may offer a faster route of administration, resulting in avoidance of reluctance to IM injection and application error. However, nasal congestion may affect IN absorption.

METHODS
• Open-label, 4-period study
• 26 subjects with seasonal allergy
• Treatments:
  A) IN 13.2 mg EPI (as 2 sprays in opposite nostrils), with nasal congestion (after nasal allergen challenge)
  B) IN 13.2 mg EPI (as 2 sprays in opposite nostrils), without nasal congestion
  C) IM 0.3 mg EPI by EpiPen®
  D) IM 0.5 mg EPI by manual syringe
• Assessment of safety, PK, blood pressure and heart rate up to 360 min postdose (adjusted for baseline)

RESULTS
Tmax (median):
- 15.1 (IN congested), 25.2 (IN), 21.5 (IM 0.3 mg) and 45.0 min (IM 0.5 mg)

Heart rate Emax (median):
- >20 bpm only for treatments 0.5 mg IM and 13.2 mg IN
- Tmax occurring earlier for IN treatments

Systolic Blood Pressure (mean): comparable across treatments, with no systolic blood pressure changes >10 mmHg

Safety: All treatments were well tolerated. Most common AEs observed with IN dosing were gastrointestinal, were generally of mild severity and resolved quickly.

CONCLUSION
• Nasal congestion enhanced peak levels of EPI after IN administration
• Total EPI exposure after 13.2 mg IN similar to exposure after 0.5 mg IM
• IN administered EPI was well tolerated

Table 1. EPI AUC_0-360 (pg•min/mL)

<table>
<thead>
<tr>
<th>EPI</th>
<th>Mean (SD)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>A) IN 13.2 mg (congested)</td>
<td>34200 (99.7)</td>
<td>A vs. C *</td>
</tr>
<tr>
<td>B) IN 13.2 mg</td>
<td>29680 (75.9)</td>
<td>B vs. C *</td>
</tr>
<tr>
<td>C) IM 0.3 mg</td>
<td>16710 (51.7)</td>
<td></td>
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<tr>
<td>D) IM 0.5 mg</td>
<td>32400 (43.8)</td>
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</tbody>
</table>

Table 2. EPI Cmax (pg/mL)

<table>
<thead>
<tr>
<th>EPI</th>
<th>Mean (SD)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>A) IN 13.2 mg (congested)</td>
<td>458.0 (117.8)</td>
<td>A vs. B &amp; C *</td>
</tr>
<tr>
<td>B) IN 13.2 mg</td>
<td>270.1 (102.5)</td>
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<tr>
<td>C) IM 0.3 mg</td>
<td>279.0 (63.4)</td>
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<tr>
<td>D) IM 0.5 mg</td>
<td>364.2 (38.6)</td>
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*p < 0.05