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 conjection 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)

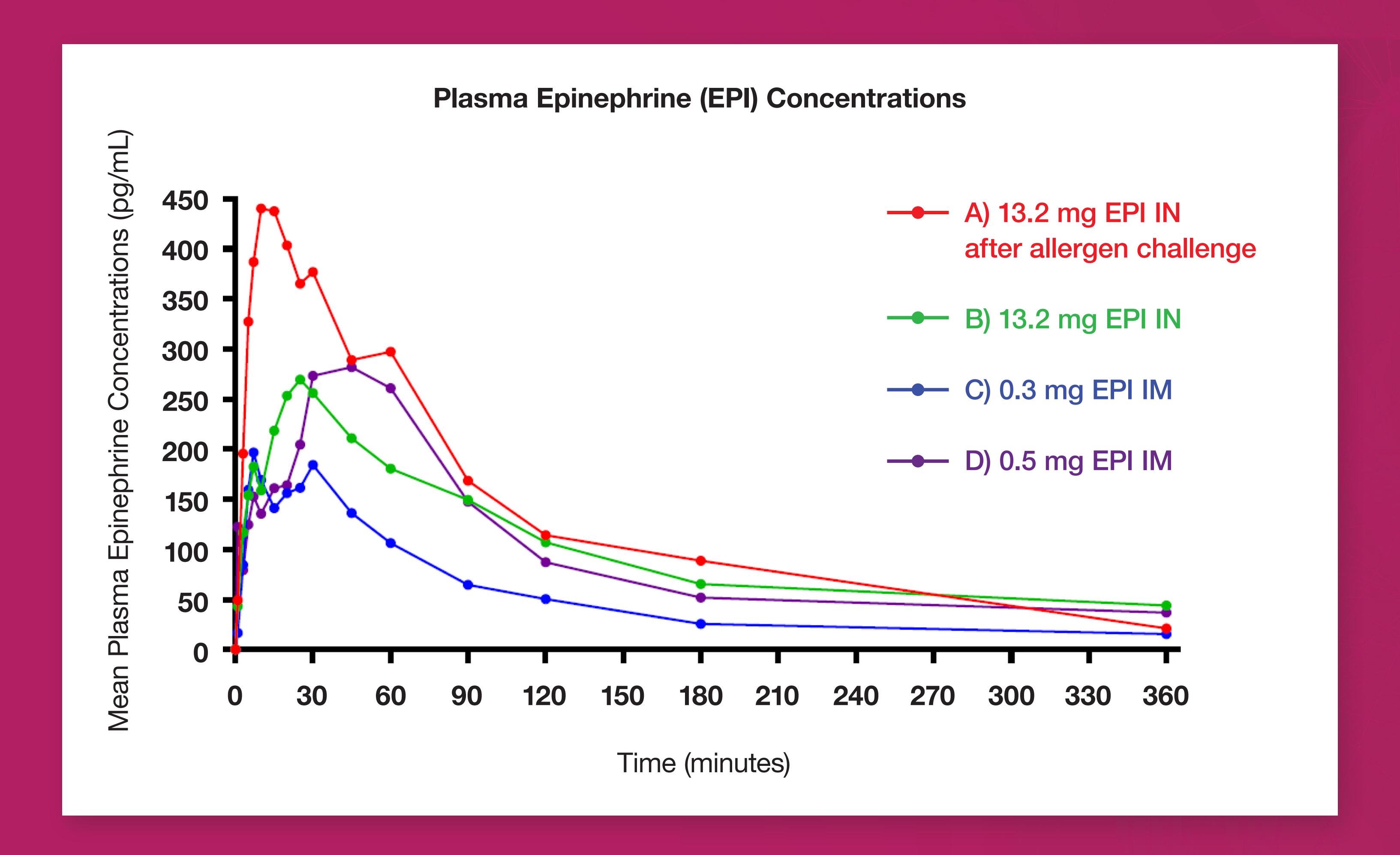
Heart rate Emax (median):

- >20 bpm only for treatments 0.5 mg EPI IM and 13.2 mg EPI IN
- TEmax occurring earlier for IN treatments

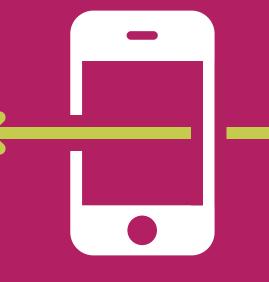
Systolic Blood Pressure (mean): comparable across treatments, with no systolic blood pressure changes >10 mmHg

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

Nasal Congestion Leads to Higher Exposure of Epinephrine Sprayed Intranasally







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Table 1. EPI AUC₀₋₃₆₀ (pg·min/mL)

EPI exposure after 13.2 mg IN similar to exposure after 0.5 mg IM

EPI	Mean (CV%)	Significance
A) IN 13.2 mg (congested)	34200 (99.7)	A vs. C *
B) IN 13.2 mg	29680 (75.9)	B vs. C *
C) IM 0.3 mg	16710 (51.7)	
D) IM 0.5 mg	32400 (43.8)	

^{*} p < 0.05

Table 2. EPI C_{max} (pg/mL)

Nasal congestion enhances peak levels after IN EPI administration

EPI	Mean (CV%)	Significance
A) IN 13.2 mg (congested)	458.0 (117.9)	A vs. B & C *
B) IN 13.2 mg	270.1 (102.5)	
C) IM 0.3 mg	279.0 (63.4)	
D) IM 0.5 mg	364.2 (68.9)	

^{*} p < 0.05

CONCLUSION

- Nasal congestion enhanced peak levels of EPI after IN administration
- Total EPI exposure after 13.2 mg EPI (with and without nasal congestion) was similar to exposure after 0.5 mg IM EPI (manual syringe), but greater than after 0.3 mg IM EPI (EpiPen®)
- IN administered EPI was well tolerated

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