

Effect of Sniff after Dosing of Epinephrine Nasal Spray

Jonathan M. Spergel, MD,¹ David Bernstein, MD,² Anne K. Ellis, MD,³ S. Shahzad Mustafa, MD,⁴ Vandana K. Patel, MD,⁵ Richard Lowenthal, MSc,⁶ Sarina Tanimoto, MD, PhD⁶
¹Division of Allergy and Immunology, Children's Hospital of Philadelphia, Department of Pediatrics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA; ²Bernstein Clinical Research Center and Division of Immunology, Allergy and Rheumatology, University of Cincinnati College of Medicine, Cincinnati, OH, USA; ³Division of Allergy & Immunology, Department of Medicine, Queen's University, Kingston, Ontario, Canada; ⁴Allergy, Immunology & Rheumatology, Rochester Regional Health System, Clinical Associate Professor of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA; ⁵Pediatric Allergy & Immunology, Carolina Asthma & Allergy Center, Charlotte, NC, USA; ⁶ARS Pharmaceuticals Operations, Inc., San Diego, CA, USA.

RATIONALE

- An FDA-approved epinephrine nasal spray is indicated for the emergency treatment of severe allergic reactions, including anaphylaxis.
- To further understand the impact of sniffing during or after intranasal administration, the pharmacokinetics of epinephrine nasal spray 2 mg with sniff were compared to epinephrine nasal spray 2 mg without sniff and intramuscular epinephrine 0.3 mg injection (IM 0.3 mg).

METHODS

STUDY DESIGN AND POPULATION

- A Phase 1, single dose, randomized, crossover study was conducted in 42 adults.
- Twenty-nine patients (69.0%) reported sniffing during or after self-administering epinephrine nasal spray 2 mg; sniffing was confirmed via video by two independent persons.
- Plasma epinephrine concentrations were assessed after administration of epinephrine nasal spray in patients who sniffed (n=29), epinephrine nasal spray in patients who did not sniff (n=12), and a single IM injection administered by study staff (n=42). One subject was excluded from the analysis due to an incomplete video recording.
- Patient demographics are presented in [Table 1](#).

Table 1: Patient Demographics

Demographic	Epinephrine Nasal Spray 2 mg with Sniff (n=29)	Epinephrine Nasal Spray 2 mg without Sniff (n=12)	IM 0.3 mg (n=42)
Age			
Mean (SD)	39.3 (8.4)	38.5 (8.8)	39.6 (8.5)
Gender			
Male	17 (58.6)	7 (58.3)	23 (54.8)
Female	12 (41.4)	5 (41.7)	19 (45.2)
Height (cm)			
Mean (SD)	171.4 (10.7)	174.8 (10.0)	171.9 (10.6)
Weight (kg)			
Mean (SD)	80.0 (14.1)	82.1 (13.5)	80.4 (13.7)
Body Mass Index (BMI)			
Mean (SD)	27.1 (3.2)	26.7 (3.0)	27.1 (3.1)

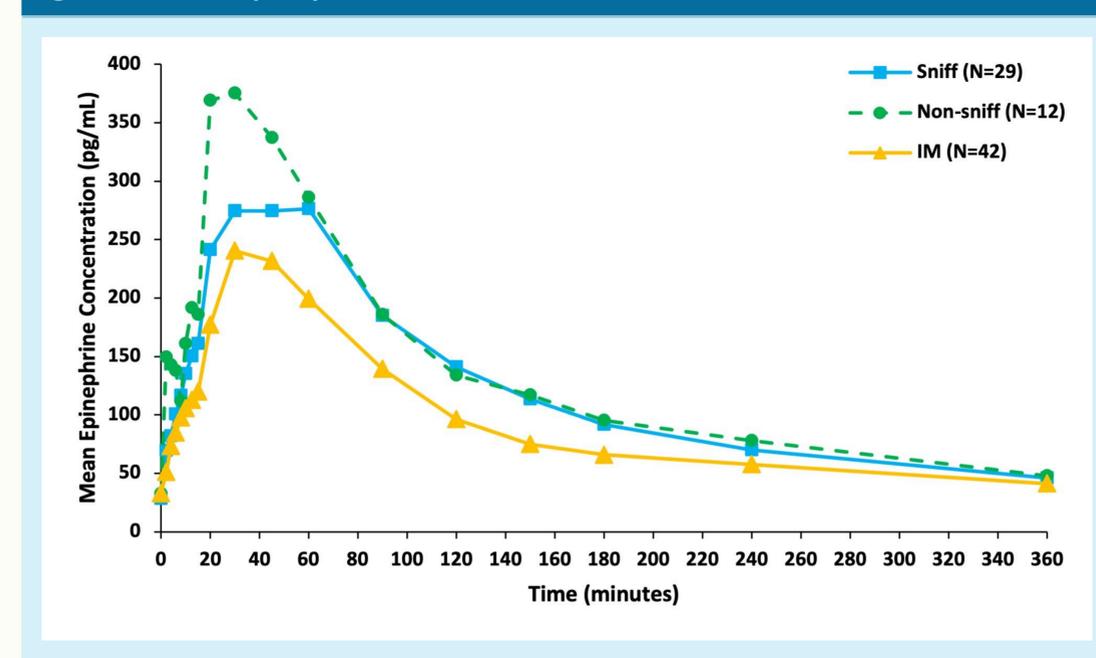
RESULTS

- Epinephrine nasal spray (without sniff) resulted in the highest mean maximum concentrations (C_{max}) (Coefficient of Variation [CV]) with 484 pg/mL (67%) (see [Table 2](#) and [Figure 1](#)).
- Epinephrine nasal spray (with sniff) and IM 0.3 mg resulted in mean C_{max} 382 pg/mL (67%) and 322 pg/mL (65%), respectively (see [Table 2](#) and [Figure 1](#)).

Table 2: Epinephrine Pharmacokinetics Parameters

Treatment	N	t_{max} (min) median (range)	C_{max} (pg/mL) Mean (%CV)	AUC _{last} (min*pg/mL) Mean (%CV)
Epinephrine Nasal Spray 2 mg with Sniff	29	30 (6 – 150)	382 (67)	44037 (61)
Epinephrine Nasal Spray 2 mg without Sniff	12	30 (12 – 240)	484 (66)	49232 (44)
IM 0.3 mg	42	45 (4 – 120)	322 (65)	33494 (41)

Figure 1: Mean Epinephrine Concentrations



CONCLUSIONS

- Sniffing may be a common reflex following intranasal drug administration.
- Sniffing during or after self-administration of epinephrine nasal spray 2 mg resulted in plasma epinephrine concentrations that were higher than IM injection, suggesting that sniffing will not have any impact on efficacy.
- There were clinically insignificant changes in C_{max} and overall exposure (AUC) due to patients who sniffed versus those who did not sniff.
- Regardless, patients should not be instructed to repeat dosing if the patient sniffs but to follow standard instructions and administer a second dose if symptoms do not improve.

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