Rationale for Second Dose of Epinephrine Nasal Spray to the Same Nostril

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RATIONALE

- In the absence of clinical improvement or if anaphylaxis symptoms worsen after initial epinephrine administration, a second dose should be administered.
- To determine the best practice for nasal administration of two consecutive doses of intranasal epinephrine, we compared epinephrine plasma levels following a second dose administered to the same nostril versus the opposite.
- To demonstrate the safety and efficacy of intranasal epinephrine, comparisons were made under various nasal conditions and relative to intramuscular (IM) injection.

METHODS

STUDY DESIGN AND POPULATION

- Repeated doses of epinephrine nasal spray 2 mg were administered during normal nasal conditions, either to the same [R/R] or opposite [L/R] (n = 39 each) nostril, and during allergic rhinitis [R/R] (n = 41) and [R/L] (n = 40).
- Repeated doses of IM injection 0.3 mg were administered [R/L] during normal nasal conditions and allergic rhinitis (n = 42 each).
- Patient demographics are presented in **Table 1**.

Table 1: Patient Demographics

Demographic	Normal Nasal Conditions		Allergic Rhinitis Conditions		
	Epinephrine Nasal Spray 2 mg [R/R] and [R/L] (n=39)	IM 0.3 mg [R/L] (n=42)	Epinephrine Nasal Spray 2 mg [R/R] (n=41)	Epinephrine Nasal Spray 2 mg [R/L] (n=40)	IM 0.3 mg [R/L] (n=42)
Age (year)					
Mean (SD)	40.4 (9.4)	42.8 (10.6)	42.8 (10.6)		
Min, Max	21, 54	24, 63	24, 63		
Gender					
Male	38	19	19		
Female	16	24	24		
Body Weight (kg)					
Mean (SD)	82.7 (12.5)	76.8 (15.4)	76.8 (15.4)		
Min, Max	55, 115	52, 108	52, 108		

RESULTS

NORMAL NASAL CONDITIONS

- Mean maximum plasma concentrations (C_{max}) following repeat doses were 1000 and 992 pg/mL for epinephrine nasal spray ([L/R] and [R/R], respectively) (**Table 2** and **Figure 1**).
- Mean epinephrine C_{max} following repeat doses was 420 pg/mL for IM 0.3 mg [R/L] (**Table 2** and **Figure 1**).

ALLERGIC RHINITIS CONDITIONS

- Mean epinephrine C_{max} following repeat doses were 852 and 581 pg/mL for epinephrine nasal spray ([R/R] and [R/L], respectively) (**Table 2** and **Figure 2**).
- Mean epinephrine C_{max} following repeat doses was 496 pg/mL for IM [R/L] (**Table 2** and **Figure 2**).

Table 2: Epinephrine Pharmacokinetics Parameters

Treatment	N	C_{max} (pg/mL) Mean (%CV)	t_{max} (min) median (range)	AUC_{last} (min*pg/mL) Mean (%CV)
Normal Nasal Conditions				
Epinephrine Nasal Spray 2 mg [R/L]	39	1000 (93.1)	30 (6-150)	86000 (77)
Epinephrine Nasal Spray 2 mg [R/R]	39	992 (75.3)	30 (4-150)	86500 (60.5)
IM 0.3 mg [R/L]	42	420 (66.5)	55 (8-122)	37311 (42.5)
Allergic Rhinitis Conditions				
Epinephrine Nasal Spray 2 mg [R/L]	40	581 (68.8)	15 (2-152)	35723 (102.8)
Epinephrine Nasal Spray 2 mg [R/R]	41	852 (73.7)	20 (2-150)	66424 (80.6)
IM 0.3 mg [R/L]	42	495 (47.0)	45 (6-150)	42821 (31.4)

Figure 1: Mean Epinephrine Concentrations – Normal Nasal Conditions

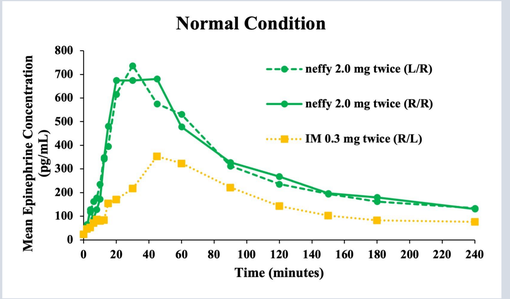
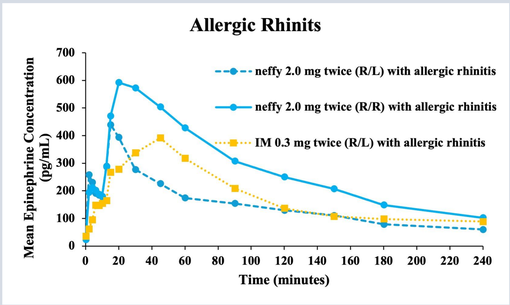


Figure 2: Mean Epinephrine Concentrations – Allergic Rhinitis Conditions



CONCLUSIONS

- Across multiple nasal conditions, mean epinephrine C_{max} via repeated doses of epinephrine nasal spray were comparable to or greater than repeated IM injections, suggesting that epinephrine nasal spray is an effective first-line therapy for the treatment of severe allergic reactions, including anaphylaxis.
- When epinephrine nasal spray was administered during rhinitis, both same and opposite nostril administration resulted in plasma epinephrine levels that were greater than IM injection; however, repeated administration to the same nostril optimized absorption.

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