Treatment of Nasal Congestion

Common cold, hay fever, or upper respiratory allergies

Dilation of nasal blood vessels

Increased nasal fluid

Narrowing of nasal passages

Nasal congestion & stuffiness

Pseudoephedrine vs. Phenylephrine

Active Ingredient	Pseudoephedrine (PSE)	Phenylephrine (PE)
Symptoms Addressed	Nasal & Sinus Congestion Sinus Pressure	
Strength/Dosing Frequency	Immediate and extended release products available for up to 24 hours of relief (6hr, 12hr, and 24hr products available)	Only available as immediate release products for about 4 hours of relief
Maximum Daily Dosage	240mg	60mg
Mechanism of Action Difference	• Works *directly* on alpha-1 adrenergic receptors found on blood vessels in nasal/sinus area (both PSE and PE) • PSE predominantly works *indirectly* through the release of norepinephrine (found in adrenergic nerve endings in the body), stimulating beta-1 and beta-2 receptors that are also on blood vessels	

Phenylephrine

Cohen BM. Clinical and physiologic "significance" of drug-induced changes in nasal flow/resistance. European Journal of Clinical Pharmacology. 1972 Nov 1;5(2):81-6.

- **Study type:** double-blind crossover placebo controlled
- **Population**: forty-eight patients with elevated Rn (nasal flow resistance) values from colds
- **Treatments**: 10.0, 15.0 and 25.0 mg single doses of phenylephrine, and placebo
- **End points**: mean Rn changes (by electronic posterior rhinometry); subjective estimates of nasal congestion (by five-ranked scale before and over 120 min)
- **Results**: All three phenylephrine doses induced a decrease from the elevated control mean Rn values which was apparent at 15 min, maximal between 30 and 90 min. The ranking of improvement for the four tablets was 25.0 mg > 15.0 mg = 10.0 mg >placebo. Subjective estimates of improvement after phenylephrine were superior to placebo effects for all three doses. Although mean per cent improvement in subjective scoring clearly separated the active tablets from placebo, the phenylephrine-induced results could not be differentiated from one another.
- **Conclusion**: Authors confirmed the ability of electronic posterior rhinometry to distinguish the efficacy of 10.0, 15.0 and 25.0 mg doses of phenylephrine from placebo at the 95% and 99% confidence limits. Mean per cent changes in Rn separated the decongestant effects of the 25.0 mg from the 10.0 and 15.0 mg doses, and differentiated all three from placebo.

ONSET: "All 3 PE doses induced a decrease from elevated control mean Rn values which was apparent at 15 min, and maximal between 30 and 90 min, and still present 120 min after therapy."

Kollar C, Schneider H, Waksman J, Krusinska E. Meta-analysis of the efficacy of a single dose of phenylephrine 10 mg compared with placebo in adults with acute nasal congestion due to the common cold. Clinical therapeutics. 2007 Jun 1;29(6):1057-70.

- **Study type:** Meta-analysis of 7 crossover studies (involving a total of 113 subjects) and the reanalysis of a parallel-group study (involving 50 subjects)
- **Population**: patients with acute nasal congestion due to the common cold
- **Treatment**: phenylephrine 10 mg
- **End points**: nasal airway resistance (NAR)
- **Results**: Significant differences in favor of phenylephrine were seen in 4 of the 8 studies ($P \leq 0.05$). Phenylephrine 10 mg was significantly more effective than placebo at the primary time points and at 90 minutes after dosing in the meta-analyses using both the fixed-effects and random-effects models ($P \leq 0.05$). At 45, 120, and 180 minutes after dosing, phenylephrine 10 mg was also significantly more effective than placebo in the fixed-effects model ($P \leq 0.05$). Between 30 and 90 minutes after dosing, percent reductions from baseline in NAR ranged from 6.0 percentage points higher with phenylephrine than with placebo (at 30 and 45 minutes after dosing) to 16.6 percentage points higher (at 60 minutes after dosing). From 60 to 180 minutes after dosing, the percent reductions from baseline were $\geq$ 20% with phenylephrine.
- **Conclusion**: Maximum and total systemic exposures following single doses of phenylephrine HCl 10, 20, and 30 mg increased disproportionally with increasing dose. Safety and cardiovascular tolerability were comparable among doses and placebo.

ONSET: “In the meta-analyses, PE was statistically significantly more effective than placebo at the primary time points, 30, and 60 minutes after dosing, and at 90 minutes after dosing”

Pseudoephedrine

Roth RP, Cantekin EI, Bluestone CD, Welch RM, Cho YW. Nasal decongestant activity of pseudoephedrine. Annals of Otology, Rhinology & Laryngology. 1977 Mar;86(2):235-42.

- **Study type:** double-blind controlled trial
- **Population**: Twenty adult male and female volunteer patients (ages 18-32 years) with symptoms of acute or chronic non suppurative rhinitis and possessed no pre-existing conditions which required administration of interfering drug therapy.
- **Treatments**: pseudoephedrine 60 mg tablet, Intranasally administered ephedrine as positive control
- **End points**: nasal resistance, plasma levels of pseudoephedrine
- **Results:** Onset of action in congested nasal passages occurred within 30 minutes following treatment; nasal resistance was reduced by a mean value of 52.5 ±6.2% compared to control. This highly significant decrease, which was the greatest degree of decongestion, was essentially maintained for an additional 210 minutes. Concentration of pseudoephedrine in plasma for 16 subjects rose to 261 ± 34 ng/ml by 30 minutes, reached a peak level of 306 ± 42 ng/ml at 60 minutes, and declined to 189.4 ± 25 ng/ml by 240 minutes after treatment. The mean nasal decongestant response (CI% of baseline) of 57.2% was associated with a mean peak of plasma pseudoephedrine level of 274 ng/ml.
- **Conclusion**: Results suggest that pseudoephedrine is an orally effective nasal decongestant.

ONSET: Onset of action in congested nasal passages occurred within 30 minutes following treatment

DURATION: Decongestion maintained for 240 minutes

> "the nasal decongestant response of patients to orally administered PSE, 60 mg tablet, had a fairly rapid onset of action and was maintained for four hours"

Taverner D, Danz C, Economos D. The effects of oral pseudoephedrine on nasal patency in the common cold: a double-blind single-dose placebo-controlled trial. Clinical Otolaryngology & Allied Sciences. 1999 Feb;24(1):47-51.

- **Study type:** placebo-controlled double-blind randomized
- **Population**: fifty-four patients with moderate to severe nasal congestion
- **Treatments:** single dose of oral pseudoephedrine 60 mg capsule or placebo
- **End points**: symptoms of congestion
- **Results:** symptoms of congestion improved significantly compared with placebo at times 60, 90, 120 and 150 min after the dose. Total nasal minimum cross-sectional area and nasal volume measured by acoustic rhinometry increased significantly compared to placebo (P= 0.018 and P= 0.003 respectively after the dose). There was no significant change in nasal area as measured by active posterior rhinomanometry after pseudoephedrine compared to placebo.
- **Conclusion**: in the acute common cold a single 60 mg dose of pseudoephedrine produces significant increases in the dimensions of the nasal cavity compared to placebo and this is associated with a reduction in the symptom of congestion.

ONSET: The reduction in symptoms after PSE administration was significantly greater than placebo at all time points between 60 and 150 min after dosing.

Table 4. Reported symptoms of nasal congestion after 60 mg pseudoephedrine orally or placebo (arbitrary units ± SD)

Time after dosing (min)	Placebo ($n = 28$)	Pseudoephedrine ($n = 24$)
Baseline	3.00 ± 0.55	2.88 ± 0.74
30	3.15 ± 0.72	2.79 ± 0.83
60	3.04 ± 0.76	2.50 ± 0.72*
90	2.89 ± 0.64	2.42 ± 0.72*
120	2.70 ± 0.67	2.29 ± 0.86*
150	2.74 ± 0.71	2.29 ± 0.75*
180	2.54 ± 0.65	2.27 ±0.83

* Indicates difference from baseline compared to placebo ($P < 0.05$).

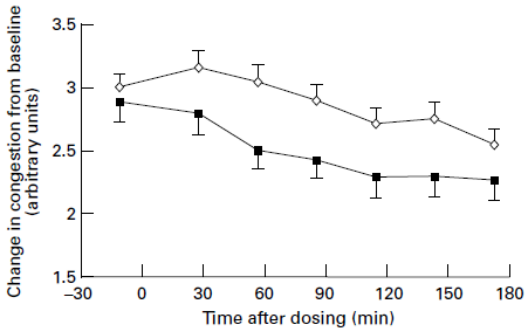

Figure 4. Reported symptoms of congestion at times after dosing with 60 mg pseudoephedrine or placebo (mean ± SE). ◇, CON placebo; ■, CON pseudoephedrine.