

# Safety, efficacy, and cost of 0.4 mg versus 2.0 mg intranasal naloxone for treatment of prehospital opioid overdose

John Thompson MPhil, Jenna Salter, Peter Bui MD, Logan Herbert MD, David Mills, Deborah Wagner PharmD FASHP, Christine Brent MD

**Background:** Intranasal naloxone is commonly used by emergency medical services personnel to treat prehospital opioid overdose. However, the optimal dose is unclear and currently no study exists comparing the clinical effect of intranasal naloxone at different doses. Objective: The goal of this investigation was to compare the safety, efficacy, and cost of 0.4 mg versus 2.0 mg intranasal naloxone for prehospital treatment of presumed opioid overdose.

**Methods:** A retrospective, cross-sectional study was performed of two hundred eighteen (218) consecutive adult patients receiving intranasal naloxone in either of two neighbouring counties in Southeast Michigan, USA: one that uses a 0.4 mg protocol and one that uses a 2.0 mg protocol. The primary outcomes were response to initial dose, requirement of additional dosing, and incidence of adverse effects. Unpooled, two-tailed, two-sample t-tests and chi-squared tests for homogeneity were performed with statistical significance defined as  $p < 0.05$ .

**Results:** There was no statistically significant difference between the two populations in age, mass, gender, or proportion of known exposures identified as heroin. There was no statistically significant difference in response to initial dose, requirement of redosing, or total number of doses by any route. The overall rate of adverse effects was 2.1% under the lower dose protocol and 29.0% under the higher dose protocol ( $p < 0.001$ ). The lower dose protocol was 79% less costly.

**Conclusion:** This study cannot conclude whether the observed difference in rate of adverse effects was due to the difference in initial dose or to a confounding factor such as differences in reporting. However, the observation that higher total doses of naloxone carry greater risk of adverse effects is supported by previous investigations. In this study, treatment of prehospital opioid overdose using intranasal naloxone at an initial dose of 0.4 mg was equally effective during the prehospital period as treatment at an initial dose of 2.0 mg, was associated with a lower rate of adverse effects, and represented a substantial cost savings.

**Table 1. Demographics and Main Results, by County<sup>a</sup>**

	Oakland County	Washtenaw County	p-value
Total number of patients	94	124	... <sup>b</sup>
Mean age, yr (n, S.D.)	38.2 (92, 14.9)	37.4 (124, 13.0)	0.70
Mean mass, kg (n, S.D.)	83.9 (19, 20.6)	76.1 (124, 18.7)	0.13
% male	70.2	64.5	0.38
% known exposures identified as heroin (n)	85.7 (35)	88.1 (67)	0.74
Mean initial intranasal dose, mg (n, S.D.)	0.48 (92, 0.28)	1.77 (121, 0.75)	<b>&lt;0.001</b>
Subjective response to initial dose <sup>c</sup> , %	Y: 39, N: 45, U: 16	Y: 54, N: 35, U: 11	0.10
% patients requiring redosing	58.5	54.8	0.59
Mean number of doses by any route (S.D.)	1.77 (0.74)	1.67 (0.70)	0.33
Mean number of intranasal redoses (S.D.)	0.51 (0.60)	0.17 (0.42)	<b>&lt;0.001</b>
Mean number of intramuscular redoses (S.D.)	0.06 (0.29)	0.24 (0.43)	<b>&lt;0.001</b>
Mean number of intravenous redoses (S.D.)	0.19 (0.47)	0.26 (0.49)	0.31
% patients with adverse effects	2.1	29.0	<b>&lt;0.001</b>

<sup>a</sup> Data were available for 100% of patients unless otherwise noted. Statistically significant results ( $p < 0.05$ ) are in bold. <sup>b</sup> Not applicable. <sup>c</sup> Categorized as “yes,” “no,” or “unclear.”

**Figure 1. Adverse Effects, by County**

Fig. 1: Adverse effects observed in patients treated with intranasal naloxone in A) Oakland County, which used a 0.4 mg protocol, or B) Washtenaw County, which used a 2.0 mg protocol.

