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High-Dose Nitroglycerin for Sympathetic Crashing Acute Pulmonary Edema

Sympathetic crashing acute pulmonary edema (SCAPE) is a subset of hypertensive heart failure which develops rapidly due to an abrupt increase in catecholamine release, subsequently leading to increased pulmonary capillary permeability and flooding of alveolar space. Preload and afterload reduction is key and is managed with non-invasive ventilation (NIV) and pharmacologic agents such as nitroglycerin. However, nitroglycerin has dose-dependent afterload reduction that requires doses >50-150 mcg/min.

Pharmacology

Nitroglycerin (NTG)

Mechanism of Action	Nitroglycerin, an organic nitrate, is **a vasodilating agent that relieves tension on vascular smooth muscle and dilates peripheral veins and arteries (at higher doses)**.
Dose	• Chest pain: 5-400 mcg/min (starting at 5 mcg/min) • Pulmonary edema/afterload reduction: 50-400 mcg/min ○ **Titrate to symptom improvement and tolerated blood pressure**
Administration	• IV infusion**: 50-400 mcg/min until symptom resolution** • IV bolus: **400-2000 mcg in syringe over 2-5 min (check hospital policy)** • 400 mcg Sublingual tablet: **2-4 tablets (equivalent to 160-320 mcg/min of IV nitroglycerin)** • Ointment: slow onset **30-60 min**
PK/PD	• Onset: **IV 1-5 min**; sublingual 1-3 min • Peak: IV/sublingual 3-15 min • Duration: **IV 5-10 min, sublingual 10-60 min** • Elimination: 22% renal
Adverse Effect	• Headache • **Hypotension** • **Syncope** • Rebound hypertension • Tolerance with prolonged use ~24 hours
Warnings and Drug Interactions	• **PDE inhibitors** • **Aortic stenosis**, preload-dependent cardiomyopathy, hypertrophic obstructive cardiomyopathy, hypotension at any time
Compatibility	• Incompatible with levofloxacin, SMX-TMP, daptomycin, and phenytoin

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Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
Patrick, 2020	Observational n=48	IV NTG 1 mg bolus by EMS	**High dose NTG associated with:** • Decreased SBP by 31 mmHg from baseline • Decreased HR by 10 beats per minute • Increased 02 saturation from 86% to 98% • 1/48 (2%) had symptomatic hypotension
Hsieh, 2018	Case report n=3	Sublingual NTG 0.6 mg/tab x 3 doses IV NTG bolus 1 mg every 2 min* IV NTG infusion 40 mcg/min* *If prior therapy failed	**High dose NTG associated with:** • Normalize respiratory status • No intubation + no ICU admission
Paone, 2018	Case report n= 1	IV NTG infusion 400 mcg/min titrated by 50 mcg/min	**High dose NTG bolus associated with:** • Symptomatic resolution @ 6 minutes
Wilson, 2016	Observational n=395	IV NTG bolus 500–2000 mcg Q3–5 min vs IV NTG infusion 20–35 mcg/min vs IV NTG bolus + infusion	**High dose NTG bolus associated with:** • Decreased ICU admission • Shorter LOS • No differences in adverse outcomes (intubation)
Levy, 2007	Observational n=29	IV NTG Bolus 2 mg IV Q3 min	**High dose NTG bolus associated with:** • Reduced intubation, need for bi-level positive pressure ventilation, and ICU admission
Sharon, 2000	RCT n= 40	IV bolus isosorbide 4 mg Q4 min vs Isosorbide infusion starting @ 10 mcg/min + BiPAP	**High dose isosorbide bolus associated with:** • Decrease intubations, MI, mortality, and improved PaO2
Cotter, 1998	RCT n= 104	IV isosorbide dinitrate 3 mg Q5 min + furosemide 50 mg vs IV isosorbide infusion 16 mcg/min titrate Q15min + furosemide 80 mg Q15 min	**High dose isosorbide bolus associated with:** • Reduction in mechanical ventilation and MI • Improvement in Pa02 and RR • Less adverse effects

References

1. Nitroglycerin. Micromedex [Electronic version].Greenwood Village, CO: Truven Health Analytics. Retrieved March 5, 2020, from http://www.micromedexsolutions.com/
2. Kramer K. Am Heart J. 2000;140:451–5.
3. Agrawal N. *Crit Care Med.* 2016;20:39–43.
4. Mebazaa A. *Eur J Heart Fail.* 2015;17:544–58.
5. Viau DM. *Heart.* 2015;101:1861–7.
6. McMurray JJ. *Eur J Heart Fail.*2012;14:803–69.
7. Yancy CW. *J Am Coll Cardiol.* 2013;62:e147–239.
8. Hsieh Y. *Turk J Emerg Med.* 2018; 18(1): 34–36.
9. Wilson SS. *Am J Emerg Med.* 2017;35(1):126–31.
10. Levy P. *Ann Emerg Med.* 2007;50:144–52.
11. Sharon A . *J Am Coll Cardiol.* 2000;36(3):832-7.
12. Cotter G. *Lancet.* 1998;351(9100):389-93.
13. Paone S. *Am J Emerg Med*. 2018;36(8):1526.e5-1526.e7.
14. López-Rivera F. Am J Case Rep. 2019 Jan 21;20:83-90.
15. Clemency BM, Prehosp Disaster Med. 2013 Oct;28(5):477-81.
16. Patrick C. Prehosp Emerg Care. 2020 Jan 27:1-7.

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