

## Nitroglycerin, stroke and hypertension: a word of caution

*Paul E. Marik, Joseph Varon*

The ENOS trial investigators performed a large multicenter trial investigating the role of a daily nitroglycerine patch in hypertensive patients with an acute stroke. (1) The reasoning for the choice of this agent in patients with an acute stroke is puzzling. Nitroglycerine is a potent veno-dilator and only in high doses does this drug reduce arterial tone. (2) This agent reduces blood pressure predominantly by reducing venous return and cardiac output. (2) It would appear counter-institutive to use a drug which reduces cardiac output, and therefore organ blood flow, in patients who have suffered an acute ischemic stroke. Rashid and coworkers suggest that nitroglycerine maintains cardiac output; (3) however, in this study the authors used a finger probe to measure cardiac out-

put, a method which remains invalidated. (4) Nitroglycerin causes dilation of intracerebral capacitance vessels which may increase intracranial pressure (ICP). (5,6) The combination of reduced mean arterial pressure and raised ICP may cause a significant fall in cerebral perfusion pressure (CPP). Tolerance develops rapidly to nitroglycerin, and the continued use of this agent without a drug-free interval goes against current dosing strategies. This may explain the short-lived antihypertensive effect, and the limited toxicity of nitroglycerine noted in the ENOS trial. We suggest that clinicians interpret this study carefully, as a compromise in CPP on the basis of an inexpensive and easy-to-administer agent is not justified.

---

From Eastern Virginia Medical School, Norfolk, VA, USA (Paul E. Marik), and The University of Texas Health Science Center at Houston, The University of Texas Medical Branch at Galveston, University General Hospital, Houston, TX, USA (Joseph Varon).

**Address for correspondence:**

Paul E. Marik MD, FCCP, FCCM  
Eastern Virginia Medical School  
825 Fairfax AV, Suite 410, Norfolk, VA 23507, USA  
Tel: +1-757-446.8910  
Fax: +1-757-446-5242  
Email: marikpe@evms.edu

## References

1. ENOS Trial Investigators, Bath PM, Woodhouse L, Scutt P, Krishnan K, Wardlaw JM, et al. Efficacy of nitric oxide, with or without continuing antihypertensive treatment, for management of high blood pressure in acute stroke (ENOS): a partial-factorial randomised controlled trial. *Lancet* 2015;385:617-28.
2. Marik PE, Varon J. Hypertensive crises: Challenges and management. *Chest* 2007;131:1949-62.
3. Rashid P, Weaver C, Leonardi-Bee J, Bath F, Fletcher S, Bath P. The effects of transdermal glyceryl trinitrate, a nitric oxide donor, on blood pressure, cerebral and cardiac hemodynamics, and plasma nitric oxide levels in acute stroke. *J Stroke Cerebrovasc Dis* 2003;12:143-51.
4. Marik PE. Non-invasive cardiac output monitors: a state-of-the-art review. *J Cardiothorac Vasc Anesth* 2013;27:121-34.
5. Lagerkranser M. Effects of nitroglycerin on intracranial pressure and cerebral blood flow. *Acta Anaesthesiol Scand Suppl* 1992;97:34-36.
6. Anile C, Zanghi F, Bracali A, Maira G, Rossi GF. Sodium nitroprusside and intracranial pressure. *Acta Neurochirurgica* 1981;58:203-11.