In conclusion, Kamenschikov and colleagues are to be congratulated for highlighting the promise of nitric oxide for renal protection in adult cardiac surgery. They have identified this versatile agent as a possible magic bullet for renal rescue as we continue our voyage to piece together the complex puzzle of AKI associated with cardiac surgery.

References

Commentary: Just say NO!

Jack S. Shanewise, MD, FASE

One nitrogen atom covalently bonded to 1 oxygen atom is nitric oxide. Add 1 more nitrogen and you have laughing gas—a medically useful compound produced by humans in large amounts. Add an oxygen atom to nitric oxide and you have smog—another gas produced by humans in abundance, unfortunately. Well known for many years to industrial chemical engineers, nitric oxide’s biologic function as an important molecular signal in systems regulating vascular tone was elucidated in the 1980s, earning it Science magazine’s “Molecule of the Year” award in 1992 and the 1998 Nobel Prize in Physiology or Medicine for 3 Americans: Furchott, Ignarro, and...
Murad. As a small, highly reactive free radical, nitric oxide—synthesized from arginine in vascular endothelium—passes freely through cell membranes to relax nearby smooth muscle cells before vanishing in a few seconds, making it perfect for moment-to-moment modulation of vascular tone. Nitric oxide became a drug in the 1990s with the realization that if inhaled in minute amounts (20-40 PPM), it will selectively dilate the pulmonary vascular bed and disappear before reaching the systemic vessels. Although only Food and Drug Administration-approved for persistent pulmonary hypertension in newborn infants, much, if not most, nitric oxide is used in adults to treat pulmonary hypertension and its adverse effects.

Kamenshchikov and colleagues\(^1\) studied another, even more novel way to use nitric oxide therapeutically. They gave nitric oxide to adult cardiac surgery patients at moderate risk for acute kidney injury (AKI) by blending it with the fresh gas flowing into the oxygenator of the cardiopulmonary bypass (CPB) circuit. In their randomized trial, blinded except for the perfusionists, with 48 patients in each arm, the treatment group had half as much AKI postoperatively: 20.8\% versus 41.6\% (\(P = .023\)). The treatment group also made more urine on CPB and had significantly lower levels of urinary neutrophil gelatinase-associated lipocalin, a well-known marker for acute renal injury. They also measured toxic metabolites of nitric oxide, which, as one would expect, were higher in the treatment group during CPB, but which fell quickly back to baseline. This study is important because AKI after cardiac surgery is common and, even when mild, associated with decreased long-term survival.\(^2\) The renal protective effect of nitric oxide during cardiac surgery has been observed before,\(^3\) but this study not only confirms that the benefit is real, it describes a practical and elegant method to deliver nitric oxide to the kidneys exactly when it is needed: on CPB. Among the concerns of using nitric oxide is cost, especially in the United States. The technique described in this study provides a clear means to limit its use to a relatively short, well-defined duration: bypass time. The technique also is attractive because, by keeping the nitric oxide delivery system in the operating room, it avoids the complexities of transport and setting up in an intensive care unit. This study is an important step forward in the ongoing battle against perioperative AKI and will hopefully inspire larger trials aimed at investigating long-term outcomes and cost-effectiveness.

References