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Commentary: It is safe, but is it really better?

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Lee and colleagues¹ present a retrospective comparison of del Nido (DN) versus histidine-tryptophan-ketoglutarate (HTK) cardioplegia in 456 propensity-matched patients undergoing minimally invasive cardiac surgery (MICS), usually with single cardioplegia dosing. The authors conclude that, in comparison with HTK solution, DN solution seems to have acceptable safety and efficacy with more favorable myocardial protection in MICS.¹

This is the only clinical trial in adults or minimally invasive surgery comparing HTK and DN solutions. The study is large and well powered with detailed findings. However, this study does have limitations. First, it is a retrospective, nonrandomized trial. Surgeon, time, and practice biases may have influenced the results. Second, the myocardial ischemic times in this study were 50-100 minutes, generally within the ≤90-minute range where DN and HTK have both been seen to work well. Whereas multidose HTK has been used in clamp times up to 240 minutes with reasonable success, animal and human evidence tend to suggest that single-dose HTK may be increasingly associated with myocardial injury with clamp times >120 minutes. It is not yet known whether single-dose DN can provide reliable protection in adults with clamp times much longer than 90 minutes.²

Finally, clinical assessment of perioperative myocardial protection is difficult at best. Perioperative cardiac isoenzyme levels have been famously difficult to relate to relevant clinical outcomes. Use of postoperative cardiac inotropes can be subjective and not a very sensitive measure of systolic or diastolic performance.

CENTRAL MESSAGE

Single-dose del Nido versus HTK cardioplegia in 456 propensity-matched patients undergoing minimally invasive cardiac surgery showed lower peak cardiac isoenzyme levels.

In most clinical practices, measurable adverse outcomes attributable to myocardial injury are infrequent, perhaps in the range of <5% of cases. To detect a gross 50% improvement in adverse events, each study arm could require 400 patients or more. Clinical trials are very expensive and unlikely to occur unless sponsored by an industry likely to make millions of dollars from a positive outcome. Cardioplegia and myocardial protection are not very profitable industries at present. Thus, studies like that by Lee and colleagues¹ are likely to be rare and limited to showing general safety of any 1 myocardial protection technique. We may always be dependent on animal investigations to point the way to potentially more effective myocardial protection strategies.

Although this retrospective study is not a prospective randomized trial, it provides some of the best detailed data to date showing that use of DN in MICS can be safe at 50-90 minutes of clamp time. It remains difficult to say whether single-dose DN versus single-dose HTK is truly better in terms of myocardial protection up to 90 minutes of ischemia. Unlike multidose HTK, the safety of single or multidose DN beyond 90 minutes remains to be proven.

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