

INHALED NITRIC OXIDE: TODAY AND TOMORROW

Industry Sponsored Session – Mallinckrodt Pharmaceuticals

Inhaled nitric oxide (iNO) is a pulmonary vasodilator that plays a significant role in regulating vascular muscle tone. The session looked at three topics that are relevant to the current use of iNO as well as potential uses for the future.

- Professor Graeme MacLaren, Clinical Associate Professor of Paediatrics at the University of Melbourne presented *Inhaled Nitric Oxide: Role in Critical Care Today*
- Professor Paul Checchia, Professor of Pediatric Critical Care Medicine and Cardiology and Medical Director of the Pediatric Cardiovascular Intensive Care Unit at Texas Children's Hospital in Houston spoke on the subject of *Inhaled Nitric Oxide for Children during Cardio-Pulmonary Bypass*
- Professor Warwick Butt, Director of The Royal Children's Intensive Care Unit, Melbourne presented the third topic of the session *Inhaled Nitric Oxide for Children with Brain Injury and ECMO*

In opening remarks Dr. Butt clarified that the content of the session was not underwritten by industry nor was it designed to promote nitric oxide. Rather, the session was a summary of some of the current practices using iNO, some clinical and study observations and discussion surrounding rationale for current practices, often in the absence of comprehensive evidence. (Disclosure slides were displayed for each speaker)

Dr. MacLaren reviewed some of the literature with regards to efficacy for ARDS, cardiogenic shock and rebound pulmonary hypertension. Current uses of iNO include: persistent pulmonary hypertension of the newborn; a bridge to stabilization en route; severe right ventricular failure and LVAD.

Of interest for the future he made reference to a relatively new device that might provide an alternate technique for administering iNo by fitting into the ventilator circuit.

Dr. Checchia then continued the presentation, noting that the complexity of cardio pulmonary bypass was staggering and, although a "necessary evil", probably accounted for much of the inflammatory response issues. He noted that apoptosis and nitric oxide were still somewhat of a "black box". He recounted the Houston experience where they delivered iNo during bypass at the moment of reperfusion. The small pilot demonstrated some interesting findings and was followed by a larger study. The results included a reduction in time on the ventilator and reduced time in ICU. An Australian group then followed with an RCT. The trial showed a significant difference in primary outcome of low cardiac output with the greatest impact on the youngest and most complex.

Other studies that might impact the future include:

- A group in China looked at 217 adults with renal injury and the effects of nitric oxide on the kidney
- Mouse studies looking at ischemia reperfusion with reduced infarct size and improved cardio as well as mouse studies addressing brain injury with results indicating smaller stroke burden. In the future there is the potential to look at neural outcomes in neonates.

Dr. Butt discussed use of iNO in ECMO. He also noted some current thoughts on autoregulation in brain mPTP, preventing ischemia after cardiac arrest in mice and the synergy between nitric oxide and hypothermia. He concluded that there are still many things we don't know.

A consistent theme throughout the session was the need for additional studies. Much of current practice prompts further questions rather than providing guidance for changes in practices and policies. Where do we go from here? There is interest in multi-centred trials but an abundance of issues and variations create challenges in study design and will, therefore, require continuing collaboration.