INAHTA Briefs

Issue 2008/043

Title **Safety and Efficacy of Inhaled Nitric Oxide in the Management of Hypoxemic Respiratory Failure in Adults with Acute Respiratory Distress Syndrome**

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Reference April 2007 (English). ISBN 978-0-9780024-9-7. www.ihe.ca/hta/publications.html

Aim

To examine the scientific evidence on the safety and efficacy of inhaled nitric oxide (iNO) in managing hypoxemic respiratory failure in adult patients with acute respiratory distress syndrome (ARDS) to ensure the most clinically and economically appropriate application of iNO.

Conclusions and results

One systematic review, 5 randomized controlled trials (RCT), and 1 followup study on the use of iNO in patients with ARDS were identified. The 5 RCTs varied considerably in methodology, making comparisons challenging. In 4 of the primary studies, the manufacturer/supplier of the treatment gas provided funding. Nonetheless, the results indicated that using iNO to treat ARDS does not improve mortality rates, compared to conventional ventilator management, with or without placebo gas. Also, it appears that improvements in supportive care, early treatment, and the use of evidence-based management strategies, eg, lung-protective ventilation, over the past 10 years have dramatically improved overall mortality.

However, iNO is not without complications. Although the incidence of serious adverse effects was not clinically significant in the studies presented, even a slight complication in a critically ill ARDS patient can be dangerous. While iNO has been suggested as a last resort in the most severely refractory hypoxemic patients to obviate the need for more expensive therapeutic options, eg, extracorporeal membrane oxygenation, the degree of benefit has not been established.

Recommendations

People with ARDS resulting from a nonpulmonary infection (eg, sepsis) and those with multiorgan failure or an irreversible underlying condition generally have poor outcomes. Using iNO in these patients does not appear to alter their prognosis. Hence, its use should be reconsidered.

Transient improvement in oxygenation can be expected in about 60% of people receiving iNO early in ARDS (within 72 hours). Any improvement is typically evident within 10 minutes of initiating therapy and may continue up to 48 hours. Beyond this time, continued use should be re-evaluated based on the patient's condition, including an assessment for potential complications.

iNO should be used in concentrations of less than 40 parts per million (ppm), with the best available evidence indicating a range of 5 to 10 ppm as being the most effective (when there is a response to oxygenation). Daily dose assessment or challenges should be conducted throughout iNO administration to re-establish optimal dosing. Stepwise discontinuation of iNO should be conducted if there is no ongoing positive response in oxygenation or intensity of ventilation.

Methods

All relevant systematic reviews and RCTs, published in English, were identified by systematically searching the Cochrane Library, the Centre for Reviews and Dissemination databases (National Health Service Economic Evaluation Database, HTA, Database of Abstracts of Review of Effects), PubMed, EMBASE, CINAHL, and Web of Science, plus relevant practice guidelines, regulatory agencies, and evidence-based resources and other HTA agency-related resources from January 1999 to November 2006. Methodological quality of the included studies was not assessed.

Further research/reviews required

Future studies are needed to determine whether the use of iNO alters the duration and intensity of ventilation, or obviates the need for more expensive therapies.

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ISSN 1654-501X