吸入一氧化氮運用於成年病人─南台灣一家醫學中心之十年經驗 A 10-year Experience of Inhaled Nitric Oxide in Adult Patients at a Medical Center in Southern Taiwan

鄭舒帆1、宋美儀2、鄭高珍1、柯獻欽1

奇美醫療財團法人奇美醫院內科部1、呼吸治療科2

Background: Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator, which has been used in patients with acute hypoxemic respiratory failure (e.g., acute respiratory distress syndrome, ARDS) or pulmonary hypertension (e.g., after cardiac surgery), but its role remains controversial. Recent reviews and meta-analyses concluded that iNO did not reduce mortality and might impair renal function. However, the use of iNO is not infrequent when patient's oxygenation cannot be maintained even under the use of high positive end-expiratory pressure (PEEP) and high oxygen fraction of inspired gas (FiO2). We studied the adult patients using iNO in our hospital to investigate the factors affecting the patient outcomes.
Materials and Methods: During Jan. 2002 to Dec. 2011, we retrospectively collected the adult patients (≥18 year-old) using iNO from respiratory therapeutist's records. Demographic characteristics including age and sex were recorded. The patients were sorted by three departments: cardiovascular (CV), internal medicine (excluding CV), and surgery (excluding CV). Disease severity was assessed by Acute Physiology and Chronic Health Evaluation (APACHE II) and Therapeutic Intervention Scoring System (TISS) scores. From medical charts and computer system, we recorded arterial oxygen partial pressure (PaO2), arterial carbon dioxide partial pressure (PaCO2), FiO2, serum creatinine and blood urea nitrogen (BUN) levels before and during the iNO use. The ratio of arterial oxygen partial pressure to the fraction of inspired oxygen (PaO2/FiO2, P/F ratio) was calculated. The patient's outcome (survival or mortality), durations of iNO use and mechanical ventilation were recorded. Patients died in hospital or discharged in critical condition were sorted as mortality group. Results: Totally, 330 patients were collected and 71 (21.5%) patients survived. The survivals were younger (53.8±16.7 vs. 62.6±16.8 years old, p <0.001) and had less severe disease (APACHE II 16.7±10.2 vs. 25.2±9.7, p <0.001). The duration of iNO use was not different between survivals and non-survivals (4.1±2.2 vs. 4.3±3.5 days, p =0.42). The duration of mechanical ventilation was significantly longer in the survivals (23.9±19.6 vs. 14.4±15.0 days, p <0.001). When sorted by different departments, 224 (67.9%) patients were in department of internal medicine, 48 (14.5%) in surgery, and 58 (17.6%) in cardiovascular department. The cardiovascular patients had much better outcome (50% survived) than internal medicine (14.7% survived) and surgery (18.8% survived) (p <0.001). Because the FiO2 was not registered by the computer system in the initial 97 patients, only 233 patients had P/F ratio data. During these 233 patient, the survivals (42, 18.0%) had higher P/F ratio before (120.8±91.8 vs. 74.7±47.1 mm Hg) and during (207.4±92.1 vs. 117.2±67.3 mm Hg) iNO use (p =0.003, <0.001 respectively). The P/F ratio increment was also larger in survivals (51.3±66.5 vs. 31.3±49.0 mm Hg, p =0.021). The PaCO2 before iNO use was not different between survivals and non-survivals (45.6±14.2 vs. 47.5±13.6 mm Hg, p =0.3), but the PaCO2 during iNO use was higher in the non-survivals (44.4±12.9 vs. 58.4±18.7 mm Hg, p <0.001). Before iNO use, the survivals had lower serum creatinine (1.85±1.77 vs. 2.37±1.91 mg/dL, p =0.041) and BUN (30.5±19.0 vs. 44.4±28.0 mg/dL, p <0.001)

levels. Among the total 330 patients, 99 patients had no creatinine or BUN data after iNO use. In the 231 patients having post-iNO data, the survivals still had lower serum creatinine (1.72±1.74 vs. 3.00±1.87 mg/dL, p <0.001) and BUN (39.3±26.0 vs. 61.6±32.2 mg/dL, p <0.001) levels.

Conclusions: Because the cardiovascular patients using iNO had higher P/F ratio and better outcome, we infer that the majority of iNO users in the cardiovascular department were for pulmonary hypertension. Patients using iNO for pulmonary hypertension have better outcome than those for hypoxic respiratory failure. The survivals had higher P/F ratio and less disease severity. The poor prognosis may be due to delay in iNO use. In the late stage of ARDS, pulmonary fibrosis may impede the iNO effects. Regardless of survival or not, iNO improved oxygenation significantly, but P/F ratio was increased to a greater extent in survivals. The patients tend to poor prognosis, if the PaCO2 increased significantly during the use of iNO. Increased PaCO2 represents the disease progresses and the gas exchange worsens. The initial renal function of non-survivals was worse than survivals. It represents multi-organ dysfunction already started before the use of iNO. Most ARDS patients died of multi-organ dysfunction syndrome (MODS) rather than hypoxemic respiratory failure. Once MODS began, it is difficult to reverse it. According to previous studies, iNO may deteriorate renal function. However, in the present study, renal function became worse only in the non-survivals. No adverse effect of iNO on renal function was detected in the survival group.