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Original Article

Analysis of Medical Resource Utilization and Outcome of Inhaled Nitric Oxide in Patients Undergoing Mechanical Ventilation☆

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SUMMARY

Background: Inhaled nitric oxide (iNO) is a potent selective pulmonary vasodilator, which is used in critically ill patients to improve oxygenation. It avoids systemic hypotension and ventilator-induced lung injury in patients using ventilators. This study explored the medical resource utilization and outcome, and predicted risk factors for mortality in patients using ventilators with iNO.

Methods: The database was from the National Health Insurance hospital claims data in Taiwan from 2004 to 2009. The patients using ventilators with iNO were collected and stratified by age to 20–44 years, 45–64 years, 65–74 years, and ≥ 75 years.

Results: Seven hundred and thirty ventilator patients with iNO were enrolled (63.15% male, mean age 60 years). Mechanical ventilation (MV) weaning rate was 18.25%, intensive care unit (ICU) readmission rate was 5.75%, and ICU mortality rate was 74.52%. ICU mortality rate was lower, case-mix index, MV weaning rate, and hospital costs were higher for patients aged 20–44 years and 45–64 years than in those aged 65–74 years and ≥ 75 years ($p < 0.05$). Sex, case-mix index, Charlson comorbidity index, whether MV weaning ($p < 0.001$), different age group, and implementation of tracheostomy ($p < 0.05$) were all significant risk factors in predicting mortality of patients using ventilators with iNO.

Conclusion: This study showed that the outcome differed with age in patients using ventilators with iNO.

1. Introduction

Conventional vasodilators may easily cause systemic vasodilation, which leads to hypotension; whereas inhaled nitric oxide (iNO) is a pulmonary vasodilator that selectively enters well-ventilated alveoli. There is a large affinity between NO and hemoglobin, 1500 times more than that between CO and hemoglobin. The half-life of NO is short, so it loses its activity before entering the systemic circulation. As a result, NO does not lead to systemic hypotension[1–3], but improves the V/Q (ventilation/perfusion) mismatch of patients using ventilators, reduces intrapulmonary shunts, increases arterial oxygen content, decreases the oxygen concentration of the ventilator (FiO_2), and lowers pulmonary artery hypertension[4–6]. Dellinger et al found that the survival rate and the weaning rate of 5 ppm iNO users were the highest[7]. When newborns with persistent pulmonary hypertension use iNO, the condition of oxygenation may be improved, and the treatment demand of extracorporeal membrane oxygenation may be reduced, which also decreases the expenses of hospitalization[8,9]. However, some studies found that iNO was not able to improve the condition of oxygenation, ventilator weaning rate, and prognosis in patients[10,11]; or, the improvement was observed only temporarily, and the mortality rate, length of mechanical ventilation (MV) utilization, and the number of days in the intensive care unit (ICU) were not improved[12–14].

This study explored the medical resource utilization and outcome of patient in different age groups using iNO ventilators, and predicted risk factors for mortality. Through this study, the conditions of patients using iNO ventilators will be understood further as references for future clinical applications.

☆ Conflicts of interest: The authors declare no conflicts of interest.

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2. Materials and methods

2.1. Study design and patient selection

The data were provided by the National Health Insurance (NHI) Bureau from March 1, 2004 to February 28, 2009; the targets were adult patients from around Taiwan who were in the ICU using MV with iNO (NHI registration code 57025b). Variables were statistically analyzed, including patient age, sex, case-mix index (CMI), Charlson comorbidity index (CCI), mortality rate in ICU, MV weaning rate, ICU readmission rate, tracheostomy rate, hospitalization cost, antibiotics cost, number of days using iNO, number of days in ICU, number of days hospitalized, and number of days using a ventilator. The patient medical resource utilization and outcomes were analyzed. Risk factors for mortality rate in patients using MV with iNO were analyzed according to sex, age group, CMI, CCI, MV weaning rate, and tracheostomy rate.

2.2. Measurements and variables

This study categorized patients into four age groups of 20–44 years, 45–64 years, 65–74 years and ≥ 75 years. Hospitals were categorized into three levels according to their accreditation, including medical center, regional hospital, and district hospital. Most iNO patients were found in medical centers and regional hospitals, therefore, this study excluded data from district hospitals. The regional NHI branches included Taipei, Northern, Central, Southern, Kao-Ping and Eastern Branches; only the Eastern Branch had been excluded, because no patients were using iNO. For a better annual presentation, data collected between March 1, 2004 and February 28, 2005 were presented as 2004; data collected between March 1, 2005 and February 28, 2006 was presented as 2005, and so on for the remaining data.

Amongst independent variables, medical resource utilization and disease severity were assessed using CMI and CCI values. When CMI increased, it meant that the patients in the hospital were more complicated and used more resources. The CCI values were divided into four groups, 0, 1, 2, and ≥ 3. The CCI value controls the comorbidity of patients before treatment or surgery, which avoids biased efficacy assessment. A developed comorbidity and severity calibration tool may follow up the prognosis of the patients as a good indicator. There were five scores, including 0 (no event), 1, 2, 3, and 6; the higher the score, the more severe the disease[15]. MV weaning is defined when a patient using iNO leaves the ICU without carrying a mechanical ventilator. ICU readmission is defined when a hospitalized patient leaves the ICU and returns after > 24 hours. The hospitalization expenses were the total reported to the NHI. The dependent variable was patient mortality rate. Mortality was defined when the patient's status in the NHI database changed to Code 4 and Code A, and was discharged from the hospital ICU within 24 hours due to their terminal condition[16].

2.3. Statistical analyses

Access 2007, statistics analysis system (SAS), and SPSS for Windows, version 17.0 (Chicago, IL, USA) were used in this study for data conversion and analysis. Descriptive analysis, χ^2 test, and one-way analysis of variance were used to investigate the medical resource utilization and outcomes of the patients using iNO. When the mortality risk factors of patients using iNO were investigated, in order to keep the cluster effect of the hospital on the prognosis of the patients, generalized estimating equations model and logit link function were used. Under the hypothesis of the exchangeable working correlation matrix, the data were analyzed to calculate the odds ratio and 95% confidence interval[17] of each risk factor.

3. Results

This study included 730 patients using MV with iNO; the average age was 60 years and there were 461 men (63.15%) and 269 women (36.85%). The CMI was 4.63. The CCI distribution was 28.9% for 0, 29.18% for 1, 25.62% for 2 and 16.3% for ≥ 3. The tracheostomy rate was 9.86%; the antibiotics usage rate was 97.67%; and the ICU mortality rate was 74.52% (Table 1). However, when the MV weaning rate was calculated, some NHI reporting materials were missing between 2004 and 2009; after excluding some data, the total number of patients using iNO MV was 707 and the survival rate was 18.25% (129 patients).

Table 1 also shows the distribution of patients using MV with iNO, which includes 666 patients (91.23%) from medical centers and 64 patients (8.77%) from regional hospitals. On the aspect of NHI branch, the highest number of iNO users was found in Taipei Branch, and the lowest number of iNO users was found in Kao-Ping Branch; the numbers were 498 (68.22%) and 21 (2.88%), respectively (Fig. 1). Patients using MV with iNO were mostly found in medical centers, but big differences in the distribution of iNO users in various branches were found; the number of patients in the medical centers was not proportionally related to the distribution of the branches. It is predicted that the presence of facilities and the choice of physicians are related to the number of iNO users in each hospital.

Among different age groups of the patient using MV with iNO, the analysis (Table 2) of the medical resource utilization and outcomes found that, CMI, MV weaning rate and hospitalization expense of the 20–44 years age group were higher than those of the 65–74 years and ≥ 75 years groups; the antibiotics cost of 20–44 years age group was also higher than that of the ≥ 75 years age group. However, the ICU mortality rate of the 20–44 years age group was lower than that of the 65–74 years and ≥ 75 years groups; the MV of the 20–44 years age group was also lower than that of the ≥ 75 years age group. The CMI values for the three groups mentioned were 5.70, 3.14 and 3.22 ($p < 0.001$), respectively; the MV weaning rates were 40 (25.48%), 18 (12.68%, $p < 0.05$) and 16 (8.29%, $p < 0.001$), respectively; the hospitalization costs were US$25,113, US$17,596 and US$18,507 ($p < 0.05$), respectively; the antibiotics costs were US$2,415 and US$1,714 ($p < 0.05$),

Table 1
Baseline characteristics of ventilator patients with inhaled nitric oxide.

Variable	$n = 730$
Age	60 ± 19
Sex	
Male	461 (63.15)
Female	269 (36.85)
CMI	4.63 ± 4.98
CCI	
0	211 (28.90)
1	213 (29.18)
2	187 (25.62)
≥ 3	119 (16.30)
MV weaning rate[a]	129 (18.25)
Readmission ICU rate	42 (5.75)
Tracheostomy rate	72 (9.86)
Antibiotic usage rate	713 (97.67)
ICU mortality	544 (74.52)
Hospital level	
Medical center	666 (91.23)
Regional hospital	64 (8.77)

Data are presented as mean ± standard deviation or *n* (%).
[a] $n = 707$.
CCI = Charlson Comorbidity Index; CMI = case-mix index; MV = mechanical ventilation.