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Utility and outcomes of hydroxocobalamin use in smoke inhalation patients

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ARTICLE INFO

Article history:
Accepted 31 July 2016

Keywords:
Inhalation injury
Hydroxocobalamin
Cyanokit
Burn
Smoke inhalation
Pneumonia

ABSTRACT

Introduction: Hydroxocobalamin has been available for use for suspected cyanide toxicity in smoke inhalation patients in the United States since 2006. Our study compares outcomes of patients who received hydroxocobalamin to historical controls who did not.
Methods: In this retrospective review, patients administered hydroxocobalamin (2008–2014) were compared to historical controls (2002–2008). Patients <18 years, patients who received an alternate antidote, and patients without suspicion of smoke inhalation injury were excluded. Mortality was the primary outcome. Secondary outcomes evaluated were 7-day change in creatinine, culture-proven pneumonia, days on mechanical ventilation, ventilator- free days (VFD), ICU length of stay (ICU LOS), and hospital length of stay (HLOS).
Results: A total of 138 patients in the hydroxocobalamin group and 135 in the control group were identified. Mortality rate was similar between both groups (29% vs. 28%, $p = 0.90$). Hydroxocobalamin was associated with lower pneumonia rate (23% vs. 49%, $p < 0.01$), less ventilator days (4 days vs. 7 days, $p < 0.01$), and increased VFD (20 days vs. 11 days, $p = 0.01$) compared to controls. Shorter ICU LOS (6 days vs. 10 days, $p = 0.03$) and a trend toward lower HLOS (7 day vs. 11 days, $p = 0.06$) were also found in patients who received hydroxocobalamin.
Conclusions: Routine administration was associated with lower rate of pneumonia, faster liberation from the ventilator, and reductions in intensive care unit stay. Burn centers should consider its empiric use in suspected smoke inhalation patients.
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http://dx.doi.org/10.1016/j.burns.2016.07.028
0305-4179/Published by Elsevier Ltd.

1. Introduction

House fires account for 3200 deaths and 40,000 injuries undergoing hospitalization in the United States each year [1]. Approximately 60–80% of these deaths involve smoke inhalation and elevated cyanide levels are frequently found in victims of closed- spaced fires, with the risk of death being directly related to the amount of cyanide exposure [2,3]. Manifestations of cyanide toxicity can range from confusion, headache, nausea and vomiting to seizures, bradycardia, hypotension, and respiratory or cardiac arrest [4,5]. Given the rapidly fatal cellular hypoxia attributed to cyanide, a low threshold must be maintained for prompt empiric treatment in fire smoke inhalation patients [6,7]. Hydroxocobalamin, a natural vitamin B12 derivative, has been studied as an empiric antidote for cyanide poisoning. It directly chelates cyanide to form cyanocobalamin (Vitamin B12), which is renally excreted and nontoxic [8]. Several studies have demonstrated its safety for prehospital use in the management of acute cyanide poisoning caused by smoke inhalation [9,10]. However no studies have evaluated the benefits of hydroxocobalamin compared with no antidotal intervention. We evaluated the outcomes of those who received hydroxocobalamin to historical controls, in patients with suspected inhalation injury.

2. Methods

2.1. Patient selection

Institutional review board approval was obtained before conducting this study. A retrospective review of medical records was performed to compare routine use of hydroxocobalamin against historical controls in suspected smoke inhalation patients. These include patients who were involved in enclosed space fires, presented with soot in their nares and/or oropharynx, had singed nasal hair or carbonaceous sputum, showed signs of tracheal edema such as stridorous respirations/hoarseness, or had elevated carboxyhemoglobin (COHb) levels. In 2008, the use of hydroxocobalamin was adopted by our institution; however, its empiric and routine use in suspected smoke inhalation patients became protocol late that year. The hydroxocobalamin group included suspected smoke inhalation patients who received hydroxocobalamin between 2008 and 2014. Confirmation of administration was obtained by review of medication administration records (MAR) and all charts were carefully evaluated to ensure that the patient did not receive any other antidote (i.e. sodium thiosulfate) for smoke inhalation in addition to hydroxocobalamin. The historical control group was obtained by reviewing charts of patients with smoke inhalation injury between 2002 and 2008 using the International Classification of Disease (ICD) code of 987.9: Toxic eff gas/vapor NOS. MARs and prehospital documents were thoroughly reviewed to confirm that patients in the control group did not receive any antidote. Patients who were excluded from this study include: pediatric patients (<18 years), patients who received an alternate antidote (i.e. sodium thiosulfate), and patients without suspicion or confirmed smoke inhalation.

2.2. Demographics and end points

Patient demographics including age, gender, smoking history, and history of chronic obstructive pulmonary disease (COPD) were evaluated. Injury severity was assessed using APACHE II score, 24-h fluid intake and balance, initial admission creatinine, total body surface area (%TBSA) burned, presence of altered mental status (AMS) on first evaluation determined by a Glasgow Coma Scale (GCS) of $\leq$14, need for intubation prehospital or prior to admission to the intensive care unit (ICU), and initial carboxyhemoglobin (COHb), lactate, and arterial pH values. The grade of inhalation injury determined by bronchoscopy was evaluated and then categorized into two groups: low grade (1–2) and high grade (3–4) [11]. For the bronchoscopy reports with no explicit mention of grade, a bronchoscopy grade was designated based on the description of the report using the Abbreviated Injury Score [12]. The cause of burn or inhalation injury (house fire, explosion, motor vehicle collision (MVC), or self-inflicted), and presence and location of soot (nares, oropharynx, or both) were also reviewed. The primary endpoint studied was mortality. Secondary endpoints evaluated included culture-proven pneumonia (PNA) which was also cross-referenced with daily notes for accuracy, 7-day change in creatinine, hospital length of stay (HLOS), intensive care length of stay (ICU LOS), number of ventilation days, and ventilator-free days (VFD) in order to control for the effect of mortality on ventilation days. VFDs were defined as follows [13]:

VFDs = 0: If the patient dies before 28 days.
VFDs = (28 − x): If the patient is extubated within 28 days, where x is the number of days receiving mechanical ventilation.
VFDs = 0: If the patient receives mechanical ventilation for 28 days or more.

2.3. Statistics

All analyses were performed using IBM SPSS Statistics 23.0 software (IBM Corporation, Armonk, New York, USA). Categorical variables were analyzed using Pearson chi-squared or Fisher exact test. Non-parametric statistic using the Mann–Whitney *U* test was performed to determine statistical significance for continuous variables. Multivariate logistic regression models were used to control for possible confounding variables. The probability of type 1 error of less than 5% ($p < 0.05$) was used to determine statistical significance. If data was missing from any variables, these patients were included in the analysis without replacing the missing data points.

3. Results

3.1. Patient demographics

A total of 294 patient charts were reviewed over a 13-year period. After exclusion, 277 patients met the study criteria; 138 patients were treated with hydroxocobalamin (2008–2014), and 135 patients were in the control group (2002–2008) (Fig. 1).