Clinica Chimica Acta 421 (2013) 226–229

Contents lists available at SciVerse ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

Carboxy-terminal provasopressin may predict prognosis in nursing home acquired pneumonia

Sang-Hwan Kim [a], Jae-Ho Chung [b], Jong-Chan Lee [c], Yo-Han Park [c], Jun-Hyeon Joe [c], Hee-Jin Hwang [a,*]

[a] Kwandong University College of Medicine, 579 bungil 24 Bumil-load, Gangneung-si, Gangwon-do 210-701, Republic of Korea
[b] Department of Internal Medicine, Kwandong University College of Medicine, Gangneung, Gangwon-do, Republic of Korea
[c] Department of Internal Medicine, Incheon Sarang Hospital, Incheon, Republic of Korea

ARTICLE INFO

Article history:
Received 2 January 2013
Received in revised form 21 February 2013
Accepted 21 February 2013
Available online 27 February 2013

Keywords:
Aged
Nursing home acquired pneumonia
Procalcitonin
Copeptin
Pro-atrial natriuretic peptide
Mortality

ABSTRACT

Background: This study compares biomarker (including procalcitonin, pro-ANP, and copeptin) levels to pneumonia severity scores to predict 30-day mortality in NHAP (nursing home acquired pneumonia) patients.
Methods: Seventy three patients aged ≥ 65 y, admitted to general hospitals and who fulfilled the definition of NHAP were included in the study. Data collected at admission included age, gender, nursing home admission, coexisting illness, symptoms and clinical parameters (blood pressure, pulse rate, respiratory rate and status). Additional data collected included laboratory results, radiographic findings and outcome variables. Severity of pneumonia was evaluated using a prediction rule calculated by CURB-65 criteria (confusion, urea nitrogen, respiratory rate, blood pressure, age >65 y).
Results: After adjustment for age, sex and CURB-65, copeptin (OR = 5.60, 95% confidence interval (CI) = 1.20–26.24) was associated with 30-day mortality in NHAP patients, while procalcitonin and pro-ANP were not. The areas under the receiver operating characteristic curves (AUCs) for CURB-65, in predicting mortality were 0.685 [95% CI 0.559–0.811], whereas copeptin showed slightly superior accuracy with an AUC of 0.698 (95% CI 0.568–0.827).
Conclusions: Among 3 biomakers, copeptin was the strongest predictor of 30-day mortality from NHAP. The pathophysiologic and clinical implications of this finding require further investigation.

1. Introduction

Nursing home acquired pneumonia (NHAP) is a common terminal event for residents of long-term care (LTC) facilities and the most common reason for hospital transfer [1]. Pneumonia is a leading cause of mortality in nursing home residents [2]. The incidence of pneumonia in LTC facilities is 10 times higher than in the community [3]. Compared with community-dwelling individuals, residents of LTC facilities have extensive illnesses, more functional disabilities and are at high risk of acquiring drug-resistant pathogens [4]. The use of biomarkers to assess diagnosis, prognosis, and treatment response in pneumonia is a research area of growing interest [5–7]. Infection markers like procalcitonin and C-reactive protein (CRP), neurohumoral hemodynamic markers such as pro-atrial natriuretic peptide (pro-ANP) and copeptin have been of particular interest [8–11].

Assessing the severity of NHAP can be clinically challenging [12]. Prognostic scoring systems for community-acquired pneumonia (CAP) have recently been developed to assess risk of mortality, but these methods are flawed [13]. Furthermore, prognostic scoring systems for NHAP are scarce. In the present study, biomarker levels (including procalcitonin, pro-ANP, and copeptin) are compared to pneumonia severity scores to predict 30-day mortality in NHAP patients.

2. Materials and methods

2.1. Patients

The study sample included LTC residents from the Korean Nursing Home Networks admitted to hospitals for pneumonia treatment between January 2011 and March 2012. This network was established in July 2008 to construct a health care system for nursing home residents and is composed of 35 nursing homes and one general hospital in Incheon Metropolitan City and 30 nursing homes and one general hospital in Gyeonggi Province. The present study was part of the LOVE (Long-term care of Old people Via the KorEan nursing home network) study, intended to gauge the value of the network in early detection, management and prevention of geriatric diseases among nursing home residents. Over the study period, all consecutive pneumonia patients admitted to the hospital through their nursing home were eligible. The diagnosis of pneumonia was defined according to the criteria of McGeer et al. [14] for the identification of pneumonia at an LTC facility.

All patients of ≥65 y admitted to general hospitals meeting the criteria for NHAP were included. Patients with pneumonia that developed

* Corresponding author. Tel.: +82 33 649 7441; fax: +82 33 641 1074.
E-mail address: ydsfm3624@naver.com (H.-J. Hwang).

0009-8981/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.cca.2013.02.022

Table 1
Baseline characteristics of NHAP patients.

Variables	Survivor (N = 50)	Non-survivor (N = 23)	P-value
Age (y)	79.3 ± 9.5	80.9 ± 8.0	NS
Sex (male), N (%)	23 (46.0)	11 (47.8)	NS
Comorbidity			
Cancer	2 (4.0)	2 (8.7)	NS
Cerebrovascular disease	28 (56.0)	11 (47.8)	NS
Congestive heart failure	5 (10.0)	2 (8.7)	NS
Chronic renal failure	3 (6.0)	3 (13.0)	NS
Chronic lung disease	1 (2.0)	0 (0.0)	NS
White blood cell[a]	12.3 ± 6.9	12.7 ± 9.0	NS
C-reactive protein[a]	12.5 ± 8.9	18.0 ± 13.3	NS
CURB-65[a]	2.4 ± 1.0	3.1 ± 0.9	0.007
Confusion, N (%)	26 (52.0)	12 (52.2)	NS
Blood urea nitrogen > 19 mg/dl, N (%)	30 (60.0)	19 (82.6)	NS
Respiratory rate ≥ 25/min, N (%)	6 (12.0)	6 (26.1)	NS
SBP < 90 or DBP ≤ 60 mm Hg, N (%)	10 (20.0)	13 (56.5)	0.002
Clinical outcomes			
Hospital length of stay (days)	13.0 ± 8.4	9.6 ± 7.0	NS
ICU (intensive care unit) admission	8 (16.0)	9 (39.1)	0.030
Vasopressor	7 (14.0)	13 (56.5)	<0.001
Ventilator	3 (6.0)	6 (26.1)	0.015
DNR (do not resuscitate)	5 (10.0)	19 (82.6)	<0.001

P-values were obtained by *t*-test or χ^2 test.
Values are mean ± SD or N (%).
SBP: systolic blood pressure; DBP: diastolic blood pressure; CURB-65: confusion, urea, respiratory rate, blood pressure, and age ≥ 65 y score.
[a] Values have been analyzed after log-transformation.

after being hospitalized for > 48 h, or within 14 days of leaving the hospital, were not included. Of 80 consecutive patients admitted with a provisional diagnosis of NHAP, 73 patients (91%) were included in the study. Seven patients were excluded either due to exclusion criteria or because of a non-NHAP diagnosis. The Institutional Review Board of Myongji Hospital approved this study and waived informed consent.

2.2. Measurements

Data collected at hospital admission included age, gender, nursing home admission, coexisting illness, symptoms and clinical parameters. A patient's mental status was assessed by the attending physician and mental confusion was defined by the Glasgow coma scale (GCS) score < 15 or by a new onset of disorientation to time, place or person. Additional data collected immediately after admission included laboratory results (complete blood count, CRP and urea), radiographic findings and outcome variables (requirement for ICU admission, intensive respiratory or vasopressor support (IRVS), length-of-stay (LOS) in hospital and all-cause 30-day mortality). Sputum and blood cultures were obtained on these patients. Severity of pneumonia was evaluated by the prediction rule calculated by the CURB-65 criteria (confusion, urea nitrogen, respiratory rate, blood pressure, age > 65 y) [15].

Blood samples for routine blood analysis and measurement of biological markers were collected within 24 h of subjects fulfilling the pneumonia criteria. WBC counts were quantified by an automated blood cell counter (ADVIA 120, Siemens, NY), and high-sensitivity C-reactive protein (hs-CRP) levels were measured using an ADVIA 1650 chemistry system (Siemens) To measure procalcitonin, pro-ANP and copeptin, serum was separated from blood samples when blood was drawn and frozen at −80 °C until analysis. Measurements of procalcitonin, pro-ANP, and copeptin were performed blinded in one central laboratory without knowledge of clinical parameters. Procalcitonin levels were measured by enzyme-linked immunosorbent assay (Biovender, Modrice, Czech Republic). The intra- and inter-assay coefficients of variation for procalcitonin were 3.6 ± 2.5% and 5.6%. Pro-ANP and copeptin levels were measured by enzyme-linked immunosorbent assay (USCNK, Wuhan, China). The intra- and inter-assay CVs for pro-ANP and copeptin were <10% and <12%.

2.3. Statistical analyses

All data were analyzed using a statistical software package (SPSS for Windows, ver 18.0; SPSS, Chicago, IL). Data are described as the mean ± SD in the case of normal distributions and as median and interquartile ranges in the case of non-normal distributions.

Variables such as WBC count, hs-CRP, procalcitonin and pro-ANP were logarithmically transformed to approximate a normal distribution. The NHAP patients' clinical characteristics by mortality status were compared using *t*-tests for continuous variables and χ^2 tests for categorical variables. Biomarker comparisons between groups by clinical outcomes used *t*-tests. The relative contributions to mortality of the hemodynamic biomarkers hs-CRP, procalcitonin, pro-ANP and CURB-65 were estimated using a multiple logistic regression model. Odds ratios (ORs) and 95% confidence intervals for 30-day mortality in NHAP were calculated after adjustment for possible confounders. The overall accuracy in predicting 30-day mortality was calculated as an area under the receiver operating characteristic curve (AUC). Null hypotheses of no difference were rejected for a $P < 0.05$.

3. Results

Table 1 shows the clinical characteristics of the 73 NHAP patients. There were no differences in age, sex and comorbidities between survivors and non-survivors. The CURB-65 score was lower in survivors than non-survivors (2.4 ± 1.0 vs. 3.1 ± 0.9, P = 0.007). Among the components of CURB-65, the prevalence of decreased blood pressure was higher in non-survivors (P = 0.002). The rates of ICU admission, received vasopressor or intensive respiratory support and DNR were higher in non-survivors. Results of sputum and blood cultures were not statistically different between survivors and non-survivors (data not shown).

Mean copeptin levels were significantly higher in subjects who died within 30 days than those who did not (460.4 ± 144.7 vs. 351.1 ± 160.0 pg/ml, P = 0.007), but the mean procalcitonin and pro-ANP levels did not differ by group. The procalcitonin and copeptin levels were higher in subjects admitted to the IRVS or ICU than those who were not (Table 2).

Multiple regression was used to analyze the associations between biomarkers and 30-day mortality. After adjustment for age, sex and CURB-

Table 2
Biomarker levels in NHAP patients with or without clinical outcomes.

Biomarkers	30-Day mortality			IRVS			ICU admission		
	No (N = 50)	Yes (N = 23)	P-value	No (N = 53)	Yes (N = 20)	P-value	No (N = 56)	Yes (N = 17)	P-value
Procalcitonin (pg/ml)	1985.6 ± 2618.1	3067.0 ± 2933.9	NS	1723.9 ± 2329.6	3925.0 ± 3172.0	0.009	1921.4 ± 2521.5	3663.0 ± 3107.2	0.020
Pro-ANP (ng/ml)	7.2 ± 6.5	9.2 ± 6.3	NS	7.2 ± 6.1	9.5 ± 7.3	NS	7.1 ± 6.0	10.5 ± 7.5	NS
Copeptin (pg/ml)	351.1 ± 160.0	460.4 ± 144.7	0.007	361.9 ± 161.7	448.2 ± 151.2	0.042	364.7 ± 156.9	454.1 ± 166.6	0.046

P-value by Mann–Whitney test. Values have been analyzed after log-transformation.
Pro-ANP: proatrial natriuretic peptide; IRVS: intensive respiratory or vasopressor support; ICU: intensive care unit.