Predictors of bacteraemia in emergency department patients with pneumonia

急診肺炎患者菌血症預測因子

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Objective: To determine the proportion of patients investigated in an Australian emergency department (ED) for non-hospital-acquired pneumonia with bacteraemia and to identify risk factors for bacteraemia. ***Method:*** Retrospective cohort study of patients with an ED diagnosis of non-hospital-acquired pneumonia in whom blood cultures were taken. Data collected included demographics, history of chronic obstructive pulmonary disease (COPD), immunosuppression, intravenous (IV) drug use or diabetes, prior antibiotic use, clinical features, biochemistry, haematology and blood culture results, ED disposition and pneumonia severity index (PSI) class. Outcomes of interest were the proportion of blood cultures that identified bacteraemia and identification of independent predictors of bacteraemia. Data analysis was by descriptive statistics, odds ratios (OR) and multivariate analysis. ***Results:*** Two hundred patients were studied. The bacteraemia rate was 7% (95% CI=4-11%). IV drug use (OR 16.7, 95% CI=2.65-105) and pulse rate (OR 1.29, 95% CI=1.01-1.65, per 10 beat rise) were independently associated with bacteraemia. Overall, 1/199 patients had a significant broadening of therapy based on a blood culture result (0.5%, 95% CI=0.09-2.8%). On post hoc analysis, using PSI class IV/V or known IV drug use as criteria for blood culture ordering had sensitivity 92.9% (95% CI=64.1-99.6%) and negative predictive value 98.9% (95% CI=93.5-99.9%) for bacteraemia. ***Conclusion:*** 7% of blood cultures from patients with non-hospital acquired pneumonia showed bacteraemia. Using the combination of PSI class IV/V or IV drug use as criteria for blood culture ordering shows promise. (Hong Kong j.emerg.med. 2012;19:xx-xx)

目的：確定澳大利亞急診科（ED）的非醫院獲得性肺炎患者的菌血症比例，並調查菌血症的風險因素。**方法：**回顧性世代研究，對象為ED診斷為非醫院獲得性肺炎並且有血培養的患者。收集的數據包括：人口統計資料，慢性阻塞性肺病（COPD）的歷史，免疫抑制，靜脈（IV）注射毒品，糖尿病，已經服用抗生素，臨床特徵，生化，血液和血培養結果，ED處置和肺炎嚴重指數（PSI）的分類。研究結果是血培養的菌血症比例和預測菌血症的獨立預測因子。以描述性統計，比值比（OR）和多變量分析作數據分析。**結果：**進行了200例患者研究。菌血症率為7%（95%CI=4-11%）。與菌血症相關的獨立因子有：IV藥物的使用(OR 16.7，95%CI=2.65-105）和心率（OR1.29，95%CI=1.01-1.65，每上升10次）。總體而言，1/199例患者的治療，根據血培養結果（0.5%，95%CI=0.09-2.8%）而需要擴闊。事後分析，使用PSI的第IV/V級或靜脈注射毒品作為使用血培養的標準，菌血症診斷的靈敏度為92.9%

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（95%CI=64.1-99.6%）和陰性預測值98.9%（95%CI=93.5-99.9%）。**結論：**7%非醫院獲得性肺炎患者的血培養結果顯示菌血症。使用PSI的第IV / V級或靜脈注射毒品作為使用血培養的標準，可能是有幫助的。

Keywords: Adult, bacterial pneumonia, bacteriology, diagnosis, therapeutics

關鍵詞：成人、細菌性肺炎、細菌學、診斷、治療

Introduction

Some guidelines currently promote the taking of blood cultures in patients admitted to hospital with non-hospital acquired pneumonia in order to identify pathogens and guide therapy.[1,2] Previous studies have reported that the proportion of patients with identified bacteraemia as between 2.1 and 9%.[3-10]

In the face of concerns regarding the cost effectiveness of blood cultures, some studies have attempted to identify risk factors for bacteraemia in order to guide clinicians in rational utilisation of this test. Risk factors identified have included pneumonia severity index class IV and V,[3] current smoker,[3,11] Malay ethnicity,[3] oxygen saturation <90%,[5] serum sodium concentration <130 mmol/L,[5,9] respiratory rate >30,[5,9] existing liver disease,[9,11] systolic blood pressure <90 mmHg,[9] temperature <35 or ≥40 degrees Celcius,[9] pulse rate >125,[9] blood urea nitrogen ≥30 mg/dL,[9] white cell count (WCC) <5 or >20x10^9/L,[9] alcohol use,[11] intravenous (IV) drug use[11] and HIV.[11] These risk factors have not been widely validated.

The aim of this study was to determine the proportion of patients investigated in emergency department (ED) for non-hospital acquired pneumonia in whom bacteraemia being identified and to identify risk factors for bacteraemia.

Methods

This was a retrospective cohort study conducted using explicit medical records review methodology. The study sites were two adult ED with combined annual census of adult patients of 85,000. Participants were a convenience sample of 200 patients with an ED discharge diagnosis of non-hospital acquired pneumonia treated at the ED between July 2008 and May 2009 and in whom at least one set of blood cultures was taken as part of their initial investigations. ED discharge diagnosis was made by the treating clinician with access to all the clinical and investigative data available at ED discharge. Treating clinicians were unaware of the study. Taking of blood cultures was at the discretion of treating clinicians, however it would be usual practice to collect blood cultures in patients being admitted to hospital for treatment of pneumonia or who exhibit a fever >38 degrees. Current hospital procedure has recommend the taking of two sets of blood cultures (each of one aerobic and one anaerobic culture) from different sites. This procedure was not always followed, with some patients having only a single set of cultures and others having multiple sets drawn from a single site (usually a newly sited intravenous cannula).

Patients were identified from an administrative database. Eligibility criteria included age over 18 years, having a blood culture taken within six hours of arrival in ED and availability of record for review. Data collectors were not blinded to the study's aims.

Data collected included demographics, past medical history of chronic obstructive pulmonary disease (COPD), immunosuppression, IV drug use or diabetes, antibiotic use prior to ED attendance, clinical features in ED, biochemistry, haematology and blood culture results and ED disposition. Vital sign values used were the first set recorded in the ED. Pneumonia severity index (PSI) was calculated retrospectively. Assignment of classification as 'bacteramia' (i.e. true positive culture) was performed by a researcher (MP) not blinded to the study hypothesis. Inter-rater reliability was tested on a subset of 10% of records.

The primary outcome of interest was the proportion of blood cultures that identified bacteraemia. Bacteraemia was defined as culture of a recognised pathogen from one

or more sets of blood cultures or of other organisms from two or more sets of blood culture set.[12] Secondary outcomes were identification of independent predictors of bacteraemia and the proportion of cases in which blood culture result changed the therapy.

Data analysis was by descriptive statistics, odds ratios and multivariate analysis using Analyze-It™ and Minitab™ version 16 software programs. The multivariate model was constructed using backward elimination (P<0.1) starting with all factors that were likely or significant predictors on univariate analysis (hyponatraemia, WCC <4 or >20, respiratory rate, history of IV drug use and pulse rate). The project was approved by the institutional human ethics review panel as a quality assurance study and specific patient consent was not required.

Results

Two hundred patients were studied. Characteristics of the sample are shown in Table 1. Bacteraemia was

Table 1. Characteristics of sample

Variable	Grouping	
Gender (male N, %)	–	118 (59%)
Age (median, IQR)	–	72 (60-81)
Residential care (N, %)	–	26 (13%)
Duration of symptoms (N, %)	>2 days	124 (52%)
	<2 days	75 (37.5%)
	Unknown	1
Temperature (N, %)	35-38.5 degrees C	59 (29.5%)
	<35 or >38.5 degrees C	141 (70.5%)
Past history (N, %)	Diabetes	56 (28%)
	COPD	59 (29.5%)
	Immunosuppression	4 (2%)
	Intravenous drug use	7 (3.5%)
	Antibiotics prior to emergency department	53 (26.5%)
PSI class (N, %)	I	16 (8%)
	II	47 (23.5%)
	III	39 (19.5%)
	IV	66 (33%)
	V	32 (16%)
Respiratory rate (median, IQR)	–	24 (20-29)
Pulse rate (median, IQR)	–	106 (93-124)
Oxygen saturation (N, %)	≥93%	115 (57.5%)
	<93%	79 (39.5%)
	Unknown	6 (3%)
GCS (N, %)	14-15	173 (86.5%)
	≤13	27 (13.5%)
Blood pressure <100 mmHg (N, %)	–	11 (5.5%)
Hyponatraemia (N, %)	Na <130 mmol/L	19 (9.5%)
Anaemia (N, %)	Hb ≤100	19 (9.5%)
Creatinine (median, IQR)	–	100 (80-120)
Renal dysfunction at presentation	Cr >120	44 (22%)
WCC (N, %)	<4	8 (4%)
	4-11	80 (40%)
	11-20	88 (44%)
	>20	22 (11%)
	Unknown	2 (1%)

COPD, chronic obstructive pulmonary disease; Cr, creatinine concentration; GCS, Glasgow Coma Score; Hb, haemoglobin concentration; IQR, interquartile range; Na, sodium concentration; PSI, pneumonia severity index; WCC, white cell count (x10^9/litre)

identified in 14 cases (14/200; 7%, 95% CI=4-11%): *streptococcus pneumonia* (7), *streptococcus pyogenes* (2), *staphylococcus aureus* (2), *candida albicans* (1), *escherishia coli* (1) and *corynebacterium jeikeium* (1). There were 8 false positive (contaminated) blood cultures (8/200; 4%, 95% CI=2-8%). With respect to the impact on therapy of a true positive blood culture result, 6 patients had no change in therapy, 6 had antibiotic treatment simplified, 1 had antibiotic treatment broadened and data for 1 was indeterminate. Overall, 1/199 patients had a significant broadening of therapy based on a blood culture result (0.5%, 95% CI=0.09-2.8%).

Univariate and multivariate analysis results are shown on Table 2. On univariate analysis IV drug use (OR 24; 95% CI=4.7-122.1), serum sodium concentration <130 mmol/L (OR=6.7; 95% CI=2.0-22.90), pulse >100 (OR=4.09; 95% CI=0.89-18.81) and respiratory rate >35 (OR=7.87; 95% CI=1.86-33.30) were statistically significant. Ten of the 14 true positive blood cultures were in patients in PSI class IV and V, however this did not reach statistical significance. On multivariate analysis, only IV drug use (OR=16.7; 95% CI=2.65-105, p=0.003) and pulse rate (OR=1.29, 95% CI=1.01-1.65, p=0.04, per 10 beat rise in pulse rate) remained significant.

On post hoc analysis, if we had used PSI class IV or V or known IV drug use as criteria for blood culture ordering, 13 of the 14 patients with bacteraemia would have been identified (sensitivity=92.9, 95% CI=64.2-99.6%; specificity 51.1%, 95% CI=43.7-58.4; negative predictive value=98.9%, 95% CI=93.5-99.9%). If those criteria were applied, blood cultures could have been omitted in 96 patients (48%, 95% CI=41.0-55.0).

Table 2. Univariate and multivariate analysis of factor associations with true positive blood culture

	Univariate analysis		Multivariate analysis	
Variable	**Odds ratio, 95% CI**	**p value**	**Odds ratio, 95% CI**	**p value**
Gender	0.92, 0.31-2.76	NS	–	–
History of COPD	0.38, 0.08-1.74	NS	–	–
History of diabetes	0.64, 0.18-2.52	NS	–	–
History of immunosuppression	1.67, 0.43-6.38	NS	–	–
Patient in residential care	0.92, 0.31-2.76	NS	–	–
History of intravenous drug use*	24, 4.7-122.1	<0.001	16.7, 2.65-105	0.003
Symptom duration >2 days	1.10, 0.35-2.4	NS	–	–
Pre-treatment with antibiotics	0.44, 0.1-2.04	NS	–	–
Hypotension (BP <100 mmHg)	3.19, 0.62-16.42	NS	–	–
Pulse rate# >100 bpm	4.09, 0.89-18.81	0.04	1.29 for every 10 beat rise; 1.01-1.65	0.043
Temperature <35 or >38.5 degrees C	0.74, 0.24-2.3	NS	–	–
Hypoxia	1.5, 0.5-4.5	NS	–	–
Respiratory rate >35*	7.87, 1.86-33.3	0.02	NS	-
GCS ≤13	0.47, 0.06-3.77	NS	–	–
Clear X-ray signs	1.88, 0.51-7.0	NS	–	–
Hyponatraemia* (>130 mmol/L)	6.7, 2.0-22.9	0.005	NS	–
Anaemia (Hb ≤100 g/L)	0.71, 0.09-5.7	NS	–	–
Renal impairment (Cr >120 micromol/L)	2.9, 0.9-8.8	NS	–	–
WCC <4 or >20 ($x10^9$/L)*	1.61, 0.36-7.17	NS	NS	–
PSI class IV	0.97, 0.1-9.3	NS	–	–
PSI class V	3.46, 0.38-13.57	NS	–	–

*included in multivariate model

BP, blood pressure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; Cr, creatinine concentration; GCS, Glasgow Coma Score; Hb, haemoglobin; NS, not significant; PSI, pneumonia severity index; WCC, white cell count

Inter-rater agreement of data collection was 100% for items age, gender, WCC, serum sodium concentration and ED disposition.

Discussion

This study found a similar low rate of bacteraemia to other studies.[3-10] This supports the argument that routine ordering of blood cultures in patients with non-hospital acquired pneumonia is not cost effective.

Although we found that several previously reported factors were associated with bacteraemia on univariate analysis, only pulse rate and IV drug use were independently associated on multivariate analysis. This is only the second study to report the association between bacteraemia and IV drug use in patients with a clinical diagnosis of pneumonia. In both, the association is very strong and would support a recommendation that blood cultures should be taken in this patient group, irrespective of disease severity. Unlike Cham et al,[3] we did not find that PSI class was an independent predictor of bacteraemia. This could be due to the small number of cases of bacteraemia in our sample. That said, Metersky et al[9] in a study of more than13,000 patients hospitalised with pneumonia also failed to find PSI class predictive of positive blood culture (OR of PSI class I-III vs. IV and V=0.9; 95% CI=0.7-1.1; p= 0.2). We did not have enough data to conclude whether measures of severity such as the PSI class could be associated with clinically relevant bacteraemia.

Our finding that the combination of PSI class IV or V and IV drug use had good sensitivity and excellent negative predictive value for bacteraemia (albeit with wide confidence intervals) is new. Data to calculate these is readily available and, on our estimates, could avoid of the order of 48% of blood cultures. This would be a significant cost saving in many busy hospitals. This result should be treated with some caution however as it was generated from post hoc analysis. Validation, preferably prospective, would be required.

This study has some limitations that should be considered when interpreting the results. Data was collected retrospectively. The sample was a convenience sample and some records were not available. These raise the possibility of bias, although it could be unlikely to be systematic. The data related to a single health service in Australia, so may not be generalisable to other countries. Clinician variation in the ordering and processes for acquiring blood cultures could have influenced the results. Data collection was limited to 200 cases due to staff resources for data collection; it was a trainee research project. This is unlikely to have significantly impact on the primary outcome which showed narrow confidence intervals.

Conclusion

In this sample, 7% of blood cultures from patients with non-hospital acquired pneumonia showed bacteraemia and 0.5% resulted in a broadening of therapy. IV drug use and pulse rate were the only factors independently associated with bacteraemia. The combination of PSI class IV and V or IV drug use to guide blood culture ordering shows promise.

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