Procalcitonin: Inflammatory Biomarker for Assessing the Severity of Community-Acquired Pneumonia – A Clinical Observation in Geriatric Patients

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Key Words

Community-acquired pneumonia • Pneumonia • CURB 65 • Procalcitonin

Abstract

Community-acquired pneumonia is a common disease of the elderly and involves a high mortality risk. Demographic developments are creating new challenges for acute medical treatment strategies in geriatric patients with their underlying multimorbidity. In addition to the diagnostic parameters recorded on hospital admission, such as white cell count and C-reactive protein, procalcitonin, more than the risk scores CRB- and CURB-65 evaluated to date, appears to be a promising parameter for assessing the severity of pneumonia in elderly patients to allow early detection of severe courses and initiation of suitable treatment. The decisive factor is the dynamic course of the procalcitonin values over 3 consecutive days, as demonstrated in this case series.

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Background

Community-acquired pneumonia occurs with a high annual incidence and is thus the commonest infectious disease with a total mortality of about 11% [7]. In the acute stage, about 10% of all outpatients and inpatients die, altogether more than 15% within the 6 months following diagnosis [15], with the mortality rate correlating with age and the presence of defined risk factors [8]. The need for hospital treatment is also age related. Inadequate treatment of pneumonia increases the mortality by up to 11-fold [12].

Basic statistical data show that over 70-year-old patients account for 66% of the total population. The 70- to 79-year-olds account for 26%, the 80- to 89-year-olds for 29% and the over 90-year-olds for 10% [16]. Based on the risk score CRB-65, about 82% of the patients were in risk classes 2 and 3. Hospital mortality in this population was 50% [16].

Current demographic trends clearly show that the proportion of very elderly patients in hospitals of all care categories is rising. These trends in aging are changing the nature of the challenges imposed on medical care and the management of geriatric patients in terms of multi-

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morbidity, impending disability and functional impairments, taking into account economic limitations and quality of life aspects. There is therefore a need to develop informative parameters and prognostic resources as a means of ensuring that this patient population receives the best possible treatment.

Procalcitonin as a measure for the assessment of inflammatory activity has an undisputed place in the diagnosis of sepsis [3] and respiratory tract infections [1]. Procalcitonin is also an established course control parameter for the assessment of the patient's clinical development [6, 13].

Objective

The underlying clinical principle is the use of procalcitonin assay for risk assessment in geriatric patients with community-acquired pneumonia. Various scores, such as CRB-65 or CURB-65, are already available as instruments for assessing the severity of pneumonia and for predicting mortality risk. However, these measures appear inadequate for estimating the risk of elderly and very elderly patients admitted to an acute geriatric unit because many geriatric patients already exhibit infection-unrelated deficits associated with their previous morbidities [14]. Procalcitonin as a marker of inflammation in community-acquired pneumonia should therefore not only provide evidence of bacterial infection but also reliably quantify the severity of the condition.

Method

The observation study was conducted on a 10-bed ICU for internal medicine, part of a maximum care hospital, charging all medical facilities, with the status of an academic teaching hospital affiliated to a university. It was a pilot surveillance study in which patients fulfilling the following inclusion criteria were enrolled: age over 70 years, admitted to the acute geriatric unit with community-acquired pneumonia, treatment in the intensive care unit or a general ward specialized in acute geriatric cases. Procalcitonin was assayed on admission and as a routine laboratory parameter on day 1. If the measured value was above $0.1 \mu\text{g/l}$ [1], the procalcitonin assay was repeated on days 2 and 3. Samples were collected as part of the routine blood sampling program. The measurement was performed with a PCT Immunoassay Kit (Brahms, Berlin, Germany) on a Kryptor® immunoassay system (Brahms). The CURB-65 score was recorded immediately after admission to hospital and the mortality risk was documented. The C(U)RB-65 risk score was determined on the basis of pneumonia-related disorientation, blood pressure (serum urea concentration), respiratory rate and patient age (tables 1, 2).

Table 1. CURB-65 criteria

C	Mental Confusion (confusion, disorientation)
U	Blood Urea $>7 \text{ mmol/l}$
R	Respiratory rate $>30/\text{min}$
B	Blood pressure BP diastolic $<60 \text{ mm Hg}$ or systolic $<90 \text{ mm Hg}$
65	Age >65 years

Table 2. CURB-65 management groups

CURB-65 score	Management groups	
	mortality risk	treatment
0 or 1	low (1.5%)	outpatient
2	moderate (9.2%)	inpatient supervision
3 or 4	high (22%)	inpatient/intensive care

The procalcitonin values determined were correlated with the recorded laboratory parameters C-reactive protein, white blood count and the CURB-65 point score. The initial values on admission and the results measured over the time course were compared and were considered in context with the severity of the disease and the mortality. The individual results of the two groups, patients who died and patients who survived, were considered separately and correlated.

Results

Patient Sample

Over the surveillance period, 68 procalcitonin values and the corresponding C-reactive protein and white cell count values were determined as routine laboratory parameters in 17 elderly patients. The mean age was 82 years (70–96 years). The male:female gender ratio was 7:10. Grouped into age clusters, 23.5% ($n = 4$) were 70–75 years, 47.1% ($n = 8$) were 76–85 years and 29.4% ($n = 5$) were over 85 years old. The patients' coexisting diagnoses were chronic renal insufficiency, chronic heart failure, chronic obstructive lung diseases, cerebrovascular diseases with and without cognitive deficits and diabetes mellitus.

Measurement Results

The mean CRB-65 index was 2.4 points and therefore predicted a mortality risk of 8.2%. The mean CURB-65 index was 3.3 points and therefore predicted a mortality risk of 22%. The mean procalcitonin value on admission was 3.0 ng/l . The white blood count showed a range of dispersion of $5.8\text{--}26.2/\text{nl}$, C-reactive protein a measure-

Fig. 1. White blood count on admission and value comparison between deceased and surviving patients.

Fig. 2. C-reactive protein and procalcitonin on admission.

ment range of 0.5–42 mg/dl. 58.8% (n = 10) of the patients had a pre-existing demential syndrome. 82.4% (n = 14) were suffering from pre-existing renal insufficiency with lowered estimated glomerular filtration rate (eGFR, calculated using the MDRD formula [9]) with less than 60 ml/min and elevated urea. 70.6% (n = 12) of the patients were discharged, 11.8% (n = 2) were transferred to a different department and 17.7% (n = 3) died in the hospital. The diagnosis of pneumonia was confirmed by the detection of a pulmonary infiltrate, all patients received antibiotic treatment in accordance with the guidelines, the first dose of antibiotic being administered on average within the first 5 h after admission to hospital. In 70.6% (n = 12) the initial antibiotic therapy was correct and did not have to be modified after receiving the results of the antibiotic sensitivity test.

Detection of Infectious Agents

Escherichia coli and *Klebsiella pneumoniae* were detected in 41.2% of the cases, *Streptococcus pneumoniae* in 17.7% and methicillin-resistant *Staphylococcus aureus* in 5.9% of cases. A microbiological test for infectious agents was done in all patients and in 64.7% (n = 11) a pathogen could be identified.

CURB-65 on Admission and Clinical Outcome

An evaluation of the recorded CURB-65 risk scores based on assignment to the groups dead patients and surviving patients revealed no definite correlations between the documented point scores and the further clinical course.

White Cell Count on Admission and Clinical Outcome
An evaluation of the white blood count on admission in the study groups also failed to reveal a homogeneous pattern in terms of risk estimation of the further clinical course. Both the deceased patients and the survivors showed elevated white blood counts, so that a reliable prediction about sequel is not feasible (fig. 1).

C-Reactive Protein and Procalcitonin on Admission

A comparison of the C-reactive protein and procalcitonin values measured on admission also did not allow an assessment or prognosis of the severity and the further clinical course. Considered overall, both initially recorded parameters were sensitive for the detection of inflammation (fig. 2).

C-Reactive Protein, White Blood Count and Procalcitonin over the Time Course

A comparative analysis of the measured laboratory data in relation to the time course and the absolute change in the results shows a completely different picture. In contrast to the analysis of the initial individual values, a consideration of the dynamic development (difference amounts, day 0 enrollment – day 1) allows a risk identification for the further clinical course based on the measured procalcitonin values. Although C-reactive protein and white blood count still do not exhibit a homogeneous pattern capable of interpretation, the trend for procalcitonin is clearly apparent. The steepest rise in the values measured for procalcitonin was found in the group of patients who died. The group of patients

Fig. 3. C-reactive protein, white blood count and procalcitonin over time (* patient 15: additionally severe soft tissue infection). Dynamic course value day 0 (admission) – value days 2/3 = value Δ PCT/CRP/WBC plotted on the ordinate. Left side of the bar, patients who died; right side of the bar, survivors.

who survived did not show this dynamic change process (fig. 3).

The only patient from the group of survivors who showed an appreciable rise in procalcitonin suffered from severe, superinfected cellulites, so that the values measured for procalcitonin were also caused by additional infection.

Discussion

In daily clinical practice it is important to select a chemistry parameter which is dependably informative, readily available and sufficiently sensitive to reliably measure the desired outcome variable. The cut-off for procalcitonin was chosen as the low level of 0.1 $\mu\text{g/l}$ [1] because pneumonia is a directly organ-related disease and the initial induction of procalcitonin is therefore usually low [11]. The results obtained in this observation study show that procalcitonin is a sensitive biomarker for the detection of inflammation. Since antimicrobial therapy should be instituted as soon as possible and a delay in starting therapy is associated with increased mortality [4], procalcitonin is a very effective parameter for early detection of bacterial infection [5] and for instituting the decisive initial and calculated antibiotic therapy. The clinical parameters in CURB-65 have been described as independent

predictors for a fatal outcome for inpatients with community-acquired pneumonia [15], and patients who do not exhibit a risk in any of these clinical parameters have a low mortality risk (approximately 1%) [10]. A direct comparison of the CURB-65 results on admission between the two groups – patients who died and patients who survived – reveals no definite assignment to the further clinical course. A consideration of all studied patients reveals no uniform pattern based on the CURB-65 results. No prognosis for the survival of the studied patients can be derived from the static result of CURB-65. It is already clearly apparent, however, that the evidential value of the conventional measurement and scoring methods is limited in geriatric patients. Confusion as a measurement criterion is a parameter to be considered just as critically as the serum urea concentration, since it is almost routinely increased in this patient population and mostly, the findings are not defined as appearing new.

A direct comparison of the white cell count on admission between the two groups of patients reveals no correlation. Although this inflammatory parameter is initially elevated in the patients who died during the further course, the group of survivors shows no homogeneous pattern of absolute white blood counts during the further course of the disease. No predictive statement can therefore be derived from this result. A comparison of procalcitonin with C-reactive protein on admission shows that both parameters detect the bacterial infection of community-acquired pneumonia and that procalcitonin reacts more sensitively. In this case too, however, a statement regarding the further clinical course is not possible on the basis of the initially measured laboratory values. The evaluation of the change in the measured values over time, however, presents a completely different picture. Procalcitonin shows much more sensitive kinetic behavior than C-reactive protein or white cell count. The dynamic development with the rise in procalcitonin values during the further course allows conclusions on the severity of the community-acquired pneumonia. A comparison of the values measured on days 2 and 3 shows a steep rise to substantially increased procalcitonin values in the group of severely ill patients and patients who died. In this case, however, white cell count and C-reactive protein showed no definite time-related increase over the 3 days. For a reliable estimation of the further course of the disease is of great importance for the therapy to be initiated in these aged patients and since the decision has a significant influence on convalescence and mean hospital stay with all its economic risks in the event of complications, an informative parameter must be determined

for evaluation purposes. The clear dynamics seen in the increase in procalcitonin was apparent in the group of patients who died. Since this development was not observed in the group of survivors of the CURB-65, repeated determination of procalcitonin in the first 3 days of the acute illness is probably suitable for discriminating severe courses of community-acquired pneumonia in geriatric patients at an early stage and for initiating suitable therapeutic interventions.

Conclusions

Procalcitonin assay may be a promising parameter for detecting infection and estimating the severity of the further clinical course based on the development of the absolute values over time in geriatric patients admitted to hospital with community-acquired pneumonia. In multimorbid geriatric patients, procalcitonin assay is an easy-to-record and sensitive prognostic criterion and offers the advantage that the treatment can be tailored to suit the individual patient's condition and the severity of

the pneumonia. A dynamic analysis of the procalcitonin values shows that the course of the increase in the measured values is capable of assessment in the seriously ill patients. While the existing scores certainly continue to be important for outpatient medicine [2], in daily clinical practice in an acute geriatric unit, however, they are of only limited utility. Since no conclusive statement can yet be made because of the small number of cases analyzed in this case series, continued clinical observation in a follow-up study will be of major importance to assure appropriate allocation of available resources in the patients' interest and to secure maximum success of treatment while remaining within economic constraints.

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