Original articles

Impact of management guidelines on the outcome of severe community acquired pneumonia

N A Hirani, J T Macfarlane

Abstract

***Background* – Ten years ago we published a study of 50 adults with severe community acquired pneumonia admitted to our intensive care unit and subsequently introduced guidelines for the management of severe community acquired pneumonia which are largely in accordance with those of the British Thoracic Society. The results of a follow up study are now reported in order to assess their impact on the outcome of this disease.**

***Methods* – Fifty seven cases of severe community acquired pneumonia admitted to our ICU between 1984 and 1993 were studied. Causal pathogens, clinical and laboratory features of severity, antibiotic therapy and mortality were studied and, where possible, compared with results from the previous study.**

***Results* – *Streptococcus pneumoniae*, *Legionella pneumophila* and *Staphylococcus aureus* were the most frequent causes of severe community acquired pneumonia, as in the previous study. The intensity of microbial investigation has increased, particularly with regard to pneumococcal and *Legionella* antigen testing, the latter allowing earlier diagnosis of *Legionella* infection than previously. In spite of this, no pathogen was identified in 33% of cases compared with 18% previously. Indices of severity of illness were widely recognised, and a decrease in unplanned transfers to the ICU following "unexpected" cardiorespiratory arrest from 25% to 7% ($p<0.02$) was found. Antibiotic therapy largely reflected guideline recommendations with 98% receiving a beta-lactam agent and 91% erythromycin. The overall mortality was 58% compared with 54% previously.**

***Conclusions* – Management guidelines for severe community acquired pneumonia have been widely adopted but without a reduction in mortality in our hospital. Factors other than early diagnosis, appropriate antibiotics, or prompt ICU transfer may influence the outcome in severe community acquired pneumonia.**

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Keywords: severe community acquired pneumonia, guidelines, mortality.

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Community acquired pneumonia is a frequent cause of hospital admission with approximately 50 000 cases presenting per year in the UK.[1] Of these, most are treated on the medical ward without complication, but a few require transfer to the intensive care unit (ICU).

Ten years ago we reported that severe community acquired pneumonia accounted for 10% of all ICU medical admissions in our 1400 bed teaching hospital and that the mortality in these patients was high (54%).[2] *Streptococcus pneumoniae*, *Legionella pneumophila*, and *Staphylococcus aureus* were the principal pathogens identified. Certain clinical and laboratory features associated with severe pneumonia were identified and we noted that a quarter of patients eventually requiring ventilation were only transferred following an unexpected cardiorespiratory arrest on the medical ward. In reporting this study we recommended and instituted locally guidelines for the management of severe community acquired pneumonia and have continued to publicise these through a series of hospital newsletters, presentations, and ward notices. These emphasised the importance of full investigations, assessment of poor prognostic indicators, administration of appropriate empirical antibiotics, and consideration of early ICU transfer (fig 1). Our findings and guidelines are very similar to those recently published by the British Thoracic Society (BTS)[3] following a national study of severe community acquired pneumonia.[4] We now report a follow up study to assess the impact of local and, indirectly, national guidelines on the outcome of severe community acquired pneumonia.

Methods

All patients with a diagnosis of severe community acquired pneumonia admitted to the ICU of Nottingham City Hospital between January 1984 and December 1993, excluding 1986 for which no data are available, were identified. Complete documentation was available for 57 of these 58 patients. Patients known to be immunocompromised through underlying disease or immunosuppressive drugs other than low dose oral steroids were excluded.

Normal practice included the collecting of blood, respiratory secretions, and urine for investigation. Serum was examined for com-

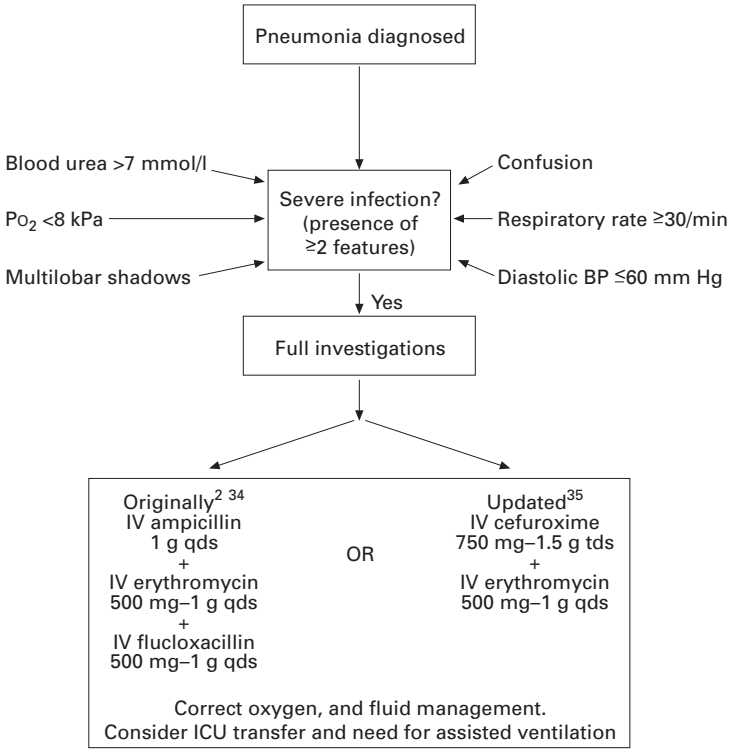

Figure 1 Our recommendations for initial management of patients with severe community acquired pneumonia of unknown cause.

Table 1 Causes of severe community acquired pneumonia in Nottingham

	1972–1981 (n=50)		*1984–1993 (n=57)*	
Pathogen	*Cases*	*Deaths*	*Cases*	*Deaths*
Streptococcus pneumoniae	16(32%)	12(75%)	10(18%) [56(19–82)]*	4(40%)
Legionella pneumophila	15(30%)	5(33%)	9(16%) [46(22–64)]	5(56%)
Staphylococcus aureus	5(10%)	5**(100%)	7***(12%) [68(48–80)]	5(72%)
Chlamydia psittaci	0	0	3	3
Pneumocystis carinii	Not done	Not done	3	2
Mycoplasma pneumoniae	1	0	0	0
Influenza A	0	0	3	2
Varicella zoster	2	0	0	0
Respiratory syncytial virus	0	0	1	0
Mycobacterium tuberculosis	1	0	1	1
Pseudomonas aeruginosa	0	0	1	1
Listeria monocytogenes	1	0	0	0
Streptococcus milleri	0	0	1	1
Unknown	9(18%)	5(56%)	19(33%)	8(42%)
Total	50	27(54%)	57	33(58%)

* Age profile (years) for 1984–1993 data shown in square brackets as median (range).
** Two cases associated with coexisting influenza A infection.
*** Including four cases associated with influenza virus (two influenza A and two influenza B) of which three died.

plement fixing antibodies to the common viral and atypical pathogens, and by indirect immunofluorescence for antibodies to *Legionella pneumophila*. Paired samples were tested 10–14 days apart where possible. A fourfold or greater rise in titre to 1:128 was considered evidence of infection, as was a single titre of at least 1:512 for viral or atypical antibodies and at least 1:256 for *Legionella* antibodies.

A significant number of blood, sputum, bronchopulmonary, and urine specimens were tested for pneumococcal polysaccharide capsular antigen (PCA) by countercurrent immunoelectrophoresis (CIE),[5] and *Legionella* antigen by direct immunofluorescent staining or enzyme linked immunosorbent assay (ELISA).[6] These tests, together with those for *Pneumocystis carinii*, were not available as routine in our previous study. In addition, necropsy consolidated lung tissue (formalin fixed paraffin sections) was examined by CIE for PCA and indirect immunofluorescent antibody testing (IFAT)[7] and immunoferritin electron microscopy (IFEM)[8] for *Legionella* species antigen. A positive test for either pathogen in any specimen was considered evidence of infection.

The results were analysed and, where appropriate, comparisons were made with the findings of the previous 10 year study in which the inclusion and exclusion criteria were identical.

The statistical tests used were the Student's *t* test, χ^2 test after Yates' correction factor, or Fisher's exact test.

Results

Of the 57 patients studied (38 men) the mean age was 57 years (range 15–83) and 34 (62%) were aged over 60 years. A significant coexisting illness (principally chronic cardiac and respiratory conditions) was present in 21 cases (37%). In 28 cases antibiotics had been given prior to hospital admission. The patient profile in the original 10 year study was similar with 52 patients (66% men) of mean age 51 years (range 24–73), 44% with coexisting illness and 40% receiving antibiotics prior to admission to hospital. Only the proportion of patients aged over 60 years (14/52) was significantly different ($p<0.02$).

All patients underwent blood cultures and initial serological testing and 28 (50%) had further serological testing 7–14 days later. Bronchoscopies were performed on 24 patients (42%).

AETIOLOGY

Streptococcus pneumoniae, *Legionella pneumophila*, and *Staphylococcus aureus* were the most important pathogens over the period of the two studies (table 1). The number of cases in which a causal pathogen was identified fell from 82% to 67% during the last 10 years.

Pneumococcal pneumonia accounted for 10 cases (18%) of severe community acquired pneumonia in this study compared with 16 (32%) between 1972 and 1981. Investigations for pneumococcal infection were more intensive in this study. Blood cultures, performed on all patients, were positive in nine cases (six *S pneumoniae* and three *S aureus*). Pneumococcal PCA was tested for in 20 (42%) of the non-bacteraemic patients of which eight (40%) were positive. In our previous study 16 (31%) patients in total were tested with seven (44%) positive results.

Legionella pneumophila (all serogroup 1) was identified in nine cases (16%) in this study and in 15 cases (30%) previously. Investigations for *Legionella* species have been more intensive since the introduction of the guidelines and all 57 patients underwent serological testing yielding four positive results compared with 27 patients (50%) and eight positive results

Table 2 Presence of markers of severity in community acquired pneumonia

	Survivors (n=24)	*Deaths (n=33)*	*Total (n=57)*
Pre-existing illness	11(46)	10(32)	21(37)
Respiratory rate ≥30/min	12(50)	18(56)	30(53)
Diastolic BP ≤60 mmHg	2(8)	7(21)	9(16)
Acute confusion*	3(13)	6(21)	9(41)
Blood urea >7 mmol/l	13(54)	22(67)	35(61)
Arterial Po_2 <8 kPa	15(63)	23(70)	38(67)
WCC <4 or >20 × 10^9/l	3(13)	7(21)	10(18)
Serum Na <130 mmol/l	8(33)	6(18)	14(25)
Serum albumin <30 g/l	6(25)	11(33)	17(30)
Multilobar shadows	6(25)	10(30)	16(28)

Values in parentheses are percentages.
* Data only available on 11 patients.

previously. In addition, 34 samples (sputum, tracheal aspirate, bronchial lavage fluid, and urine) were tested for *Legionella* antigen by direct immunofluorescent staining or ELISA, yielding three positive results. These tests were not performed in the earlier study. As a result, legionnaires' disease tended to be diagnosed earlier with seven of the nine cases being diagnosed before death. All nine cases received rifampicin and four of the seven diagnosed early and given erythromycin and rifampicin within 48 hours of ICU admission survived. In the previous study only four of the 15 cases were diagnosed before death. There is a clear seasonal variation in the incidence of legionnaires' disease. Over the period of both studies it accounted for 44% of the cases of severe community acquired pneumonia between June and September compared with 18% between October and May. Of the nine cases in this study, six (67%) had recently returned from abroad. This information was recorded in 30 of the 48 non-*Legionella* cases of which three (10%) had recently travelled abroad ($p<0.002$).

Staphylococcus aureus pneumonia often occurs in association with influenza infection as noted in six of the 12 patients over the period of both studies, five of whom died. Again there is a seasonal variation with eight of the 12 cases occurring between December and February. There were three cases of *Pneumocystis carinii* infection, all of which occurred after 1990. In each case the severe pneumonia was the presenting feature of previously undiagnosed HIV infection. *Pseudomonas aeruginosa*, cultured from tracheal aspirate, accounted for one case of severe community acquired pneumonia in a patient with chronic lung disease and recent hospital admissions. Gram negative enteric bacilli, usually *Enterobacteriae*, were isolated in seven cases from bronchopulmonary samples after at least five days on the ICU and were considered nosocomial in origin.

CLINICAL FEATURES AND MORTALITY

Table 2 displays features highlighted as indicators of severity in pneumonia in survivors and non-survivors. Documentation of the presence or absence of at least nine out of the 10 features was recorded in 94% of cases. Acute confusion was present in nine cases (17%) and, if not commented on, was assumed to be absent. No single clinical or laboratory parameter was significantly more common in either group. Overall, 27 patients (52%) fulfilled Rule 1 of the BTS criteria for severe infection at admission[3] – namely, the presence of two or more of respiratory rate ≥30 breaths per minute, diastolic blood pressure ≥60 mmHg, and blood urea >7 mmol/l. Of these, 20 (73%) died compared with 13 (43%) of those who did not fulfil Rule 1 ($p=0.04$).

Table 3 The impact of age on mortality in severe community acquired pneumonia

Age	*Number*	*Mortality*
16–39	9(16)	4(44)
40–59	14(25)	7(50)
60–69	21(37)	13(62)
70–79	9(16)	5(56)
≥80	4(7)	4(100)

Values in parentheses are percentages.

There was a trend towards a higher mortality in older patients (table 3), although there was no significant difference in mortality in patients above and below 60 years (65% versus 48%; $p=0.35$) or above and below 70 years (69% versus 55%; $p=0.32$). This compares with the results from the earlier study in which 93% of patients aged over 60 died but only 37% of those under 60 ($p<0.01$).

Hyponatraemia (serum sodium level of <130 mmol/l) was present in eight of the nine cases (89%) of legionnaires' disease and only two of the 10 cases (20%) with pneumococcal pneumonia ($p<0.05$). No other laboratory variables were significantly different in patients with these infections. Cavitation on the initial chest radiograph was present in only two patients (one *S aureus* and one pneumococcal pneumonia).

ANTIBIOTIC THERAPY

Most of the patients received a beta-lactam agent on admission; 39 (68%) received ampicillin and 17 (30%) cefuroxime or cefotaxime. Erythromycin was administered to 91% of patients on arrival at hospital and to all patients upon ICU admission. This is in accordance with our local guidelines. Only four patients received flucloxacillin on admission of whom only one had *S aureus* pneumonia. Of the remaining six cases of *S aureus* pneumonia four had received ampicillin and two cefuroxime.

Once in the ICU a median of 3.5 antibiotics were used per patient (range 1–7). In addition to a beta-lactam agent and erythromycin, 16 patients (28%) received rifampicin including all nine cases of legionnaires' disease, and 14 (25%) received flucloxacillin including all seven cases of *S aureus* pneumonia. Twelve patients (21%) received an aminoglycoside including the one case of *P aeruginosa* infection and the five cases of nosocomial Gram negative enteric bacilli infection.

Serious adverse effects attributed to an antibiotic and resulting in its discontinuation occurred in 12 cases (20%) – seven cases of grossly deranged liver function tests (three with flucloxacillin, two with rifampicin, and two with

both), two cases of aminoglycoside associated nephropathy, and one of flucloxacillin related rash.

TRANSFER TO ICU

Of the 57 patients transferred to the ICU 55 required assisted ventilation. Of these, 37 (65%) were transferred electively within 24 hours of admission. Four patients (7%) were only transferred following a cardiorespiratory arrest on the medical ward and six patients were transferred electively after more than 72 hours. In the latter group of 10 patients six fulfilled Rule 1 of the BTS guidelines for the recognition of high risk severe community acquired pneumonia at the time of their admission and subsequently died. The four remaining patients exhibited other markers of severity when admitted and there was one death.

From the time of admission to the ICU 58% of deaths occurred within one week and, of the 11 patients ventilated for 14 days or more, only three (27%) survived. The mean duration of ventilation for survivors and non-survivors was six days.

Discussion

Following our previous study we concluded that "attempts to reduce the mortality from community acquired pneumonia must include early recognition of severe infection, rapid identification of the pathogen involved and better management of the patient".[2] Management guidelines were introduced with regard to this on the perceived view that these will improve outcome[9] whilst acknowledging the scepticism concerning the effectiveness and motives behind guidelines.[10 11] The American Thoracic Society guidelines for the management of community acquired pneumonia have recently been re-evaluated.[12] In this study we have shown that our guidelines have largely been adopted but the mortality for severe community acquired pneumonia remains high and unaltered.

Early recognition of severe pneumonia depends upon identification and recording of poor prognostic markers. Our local guidelines highlighted these and they have been verified in several subsequent studies.[13–16] We have found that the admitting doctors were aware of and recorded these markers. There is a trend towards a higher mortality in older patients and increasing age is associated with worse prognosis, both as an independent risk factor and as a consequence of co-morbid disease.[17] We have noted a trend towards older patients being admitted to our ICU with severe community acquired pneumonia over the last 20 years. This action is supported by the finding that 40% of those aged 60–80 years survived whereas they would presumably have died without intensive care.

A causal pathogen was identified in 67% of cases compared with 82% in our previous study and these figures are comparable to five recent prospective studies of severe community acquired pneumonia in which an aetiological diagnosis was made in 52–81% of cases.[18–22] The reduction in diagnostic yield occurred despite adherence to our guidelines for more intensive investigation. Our guidelines advocated CIE testing for pneumococcal PCA in non-bacteraemic cases of severe community acquired pneumonia. The specificity of PCA in urine and serum is high, but the sensitivity estimates vary.[23] In this study, 40% of non-bacteraemic cases tested for PCA were positive, demonstrating a high diagnostic yield from this test. Of the 19 cases in which no causal pathogen was identified 10 were never tested for PCA. Direct immunofluorescent staining and ELISA for *Legionella* antigen has resulted in legionnaires' disease being diagnosed earlier in the illness, allowing for a more rapid and rational use of appropriate antibiotics. That half of our patients underwent bronchoscopy is probably an underestimate, the procedure not always being recorded in the notes. However, in only four cases did bronchial washings disclose an aetiological organism where earlier tests had proven fruitless. Three of these four were *Pneumocystis carinii* pneumonia, confirming the value of this technique in this condition. We did not perform distal protected aspiration or plugged telescoping catheter brushings, techniques reported to reward a higher yield.[18 21] Only one study has found that increasing the rate of aetiological diagnosis in severe community acquired pneumonia significantly reduces mortality, and even then the authors were doubtful that the relationship was causal.[18]

Our study confirms that *S pneumoniae*, *L pneumophila*, and *S aureus* account for the majority of cases of severe community acquired pneumonia although the local incidence of legionnaires' disease has fallen.[24] New pathogens are clearly likely to emerge in severe community acquired pneumonia. We diagnosed three cases of *P carinii* pneumonia in patients not known to be infected by HIV, confirming the need now to consider this diagnosis in cases of severe community acquired pneumonia. The low incidence of Gram negative enteric bacilli associated severe community acquired pneumonia is in keeping with previous studies in the UK.[3 13] In other centres, however, up to 25% of cases of severe community acquired pneumonia are reported to be due to Gram negative pathogens, particularly *Klebsiella* spp and *Enterobacteriae*,[15 19 21] probably representing differences in patient populations. In addition, there is evidence of significant false positive diagnoses of up to 30% in severely ill ventilated patients.[25 26]

Our guidelines stressed the importance of an appropriate empirical antibiotic combination at admission to cover all likely pathogens. Initially erythromycin with ampicillin was advocated, with flucloxacillin added in winter months during possible influenza epidemics. However, the latter agent was clearly underused with four of the seven patients with *S aureus* pneumonia not receiving an antistaphylococcal agent on admission. In the latter half of the study we substituted ampicillin for a second or third

generation cephalosporin which is also the recommendation of the BTS. As the mortality in staphylococcal pneumonia is high and clinical and radiological findings are non-diagnostic,[27–29] agents with antistaphylococcal activity should be included initially for all patients with severe community acquired pneumonia. The importance of appropriate antibiotic therapy extends to the period on the ICU where they may influence the incidence of nosocomial infection[30] and where drug side effects may confound an already complex illness.[31] A fifth of patients received aminoglycosides despite the infrequent isolation of Gram negative organisms in severe community acquired pneumonia.

We have improved the timing of patient transfer from the medical ward to the ICU. Only 7% of cases were transferred following a cardiorespiratory arrest compared with 25% in the first study ($p<0.02$), although most still exhibited poor prognostic markers that should have warranted earlier ICU admission. We detected a trend towards a higher mortality in patients with delayed transfer. It is felt that the outcome in critical illness is probably improved with early ICU transfer.[32] However, Hook *et al* suggest that the ICU has had little impact on the outcome of bacteraemic pneumococcal pneumonia, merely prolonging the time to death in those destined to die,[33] and a recent study of 127 cases of severe community acquired pneumonia found no significant difference in mortality in patients transferred before or after four days from admission.[22]

Our guidelines are largely in accordance with the national BTS recommendations, which therefore enabled us to assess indirectly the working value of these recommendations for managing severe community acquired pneumonia. We found them to be practical and widely adopted locally, but there has been no reduction in mortality. It is likely that there are factors other than early establishment of diagnosis, appropriate antimicrobial therapy, or even prompt ICU transfer that influence the progression of pneumonia to a potentially fatal illness. None the less, we believe that guidelines are influential in optimising management of such patients. Comprehensive microbial investigations are essential for establishing aetiology which will govern appropriate empirical antibiotic therapy in the future. In addition, early recognition of cases likely to require multisystem support allows for planned transfer to the ICU which, for some patients at least, is life saving.

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