Impact of bacteremia in a cohort of patients with pneumococcal pneumonia*

Impacto de la bacteriemia en una cohorte de pacientes con neumonía neumocócica

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Abstract

Objective: Bacteremia is the most common presentation of invasive disease in community-acquired pneumonia (CAP) due to *Streptococcus pneumoniae*. We investigated whether bacteremia in pneumococcal CAP worsens outcomes and whether it is related to pneumococcal vaccination (PV). **Methods:** Secondary analysis of a cohort of patients with pneumococcal CAP confirmed by blood culture, sputum culture, or urinary antigen testing. Demographic, clinical, radiographic, and biochemical data were collected, as were Acute Physiology and Chronic Health Evaluation II (APACHE II) and pneumonia severity index (PSI) scores, comorbidities, and PV history. We drew comparisons between patients with bacteremic pneumococcal CAP (BPP) and those with non-bacteremic pneumococcal CAP (NBPP). **Results:** Forty-seven patients had BPP, and 71 had NBPP (confirmed by sputum culture in 45 and by urinary antigen testing in 26); 107 had some indication for PV. None of the BPP patients had received PV, compared with 9 of the NBPP patients (p = 0.043). Among the BPP patients, the mean age was higher (76.4 ± 11.5 vs. 67.5 ± 20.9 years), as were APACHE II and PSI scores (16.4 ± 4.6 vs. 14.1 ± 6.5 and 129.5 ± 36 vs. 105.2 ± 45, respectively), as well as the rate of ICU admission for cardiopathy or chronic renal failure (42.5% vs. 22.5%), whereas hematocrit and plasma sodium levels were lower (35.7 ± 5.8 vs. 38.6 ± 6.7% and 133.9 ± 6.0 vs. 137.1 ± 5.5 mEq/L, respectively), although mortality was similar (29.8% vs 28.2%). **Conclusions:** In this population at high risk for CAP due to *S. pneumoniae*, the PV rate was extremely low (8.4%). Although BPP patients were more severely ill, mortality was similar between the two groups. Because PV reduces the incidence of BPP, the vaccination rate in at-risk populations should be increased.

Keywords: Pneumococcal vaccines; Pneumonia, bacterial; Streptococcus pneumoniae; Pneumococcal infections; Mortality; Epidemiology.

Resumen

Objetivo: Bacteriemia es la forma invasiva más común de neumonía adquirida en la comunidad (NAC) por *Streptococcus pneumoniae*. Investigamos si la bacteriemia en NAC neumocócica empeora los resultados y si ella guarda relación con la vacunación antineumocócica (VAN). **Métodos:** Análisis secundario de una cohorte de pacientes con NAC neumocócica confirmada por cultivo de sangre o esputo o antígeno urinario. Se registraron datos demográficos, clínicos, radiográficos y de laboratorio, escores *Higher Acute Physiology and Chronic Health Evaluation II* (APACHE II) y *pneumonia severity index* (PSI), comorbilidades y antecedente de VAN. Se compararon pacientes con NAC neumocócica bacteriémica (NNB) vs. no bacteriémica (NNNB). **Resultados:** Cuarenta y siete pacientes tenían NNB y 71 NNNB (45 por cultivo de esputo y 26 por antígeno urinario); 107 tenían alguna indicación de VAN. Ningún paciente con NNB, pero 9 con NNNB, habían recibido VAN (p = 0,043). Los pacientes con NNB eran mayores (76,4 ± 11,5 vs. 67,5 ± 20,9 años), tenían mayor APACHE II (16,4 ± 4,6 vs. 14,1 ± 6,5) y PSI (129,5 ± 36 vs. 105,2 ± 45), más frecuentemente cardiopatía e insuficiencia renal crónica e internación en UTI (42,5% vs. 22,5%) y menor hematocrito (35,7 ± 5,8 vs. 38,6 ± 6,7%) y sodio plasmático (133,9 ± 6,0 vs. 137,1 ± 5,5 mEq/L). La mortalidad fue similar (29,8% vs. 28,2%). **Conclusiones:** Los niveles de VAN (8,4%) en esta población con alto riesgo de NAC por *S. pneumoniae* fueron extremadamente bajos. Los pacientes con NNB estaban más graves, pero la mortalidad fue similar entre los dos grupos. La VAN reduce la incidencia de NNB y es razonable incrementar el nivel de vacunación de la población en riesgo.

Descriptores: Vacunas neumocócicas; Neumonía Bacteriana; Streptococcus pneumoniae; Infecciones neumocócicas; Mortalidad; Epidemiología.

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Introduction

Infection with *Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia (CAP) worldwide. This pneumococcus is a common colonizer of the nasopharynx in many healthy individuals, especially children (the so-called carrier state) and, by contiguity with the upper airway, can cause diseases such as otitis, sinusitis, and pneumonia; less commonly, it can invade sterile body sites, such as the pleura, meninges, and blood, causing an invasive disease.[1] Bacteremia has been reported to occur in 10% of cases of CAP,[2-4] and there is evidence associating the presence of bacteremia with poor outcomes in patients with CAP.[5] In a study of CAP in the pre-antibiotic era, Tilghman et al. reported a high mortality rate (78%) in adults with bacteremic pneumococcal pneumonia (BPP), compared with 28% in those with non-bacteremic pneumococcal pneumonia (NBPP).[6] More recently, Austrian & Gold reported a 17% mortality rate in adults with BPP treated with penicillin.[7] The primary objective of the present study was to determine whether bacteremia in pneumococcal CAP was associated with predictors of poor outcomes (mortality, length of stay, complications, etc.) and whether it was related to vaccination history.

Methods

This was a secondary analysis of a prospective cohort of patients diagnosed with CAP and treated in the *Hospital de Clínicas José de San Martín* emergency room, clinical medicine ward, or ICU (or any combination of the three) between June of 1997 and May of 2001. The *Hospital de Clínicas* is the University of Buenos Aires hospital. The hospital is a referral center and a primary care center, having approximately 400 beds. Because a significant number of patients admitted to the hospital are retired social security beneficiaries, individuals over 65 years of age are predominant.

The primary objective of the present study was to determine the association between bacteremia and predictors of poor outcomes (mortality, length of stay, complications, etc.) in patients with CAP. To that end, the primary variable was mortality, chosen mainly because of its objectivity and its obvious clinical importance. Secondary variables included the following: presence of bacteremia; hospitalization; ICU admission; mortality, as predicted by scores (pneumonia severity index [PSI], mental Confusion, Urea, Respiratory rate, Blood pressure, and age > 65 years [CURB-65], and Acute Physiology and Chronic Health Evaluation II [APACHE II]); being older than 65 years; being a nursing home resident; comorbidities; and biochemical data useful in screening for the presence of comorbidities and in determining clinical severity. Our secondary objective was to determine the impact of bacteremia on the severity of the manifestations of CAP in terms of demographic variables, physical examination variables, biochemical variables, and severity rates, as well as to determine the relationship of bacteremia with pneumococcal vaccination history and the presence of various comorbidities.

The inclusion criteria were as follows: being over 18 years of age; having been diagnosed with CAP in accordance with the criteria defined by Fang et al. (i.e., presence of a new infiltrate on chest X-ray, together with one of the major criteria [fever ≥ 38.0°C, hypothermia < 35.0°C, cough, and pleuritic pain] or two of the minor criteria [dyspnea, leukocytosis > 12,000 cells/mm^3, altered level of consciousness, auscultatory signs of consolidation, and expectoration])[8]; not having been hospitalized for more than 48 h prior to symptom onset; and presenting with positive blood culture for *S. pneumoniae*, positive sputum culture for *S. pneumoniae*, positive urinary antigen test results for *S. pneumoniae*, or any combination of the three.

The exclusion criteria were as follows: having been hospitalized in the last 30 days (or presenting with any other evidence suggestive of nosocomial pneumonia); having severe immunosuppression (e.g., having been under treatment with corticosteroids at a dose greater than 20 mg per day for more than 30 days); receiving chemotherapy for a lymphoproliferative disease or any other neoplastic disease; having neutropenia of any cause (< 1,000 cells/mm^3); and being HIV-positive and having an AIDS-defining illness or a CD4+ lymphocyte count < 200 cells/mm^3.

Clinical evaluation consisted of anamnesis and physical examination, the following data having been collected: demographic data (age, gender, and nursing home residence); data on flu and pneumococcal immunizations; data on clinical parameters at admission (temperature, blood pressure, HR, and RR, as well as level of consciousness, as determined by the Glasgow coma

scale score); data on coexisting conditions (diabetes mellitus, chronic lung diseases such as COPD and asthma, chronic heart failure, chronic liver or kidney disease, neurological disease [dementia and stroke], HIV infection, and alcoholism); biochemical data (blood workup, urea, creatinine, glucose, ionography, and acid-base status); data on pneumonia severity (hospitalization and ICU admission), including APACHE II score,[9] CURB-65 score,[10] and PSI class[11]; and data on 30-day mortality (regardless of the cause) and premature death, the latter having been defined as death occurring in the first 7 days.

We defined BPP as a diagnosis of pneumonia with one or more positive blood cultures for *S. pneumoniae*. In contrast, we defined NBPP as a diagnosis of pneumonia with positivity for *S. pneumoniae* as determined by sputum culture, an immunochromatographic test (Binax Now, *S. pneumoniae* urinary antigen test; Binax Inc, Portland, ME, USA), or both and negativity for *S. pneumoniae* as determined by blood cultures.

The statistical analysis was performed with the Statistical Package for the Social Sciences, version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). We used the chi-square test or Fisher's exact test for categorical variables and the Student's t-test for continuous variables. In order to analyze discrete variables associated with mortality, we employed a predictive logistic regression model including the predictors that were found to be statistically significant by the chi-square test ($p < 0.001$). The level of statistical significance was set at $p < 0.05$.

Results

Over a 4-year period, 798 patients diagnosed with CAP were hospitalized. Of those, 158 were excluded from the analysis because they did not meet all of the inclusion criteria or because they met one of the exclusion criteria. Of the remaining 640 patients, *S. pneumoniae* was found to be the etiologic agent in 118, who were therefore selected for inclusion in the study. Forty-seven met the criteria for BPP, and 71 met the criteria for NBPP. There were 23 outpatients. Of those, 5 were found to have bacteremia due to *S. pneumoniae*.

Among the BPP patients, the mean age was higher, the most common comorbidity being heart or kidney failure (Table 1). There were no differences between the two groups in terms of gender or any of the other comorbidities investigated. None of the BPP patients had received pneumococcal vaccination, whereas 9 (12.7%) of the NBPP patients had been vaccinated ($p = 0.043$). Of those 9, 7 were hospitalized (most being over 65 years of age and having severe pneumonia), and 2 (22.2%) died, whereas 32 (29.9%) of those who had not been vaccinated died ($p = 0.624$).

In addition to having hyponatremia, the BPP patients had significantly higher RRs and creatinine levels, as well as significantly lower hematocrit levels.

Although most of the BPP patients required hospitalization and ICU admission, there were no differences between the two groups in terms of the length of hospital stay. The BPP patients were more severely ill, as determined by APACHE II and PSI scores, the latter having shown a predominance of higher risk classes among those patients. The same was true for the CURB-65 score. However, we found no differences between the two groups in terms of mortality during hospitalization (Table 2).

Regarding the diagnostic methods, microbiological findings in sputum, urinary antigen testing, or both allowed us to identify the non-bacteremic group; it is of note that, although those methods were applied to the NBPP and BPP groups, the number of patients with microbiological findings in sputum was lower in the BPP group (Table 3).

Of the 118 patients, 34 (28.6%) died of pneumococcal pneumonia. Among those patients, being over 65 years of age, being a nursing home resident, having tachycardia and hypotension at admission, having a hematocrit level < 30%, and having a $PaO_2/FiO_2 < 250$ or oxygen saturation < 90% constituted variables that were significantly associated with higher mortality. The presence of chronic renal failure, chronic heart failure, or neurological disease was associated with higher mortality, as was the presence of more than one comorbidity. Other variables associated with a poor prognosis included ICU admission, CURB-65 ≥ 2, and PSI class IV-V. However, when analyzing those characteristics in terms of the presence or absence of bacteremia, we found no statistically significant differences between the two groups (Table 4).

Logistic regression was performed to evaluate the impact of a number of variables on mortality

Table 1 - Demographic and clinical characteristics of the patients with pneumococcal pneumonia.

Variable	Groups		p
	BPP	NBPP	
	(n = 47)	(n = 71)	
Demographic data			
Age, years[a]	76.36 ± 11.46	67.79 ± 20.89	0.012
M/F gender[b]	21/26	34/37	
Nursing home resident[c]	2 (4)	11 (15.5)	0.262
Pneumococcal vaccination[c]	0 (0.0)	9 (12.7)	0.043
Comorbidity, n			
Chronic renal failure	14	5	0.001
Chronic heart disease	26	24	0.021
Chronic lung disease	12	28	0.118
Diabetes	6	9	0.989
HIV infection	0	2	0.246
Liver disease	1	2	0.816
Alcohol consumption	1	1	0.767
Neoplastic disease	4	4	0.543
Cerebrovascular disease	9	17	0.538
Presence of more than 1 comorbidity	24	32	0.523
Physical examination[a]			
Temperature, °C	37.7 ± 1.1	37.6 ± 1.2	0.638
HR, bpm	102.8 ± 16.8	100.7 ± 15.5	0.493
RR, breaths/min	29.7 ± 5.9	25.8 ± 6.7	0.001
Systolic blood pressure, mmHg	118.4 ± 23.7	117.6 ± 21.7	0.853
Diastolic blood pressure, mmHg	65.8 ± 13.5	69.5 ± 13.6	0.15
Glasgow scale score	13.9 ± 2.2	14.25 ± 1.9	0.503
Biochemical data[a]			
Leukocyte count, cells/mm^3	14268 ± 7099	12667 ± 5754	0.19
Hematocrit, %	35.7 ± 5.8	38.6 ± 6.7	0.021
PaO_2, mmHg	60.8 ± 11.8	65.1 ± 25.4	0.923
PaO_2/FiO_2 ratio	275.6 ± 73	273.9 ± 100	0.923
Arterial pH	7.40 ± 0.07	7.40 ± 0.1	0.968
Glucose, mg/dL	136.09 ± 80.2	146.9 ± 65.33	0.448
Urea, mg/dL	65.7 ± 39.81	59.4 ± 33.9	0.38
Creatinine, mg/dL	1.53 ± 0.75	1.11 ± 0.73	0.009
Sodium, mEq/L	133.9 ± 6.06	137.1 ± 5.5	0.005
Potassium, mEq/L	3.8 ± 0.5	3.8 ± 0.6	0.977
Radiological finding of pleural effusion[c]	5 (10)	2 (3)	0.078

BPP: bacteremic pneumococcal pneumonia; NBPP: non-bacteremic pneumococcal pneumonia; M: male; and F: female. [a]Results expressed as mean ± SD. [b]Results expressed as n/n. [c]Results expressed as n (%).

in patients with pneumococcal pneumonia. As shown in Table 5, only three of the variables considered were found to be independently and significantly related to mortality in those patients: presence of more than one comorbidity (OR: 8.14); ICU admission (OR: 4.85); and presence of neurological disease (OR: 4.53).

Discussion

Invasive pneumococcal disease causes high morbidity and mortality, especially in at-risk patients and older adults, as well as having a higher incidence in patients with lung disease, heart disease, and diabetes. The incidence of infection, especially bacteremia, empyema, and meningitis, in

Table 2 - Variables associated with mortality in patients with pneumococcal pneumonia.

Severity criteria	Groups		p
	BPP	NBPP	
	(n = 47)	(n = 71)	
Hospitalization[a]	44 (97.8)	51 (77.4)	0.005
Length of hospital stay (in days)[b]	6.6 ± 4.5	8.12 ± 8.56	0.27
ICU admission[a]	20 (42.5)	16 (22.5)	0.028
PSI, n	46	70	
PSI (t-test)[b]	130 ± 36	105 ± 45	0.002
PSI class[a]			
I	0 (0.0)	13 (18.6)	0.016*
II	0 (0.0)	3 (4.3)	
III	8 (17.4)	9 (12.9)	
IV	18 (39.1)	22 (31.4)	
V	20 (43.5)	23 (32.9)	
APACHE II[b]	16.38 ± 4.63	14.00 ± 6.50	0.031
CURB-65[b]	2.65 ± 0.70	2.12 ± 1.20	0.012
0[a]	0 (0.0)	10 (14.9)	0.048
1[a]	2 (5.0)	9 (13.4)	
2[a]	13 (32.5)	16 (23.9)	
3[a]	22 (55)	27 (40.3)	
4[a]	3 (7.5)	5 (7.5)	
Mortality			
Death from any cause[a]	14 (29.8)	20 (28.2)	0.849
Premature death[a]	12 (26.1)	13 (18.3)	0.316

BPP: bacteremic pneumococcal pneumonia; NBPP: non-bacteremic pneumococcal pneumonia; PSI: pneumonia severity index; APACHE II: Acute Physiology and Chronic Health Evaluation II; and CURB-65: mental **C**onfusion, **U**rea, **R**espiratory rate, **B**lood pressure, and age > **65** years. [a]Results expressed as n (%). [b]Results expressed as mean ± SD. *Chi-square test.

Table 3 - Diagnostic yield of the methods employed.

Diagnostic method	Groups		p
	BPP	NBPP	
	(n = 47)	(n = 71)	
BINAX - Urinary antigen testing[a]	11/15 (73.3)	28/41 (68.3)	0.716
Microbiological findings in sputum[b]	7 (14.9)	45 (63.4)	0.001
Resistance to pneumococcal infection[b]	4 (11.1)	6 (18.2)	0.405

BPP: bacteremic pneumococcal pneumonia; and NBPP: non-bacteremic pneumococcal pneumonia. [a]Results expressed as n/N (%). [b]Results expressed as n (%).

sterile sites varies by geographic region and ranges from 21 to 33 cases per 100,000 population.[12] In Argentina, a study conducted in the city of Tandil reported that the incidence of BPP was 2.8 cases/1,000 admissions or 17 cases/100,000 population per year.[13] Since the introduction of the pediatric 7-valent pneumococcal conjugate vaccine (PCV7) in 2002, the rate of invasive pneumococcal disease has decreased significantly in the United States, according to the Centers for Disease Control and Prevention. This reduction occurred not only among vaccinated children but also among unvaccinated adults and individuals over 65 years of age, through the so-called "herd effect".[14]

In the present study, we found certain differences between the characteristics of BPP and those of NBPP. We found that BPP was more common in older individuals than was NBPP, a finding that is in disagreement with those of previous studies.[15,16] We were unable to compare the incidence of BPP and NBPP in HIV-positive patients and intravenous drugs users with the incidence of BPP and NBPP in patients who did not have those characteristics because the incidence of HIV infection and

Table 4 - Variables associated with mortality in patients with pneumococcal pneumonia.

Variable	Patients, n	Mortality, %	p
Age > 65 years	30	33.7	0.042
Male gender	14	25.5	0.452
Nursing home resident	7	54.0	0.049
Vaccination	2	22.0	0.65
Bacteremia	14	30.0	0.049
Temperature > 38°C	16	24.0	0.220
HR > 120 bpm	12	54.0	0.003
Systolic blood pressure < 90 mmHg	3	50.0	0.230
Diastolic blood pressure < 60 mmHg	10	50.0	0.019
RR > 24 breaths/min	28	33.0	0.140
Leukocytosis	20	28.0	0.524
Leukopenia	3	50.0	0.466
Hematocrit < 30%	8	61.5	0.010
PaO_2/FiO_2 ratio < 250	16	50.0	0.012
PaO_2/FiO_2 ratio < 200	8	50.0	0.109
Urea > 50 mg/dl	20	32.0	0.780
Creatinine > 1,5 mg/dl	14	35.0	0.653
Glucose > 120 mg/dl	18	34.0	0.570
Sodium < 130 mEq/l	3	33.0	0.860
PO_2 < 60 mmHg	22	40.7	0.051
Saturation < 90%	26	50.0	0.001
Presence of comorbidities	33	36.0	0.002
Presence of > 1 comorbidity	31	55.0	< 0.001
Chronic heart disease	26	52.0	< 0.001
Chronic renal failure	10	53.0	0.012
Neurological disease	17	65.0	< 0.001
Neoplastic disease	3	37.0	0.574
Chronic lung disease	15	37.0	0.136
Liver disease	1	33.0	0.860
Diabetes	5	33.3	0.679
Hospitalization	34	35.8	0.001
ICU admission	21	58.0	< 0.001
PSI (class IV-V)	33	97.0	0.001
CURB-65 ≥ 2	29	96.6	0.001

PSI: pneumonia severity index; and CURB-65: mental Confusion, Urea, Respiratory rate, Blood pressure, and age > 65 years.

Table 5 - Logistic regression predicting the likelihood of death in patients with pneumococcal pneumonia.

Variable	OR	95% CI		p
		Lower limit	Upper limit	
ICU admission	4.85	1.57	14.92	0.006
Neurological disease	4.53	1.33	15.39	0.015
More than 1 comorbidity	8.14	1.82	36.22	0.006

intravenous drug use in our hospital population was zero. One third of our population had been diagnosed with COPD, a comorbidity that tended to be more common in NBPP patients (p = not significant). We found a predominance of BPP in patients with chronic heart disease or chronic renal failure, as has been reported, especially in elderly individuals who present with neutrophil dysfunction, decreased production of immunoglobulins, and malnutrition.[17]

Regarding clinical manifestations, the only significant difference between BPP patients

and NBPP patients was that the former were more tachypneic. However, the BPP group was predominantly composed of elderly individuals, in whom tachypnea is more common,[18] Tachypnea is also a well-known indicator of severity found in many patients with bacteremia.

The BPP patients were found to have lower hematocrit levels and higher creatinine levels, as well as having hyponatremia, which is in agreement with previous reports by other authors.[19-22] We found a trend toward radiological evidence of pleural effusion, a finding that has previously been described in association with BPP.[19,20]

Bacteremia has traditionally been associated with poor outcomes in patients with CAP. In a study of CAP in the pre-antibiotic era, Tilghman et al. drew attention to the significant mortality in adults with BPP (78%), compared with 28% in those with NBPP.[6] More recently, Austrian & Gold reported a 17% mortality rate in adults with BPP treated with penicillin.[7]

In a recent study conducted in Canada and involving 1,154 patients with invasive pneumococcal disease, Marrie et al. found that being 18-40 years of age and receiving concurrent treatment with two antibiotics were associated with lower mortality.[23] The use of two antibiotics in combination for the treatment of severe forms of BPP is in line with the observations of Baddour et al.,[24] as well as with the Infectious Diseases Society of America/American Thoracic Society CAP management guidelines.[25] In addition, Marrie et al. observed that although premature death was not associated with comorbidities, it was associated with the presence of complications such as altered mental status, need for oxygen or mechanical ventilation, and cardiac arrest, all of which are indicators of the severity of the infection itself.[23] The mortality rate found by Marrie et al. in the aforementioned study was 14.1%, which is very similar to the 17% rate reported by Austrian & Gold in 1964, supporting the hypothesis of Austrian & Gold that, despite appropriate antibiotic therapy, invasive pneumococcal disease continues to have high mortality, which occurs during the first 3 days, in which the effect of antibiotics in reversing the fatal outcome seems to be nonexistent.[7,23]

Because a proportion of patients might die in the first days despite antibiotic use, it is clear that this group of patients would benefit from prevention. In Latin American countries, the pneumococcal polysaccharide vaccine is indicated for individuals over 65 years of age, those aged 2-64 years with comorbidities, and those cared for in nursing homes, as well as for immunocompromised individuals, according to different guidelines.[26,27] The 23-valent pneumococcal polysaccharide vaccine (PPV23) is well tolerated when administered for the first time but is seldom administered in the region, even to patients for whom it is clinically indicated.[28] In the present study, we confirmed the ability of PPV23 to prevent, in a significant manner, the development of BPP. However, 9 patients had NBPP despite having been vaccinated. A meta-analysis evaluating the effectiveness of PPV23 in function of patient age and risk level concluded that the vaccine is effective in preventing pneumococcal bacteremia in elderly individuals in general (65%) but less so in high-risk elderly individuals (20%), as well as showing little or no effectiveness in preventing pneumonia—the vaccine being even harmful (−16%)—in high-risk groups.[29] However, a recently published randomized controlled trial conducted in Japan and involving elderly nursing home residents (mean age > 84) demonstrated the usefulness of PPV23 in preventing NBPP.[30] Given that *S. pneumoniae* is the most common cause of pneumonia (25-50%), it would be very important to have a vaccine that can also protect against all forms of pneumococcal disease. Below the age of 2 years, the response to PPV23 is unsatisfactory, PCV7 being therefore indicated. It has been demonstrated that PCV7 can reduce the incidence of invasive and noninvasive pneumococcal disease, as well as reducing oropharyngeal colonization in children.[16] In this sense, there are expectations regarding the potential usefulness of conjugate vaccines that cover a larger number of serotypes and are close to being approved for use in adults.

In conclusion, BPP affects patients who are older and who are more severely ill. However, we found no significant differences between BPP patients and NBPP patients in terms of the length of hospital stay and mortality. Although it is more common in patients who are more severely ill, bacteremia does not determine severity; rather, it is an effect of disease severity. Although the pneumococcal polysaccharide vaccine prevents BPP, the levels of protection that the vaccine confers are not enough to prevent NBPP or colonization.

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