

## Background

Community-acquired pneumonia (CAP) is a severe illness associated with a significant morbidity and an estimated 30 day-mortality rate over 20% [1-2]. The establishment of therapeutic strategies aimed at the reduction of this significant mortality have been published as guidelines across the world [3-6]. The favourable impact of these guidelines has been reported, with a reduction in mortality [7,8].

However, differences exist between strategies, more particularly regarding microbial investigations [3-6]. If all guidelines recommend performing blood cultures, they are more controversial about the clinical benefit of urinary antigen tests (UAT) for *S. pneumoniae* and *Legionella*, the 2 main pathogens which have to be considered when providing care to patients with severe CAP.

In France [5], both tests are proposed for CAP requiring intensive care admission, while UAT for *Legionella* is proposed in case of suggestive clinical presentation or in case of acknowledged outbreak. In US guidelines [4], some comorbidities are indicative of *S. pneumoniae* UAT for in-patient management, with no regard to the severity of the disease, while in Japan, both tests are advised for all hospitalized patients [6].

The absence of consensual consideration for these UAT may come from variable interpretations of their sensibility, specificity and predictive values [9-12]. Finally there are few studies on the clinical impact of targeted therapy and their results are not unanimous [13-16].

## Objectives

**A positive *Streptococcus pneumoniae* or *Legionella* UAT in patients diagnosed with a CAP could lead to targeted therapy or reassessment antibiotic therapy with narrowing bacterial spectrum. We report herein a multicenter audit aimed to quantify such therapeutic simplification in sCAP and its link with the patient's in-hospital survival rate.**

## Methods

- Retrospective multicenter audit of all patients presenting with sCAP and for whom an UAT – *Streptococcus pneumoniae* or *Legionella* - was positive. Positive tests selected using the laboratories' information system.
- Patients admitted from January 2010 to December 2013 in 8 medical centers included: 1 teaching hospital, 6 public hospitals and 1 private clinic.
- Co-morbidities defined by the specific treatment administered before hospital care, or diagnosis newly established during the hospital stay. For diseases without specific treatment, the patient's medical records were used.
- Use of the Pneumonia Severity Index (PSI) to assess disease severity.
- Antibiotic treatments and the PSI extracted from patient's charts.
- Targeted antibiotic treatment defined as follows: amoxicillin for pneumococcal UAT and a macrolid or a non-pneumococcus fluoroquinolone for *Legionella* UAT. Antibiotic simplification was defined by the use of targeted antibiotic therapy only or by narrowing the spectrum of the initial antibiotic therapy (withdrawal of one molecule or one narrower antibacterial spectrum molecule).
- Logistic regression used for multivariate analysis of the impact of antibiotic simplification on in-hospital survival.

## Results

- 564 patients presenting with sCAP and positive UAT were included, of which 470 were pneumococcus infections (83%) and 94 legionellosis (17%). The mean (±std) of PSI score was 428±28; 40% of the patients were class 5 PSI score. Intensive care requirement was necessary for 39% of the patients.
- A targeted therapy was prescribed in 55 cases (9.7%) and antibiotic narrowing was performed in 78 cases (13.8%). Thus, antibiotic simplification concerned a total of 133 cases (23.6%).
- Table 1 shows the main characteristics of patients according to their antibiotic treatment and simplification. As antibiotic simplification was associated with a higher rate of survival, we searched for risk factors of unfavorable outcome (see Table 2).

## Conclusions

- Antibiotic simplification on the basis of positive UAT for *S. pneumoniae* or *L. pneumophila* in the context of CAP was associated with a lower rate of unfavourable outcome, compared to patients who did not have therapeutic reassessment.
- Few studies aimed to know the clinical impact of targeted therapy on the basis of positive UAT. In a prospective study including 219 patients with non-severe CAP, 48 had positive UAT and were treated by amoxicillin with a rapid favourable outcome in 92% [14]. In another prospective randomised study, UAT for *S. pneumoniae* did not carry substantial therapeutic benefit [15]. However the antibiotic consensus included at least 2 days of intra-venous large-spectrum antibiotic therapy before targeted treatment; moreover, only 25 out of 194 patients had positive UAT. A retrospective monocentric study including 152 patients presenting with positive UAT for *S. pneumoniae* or *L. pneumophila* who benefited from targeted therapy despite high PSI score showed a very low percentage of unfavourable outcome [16]. Considering legionellosis, it has been reported that early targeted therapy based on positive UAT reduced the risk of intensive care admission and death by 38% [17].
- The main question is why simplified antibiotic therapy in CAP is associated with a better outcome? Two hypotheses may be drawn: first, physicians who simplified the antibiotic therapy had more knowledge in clinical microbiology and infectious diseases leading to global better care; second, the excess of antibiotic therapy might be harmful. In the context of suspected ventilator-associated pneumonia, Singh *et al* have demonstrated that stopping antibiotics in the absence of clinical improvement on day 3 was associated with a higher survival rate compared to antibiotic continuation [18].

**Table 2: Risk factors associated with unfavorable outcome. We excluded patients who died before the third day of antibiotic treatment (n = 24). Only the main antibiotic therapy are indicated.**

	Favorable outcome	Unfavorable outcome	P	Multivariate analysis AOR (95% CI), P value
Age (years)	76±14	77±12	0.868	
Sex-ratio (M/F)	1.36	1.56	0.567	
Intensive care admission	156 (35.1)	49 (52.9)	0.001	
<b>Comorbid conditions</b>				
- cardio-vascular	266 (58.7)	55 (53.2)	0.433	
- diabetes	71 (10.3)	9 (15.7)	0.200	
- neurological and/or psychiatric	108 (23.8)	28 (32.2)	0.100	
- pulmonary	156 (34.4)	31 (35.6)	0.830	
- cancers and/or immunodepression	82 (18.1)	27 (31.0)	0.005	
- alcoholism and/or liver diseases	59 (13.0)	11 (12.6)	0.922	
- chronic renal failure	34 (7.5)	6 (6.9)	0.842	
PSI score	123±26	146±28	<0.001	
<b>PSI 5</b>	<b>150 (33.1)</b>	<b>59 (67.8)</b>	<b>&lt;0.001</b>	<b>4.16 [2.51 - 6.90], &lt;0.001</b>
<b>Microbial data</b>				
- bacteremia	54 (11.9)	10 (11.5)	0.910	
- Co-infection	31 (6.8)	3 (3.4)	0.232	
<b>Main antibiotic therapy</b>				
Inadequate first line antibiotic therapy	8 (2.0)	2 (2.8)	0.712	
One course of antibiotic therapy	258 (56.9)	41 (47.1)	0.091	
<b>single antibiotic therapy</b>	<b>194 (42.8)</b>	<b>21 (21.3)</b>	<b>0.001</b>	<b>0.47 [0.27 - 0.84], 0.007</b>
amoxicillin alone	48 (10.6)	2 (2.8)	0.014	
unchanged antibiotic combinations	62 (13.7)	20 (23.0)	0.026	
<b>Main antibiotic reassessments</b>				
combination to single antibiotic	74 (16.3)	4 (4.6)	0.004	
reassessment to targeted antibiotic	45 (9.9)	2 (2.3)	0.020	
antibiotic strengthening	28 (6.2)	14 (16.1)	0.001	
<b>Antibiotic simplification</b>	<b>127 (28.0)</b>	<b>5 (5.7)</b>	<b>&lt;0.001</b>	<b>0.14 [0.05 - 0.37], &lt;0.001</b>
≥ 3 courses of antibiotics	41 (9.0)	16 (18.4)	0.009	
Health-care associated infection	40 (8.8)	8 (9.2)	0.912	

**Table 1: Comparability of the groups, depending on the simplified antibiotic therapy.**

	Simplified therapy n = 133 (23.6)	No simplified therapy n = 431 (76.4)	p
Age (years, mean±sd deviation)	74±15	77±13	0.032
Sex-ratio (M/F)	1.22	1.46	0.356
ICU admissions	51 (38.3)	172 (39.9)	0.747
Main comorbid conditions			
- cardio-vascular	70 (52.6)	264 (62.6)	0.077
- diabetes	23 (17.3)	60 (13.9)	0.337
- neurological and/or psychiatric	23 (17.3)	117 (27.1)	0.021
- pulmonary	45 (32.3)	155 (35.5)	0.033
- cancers / immunodepression	24 (18.0)	96 (22.3)	0.297
- alcoholism / liver diseases	16 (12.0)	58 (13.5)	0.670
PSI score (n = 710, 84%)	124±26	130±29	0.046
PSI 5	49 (36.8)	179 (41.5)	0.335
Microbial data			
- <i>S. pneumoniae</i> / <i>L. pneumophila</i>	114 (9)	356 (75)	0.399
- blood culture performed	105 (78.9)	339 (78.6)	0.942
- positive for <i>S. pneumoniae</i>	15 (14.4)	41 (11.7)	0.454
Conclusion	7 (5.2)	27 (6.2)	0.671
Death	6 (4.5)	105 (24.4)	<0.001

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