

Amoxicillin (AMX) plus temocillin (TMO) for treatment of severe hospital-acquired pneumonia (HAP) compared to piperacillin/tazobactam (PIP/TAZ)

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Objectives: Overuse of broad-spectrum antibiotics is known to be associated with selection of resistant bacteria and may contribute to other undesirable adverse events such as Clostridium difficile-associated diarrhoea (CDAD). Following an update of our guidelines in November 2011, we aimed to evaluate the efficacy and safety of two narrow-spectrum antibiotics (AMX+TMO) instead of PIP/TAZ as first-line treatment for severe HAP. This combination deemed suitable because of our low incidence of Pseudomonas aeruginosa. **Methods:** Between January 2011 and July 2012, data from 186 patients with severe HAP (defined as new/persistent otherwise unexplained infiltrates on chest X-ray + increased oxygen requirement + temperature $<36^{\circ}\text{C}$ or $>38.4^{\circ}\text{C}$ + CURB-65 score >2) and treated empirically with AMX+TMO or PIP/TAZ were reviewed retrospectively. Any patient who had treatment for <3 days or penicillin allergy was excluded. **Results:** 150 patients were finally included, 75 in each group. 38 were admitted to an intensive or high dependency unit among which 27 patients developed acute lung injury/acute respiratory distress syndrome (ALI/ARDS). For each group, clinical outcomes, ALI/ARDS and adverse events rates are tabulated as attached. Co-morbidities such as chronic obstructive pulmonary disease, diabetes, stroke and cancer were observed in 70% and 68% of the clinical failures in AMX+TMO and PIP/TAZ groups, respectively. Mean duration of therapy was similar in both groups: 6.8 days in AMX+TMO group versus 7 days in PIP/TAZ group. From respiratory culture, P. aeruginosa grew in 2 samples in the PIP/TAZ group but not from the AMX+TMO group. **Conclusions:** This is the first study evaluating the combination of AMX+TMO for empirical treatment of severe HAP. Our data show that this combination is as effective as PIP/TAZ but induces significantly fewer cases of severe diarrhoea and CDAD. Moreover, it allowed us to decrease the use of PIP/TAZ by 31%. In centres with low incidence of Pseudomonas aeruginosa, those data support the use of AMX+TMO as empirical treatment of severe HAP.

		AMX+TMO (n=75)	PIP/TAZ (n=75)	P value (Fisher exact t-test)
Clinical outcome (%)	Success	81.3	78.6	NS
	Failure	13.3	16.0	NS
	Relapse	2.7	2.7	NS
	Undetermined	2.7	2.7	NS
Lung injury (%)	ALI/ARDS	16.0	20.0	NS
	Recovered from ALI/ARDS	50.0	53.3	NS
Adverse events (%)	Severe diarrhoea ¹	2.7	28.0	<0.0001
	CDAD	0	8.0	<0.05

¹Type 6 or 7 stool, Bristol chart