ANTIMICROBIAL CONSUMPTION AND INCIDENCE OF ANTIMICROBIAL RESISTANCE IN MICROORGANISMS OF NOSOCOMIAL INTEREST IN AN ITALIAN NEUROMUSCULAR REHABILITATION CENTER

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Introduction: Antibiotic resistance is a serious threat to public health above all in Europe. Particularly, Italy is placed among the first European countries with the highest rate of antibiotic-resistant microorganisms and with the highest consumption of antibiotics for systemic use [1]. In the last years, institutions have started to give more importance to the healthcare-associated infections (HAI) which occur not only in intensive care units (ICU) and long-term care facilities (LTCF), but also in rehabilitation hospitals. The rehabilitation phase often requires long pathways within specific settings during which the possible HAI risk compromising or prolonging the rehabilitation, as well as their outcomes.

The aim of the study was to take a snapshot of the situation related to incidence of antimicrobial resistant microorganisms and to systemic antimicrobial consumption in an Italian rehabilitation center during a two-year period (2014-2015) in order to provide an internal and external benchmark.

Materials and methods: Data about microorganisms isolated from patients admitted to neurorehabilitation hospital were retrospectively obtained from the diagnostic laboratory of the hospital. Microorganisms identification and antimicrobial susceptibility testing were performed using the automatic system Vitek®2 Compact (Biomerieux). Data on antimicrobial consumption were obtained from the hospital pharmacy on six-monthly basis.

For each identified species it has been calculated: the isolation density, the antibiotic resistance rates, and the incidence density of resistant isolates per 1000 patient-days (IDRI). We have expressed antibiotic consumption as Defined Daily Dose (DDD) per 1000 patient-days to conform us to the use of the ATC/DDD system, recognized by WHO as an international standard for drug utilization studies since 1996.

Results: During the study period, 420 patients generating 57.737 patient-days with an average length of stay of 104.61 days were admitted. On average for each semester, 216±17.2 microbial isolates were isolated; of these 64.6% were Gram-negatives, 23.1% Gram-positives and 12.3% were fungal species. Figure 1 shows the isolation rate of all the microbial species. **The most frequently isolated microorganism was *Klebsiella pneumoniae* (19.3%), followed by *Proteus mirabilis* (18.2%) and *Escherichia coli* (9.5%).** Particularly we observed a significant increasing trend for piperacillin/tazobactam - resistant *K. pneumoniae* from 1.47 to 3.32 in 2015 (p-value=0.04) (Table 1). This species showed an increasing trend from 2014 to 2015 in IDRI for each antibiotic class except for colistin, differently from what was reported for *P. mirabilis*, *E. coli*, *P. aeruginosa*. In the two years studied, 631 and 625 DDD were administered, respectively. Figure 2 shows the consumption of antimicrobials; it increased from 282.7 in the first semester of 2014 to 353.5 in the second semester of 2015. Among all antimicrobials used, carbapenems have always been the most prescribed antibiotic class (31% of the total antimicrobial usage density), followed by penicillins (13%), fluoroquinolones (11.3%), glycopeptides (10.6%), azoles (8.3%) and colistin (8.2%). Particularly, the consumption of piperacillin/tazobactam and teicoplanin were significantly increased (p-value 0.01 and p-value=0.02, respectively).

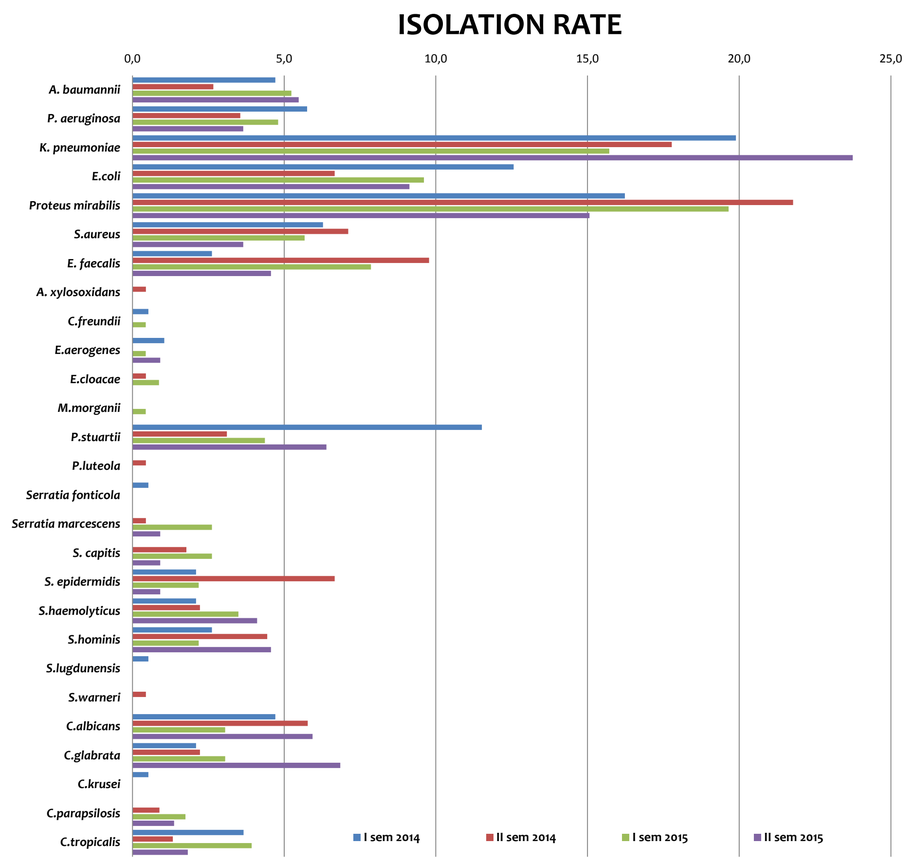

Figure 1. Isolation rate of all hospital microbial species isolated. Sem, semester.

INCIDENCE DENSITY OF RESISTANT ISOLATES (*per* 1000 patient-days)	Antibiotics	I sem 2014	II sem 2014	I sem 2015	II sem 2015	p-value
A. baumannii	Carbapenems	0.56	0.42	0.84	0.68	0.4431
	Aminoglycosides	0.56	0.35	0.84	0.68	0.4750
	Fluoroquinolones	0.56	0.42	0.84	0.81	0.2538
	Colistin	0.07	0.00	0.00	0.00	0.2254
P. aeruginosa	Extended-spectrum cephalosporins	0.68	0.48	0.58	0.41	0.2101
	Carbapenems	0.70	0.42	0.56	0.41	0.3143
	Aminoglycosides	0.67	0.42	0.52	0.34	0.2069
	Fluoroquinolones	0.56	0.48	0.70	0.47	0.9439
	Piperacillin-tazobactam	0.56	0.48	0.56	0.41	0.3168
	Colistin	0.07	0.00	0.00	0.00	0.2254
K. pneumoniae	Third-generation cephalosporins	2.39	2.29	2.38	3.12	0.2358
	Fourth-generation cephalosporins	2.39	2.15	2.24	3.05	0.3410
	Carbapenems	1.68	1.52	1.54	2.44	0.3222
	Aminoglycosides	1.58	1.11	1.61	2.37	0.2888
	Fluoroquinolones	2.46	2.35	2.31	3.26	0.3184
	Piperacillin-tazobactam	1.47	2.22	2.31	3.32	0.0419
	Fosfomycin	1.61	1.59	1.75	2.92	0.1752
	Trimethoprim/sulfamethoxazole	1.61	1.52	1.61	0.68	0.2257
	Colistin	0.56	0.62	0.49	0.27	0.1555
E. coli	Third-generation cephalosporins	1.12	0.69	1.12	0.81	0.7039
	Fourth-generation cephalosporins	0.84	0.55	1.05	0.81	0.7389
	Carbapenems	0.14	0.14	0.14	0.00	0.2238
	Aminoglycosides	0.46	0.21	0.56	0.14	0.6081
	β-lactam/inhibitor	0.84	0.42	0.63	0.68	0.7963
	Piperacillin-tazobactam	0.14	0.14	0.14	0.27	0.2272
	Fosfomycin	0.21	0.07	0.14	0.00	0.6984
	Trimethoprim/sulfamethoxazole	0.91	0.48	0.77	0.88	0.9042
P. mirabilis	Fluoroquinolones	1.26	0.83	1.26	0.95	0.6984
	Third-generation cephalosporins	2.03	2.98	2.80	1.97	0.9042
	Fourth-generation cephalosporins	1.96	2.49	2.31	1.76	0.6907
	Carbapenems	0.49	0.76	0.63	0.27	0.5122
S. aureus	Methicillin	0.70	0.90	0.91	0.54	0.6559
	Rifampicin	0.28	0.90	0.42	0.41	0.9518
	Fluoroquinolones	0.84	0.97	0.91	0.54	0.3470
	Linezolid	0.00	0.00	0.00	0.00	-
	Vancomycin	0.00	0.00	0.00	0.00	-
	Hlr - aminoglycosides resistance	0.21	1.25	0.63	0.47	0.9484
E. faecalis	Vancomycin	0.28	0.35	0.00	0.07	0.2338
	Aminopenicillins	0.28	0.35	0.28	0.07	0.2495
	β-lactam/inhibitor	0.21	0.14	0.07	0.00	0.00004
	Teicoplanin	0.28	0.28	0.00	0.00	0.1027
	Linezolid	0.00	0.00	0.00	0.00	-

Table 1. Incidence density of resistant isolates per 1000 patient-days (IDRI) assessed on six-monthly basis. Sem, semester.

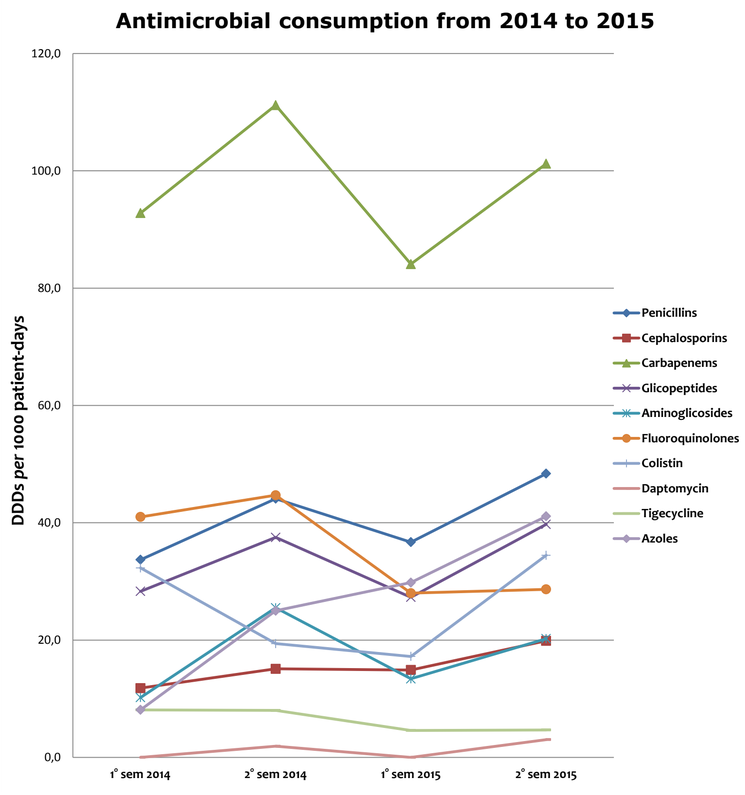

Figure 2. Consumption of antibiotic classes (DDDs per 1000 patient-days) over the study period. Sem, semester.

Discussion: Serious infections caused by ESBLs and fluoroquinolones resistant Enterobacteriaceae have led to an increased dependence on carbapenems as therapeutic options. As a consequence, the spread of Carbapenem-Resistant-Enterobacteriaceae (CPE) has been observed. The increased IDRI to carbapenems we observed, reflects the dramatic situation in the Mediterranean area, in which the strains of Enterobacteriaceae have spread in endemic form. We compared our data with those obtained from intensive care units (ICUs) [2] and from long-term care facilities (LTCFs) [3]. **Despite only the 23.5% of the bed of our hospital corresponds to ICU-bed, our results are similar to those of a recent study performed in Sicilian ICUs** by Agodi et al. (2015), in detail, RR%: carbapenem-resistant K. pneumoniae 65.2% vs. 59.2%; carbapenem-resistant A. baumannii 91.65% vs. 96.6%; third generation cephalosporin-resistant K. pneumoniae 91.45% vs. 81.6%. **By DDD comparison, our data seem to have, in all classes of antibiotics, lower values than the ICUs, (except for glycopeptides), and higher values than LTCFs.**

Conclusions: Results suggest the need for a continuous monitoring of antimicrobial consumption and bacterial resistance trend, since the adaptability of bacteria accelerates while searching for new molecules is currently stopped.

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