Antimicrobial susceptibility of Gram-negative organisms from intra abdominal infections and evolution of isolates with extended spectrum β-lactamases in the SMART study in Spain (2002-2010)

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ABSTRACT

Introduction. The SMART (*Study for Monitoring Antimicrobial Resistance Trends*) surveillance study records the antimicrobial susceptibility of Gram-negative bacilli obtain from intraabdominal infections with special focus in isolates with extended spectrum β-lactamases (ESBLs).

Material and Methods. The antimicrobial susceptibility of 8,869 isolates was analyzed by microdilution during the SMART study performed in Spain from 2002 to 2010. Isolates were recovered in 16 centres.

Results. *Escherichia coli* was the most prevalent pathogen (60.9% from intraabdominal infections acquired in the community and 49.9% in those from nosocomial origin) followed by *Klebsiella pneumoniae* (8.9% *vs* 9.2%). *Pseudomonas aeruginosa* was more common in intraabdominal infections from nosocomial origin (5.6% community and 8.6% nosocomial). Frequency of ESBL-producing isolates was: *E. coli,* 8.7%; *K. pneumoniae,* 8.4%; *Klebsiella oxytoca,* 1.4%; and *Proteus mirabilis,* 1.6%. Overall, ESBL-producing isolates were more frequently isolated from elderly patients (6.8% >60 years). Ertapenem and meropenem were the most active antimicrobials (susceptibility range with EUCAST criteria, 89.0-100%) when considering all Enterobacteriaceae isolates and also against ESBL producers (95.5-100%). Susceptibility of amoxicillin/clavulanic acid and piperacillin/tazobactam was lower, particularly among ESBL-producing isolates. Nevertheless, ertapenem maintained a good activity (susceptibility >95%) in ESBL-producers that were resistant to amoxicillin/clavulanic acid, piperacillin/tazobactam or fluoroquinolones.

Conclusions. Antimicrobial susceptibility data from the SMART-Spain study reinforce current therapeutic guidelines of intraabdominal infections that include ertapenem as the empirical choice for treatment. This is also supported by the high frequency of ESBL-producers in our geographic area.

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Key words: surveillance study, intraabdominal infections, carbapenems, extended spectrum β-lactamases.

Sensibilidad de microorganismos gramnegativos de infecciones intraabdominales y evolución de los aislados con β-lactamasas de espectro extendido en el estudio SMART en España (2002-2010)

RESUMEN

Introducción. El estudio SMART (*Study for Monitoring Antimicrobial Resistance Trends*) tiene como objetivo monitorizar la sensibilidad a los antimicrobianos de los microorganismos gramnegativos aislados en la infección intraabdominal, con especial seguimiento de los que producen β-lactamasas de espectro extendido (BLEE).

Material y métodos. Se han analizado por microdulución los datos de sensibilidad de 8.869 aislados recogidos en el estudio SMART en España entre 2002 y 2010 en el que han participado 16 centros.

Resultados. *Escherichia coli* fue el patógeno más frecuente (60,9% en la infección intraabdominal adquirida en la comunidad y 49,9% en la nosocomial) seguido de *Klebsiella pneumoniae* (8,9% *vs* 9,2%). *Pseudomonas aeruginosa* fue más habitual en la infección nosocomial (5,6% comunitaria y 8,6% nosocomial). La frecuencia de aislados con BLEE fue: *E. coli* 8,7%, *K. pneumoniae* 8,4%, *Klebsiella oxytoca* 1,4% y *Proteus mirabilis* 1,6%. En los pacientes de mayor edad aumentó la proporción global de aislados con BLEE (6,8% en pacientes >60 años). Ertapenem y meropenem fueron los antimicrobianos más activos en el conjunto de las enterobacterias (rango de sensibilidad con criterios EUCAST, 89-100%) y también entre los aislados con BLEE (95,5-100%). La actividad de amoxicilina/ácido clavulánico y piperacilina/tazobactam fue considerablemente inferior, en particular en los aislados con BLEE. Ertapenem mantuvo una buena actividad (sensibilidad >95%) en los productores de BLEE resistentes a amoxicilina/ácido clavulánico, piperacilina/tazobactam o fluoroquinolonas.

Conclusiones. Los datos de sensibilidad del estudio SMART en España avalan las guías terapéuticas actuales de infección intraabdominal que sitúan al ertapenem como tratamiento empírico de elección, teniendo en cuenta sobre todo la elevada frecuencia de aislados con BLEE en nuestro medio.

Palabras clave: estudio de vigilancia epidemiológica, infección intraabdominal, carbapenems, β-lactamasas de espectro extendido.

INTRODUCTION

The increase in antimicrobial-resistant organisms, not only in the hospital but also in the community, is alarming and within them the extended-spectrum β-lactamases (ESBL) producers are of concern[1]. To monitor their impact, one of the measures recommended has been the implementation of epidemiological surveillance programs on resistance and the use of data collected in the design of therapeutic guidelines[2,3]. The SMART study (*Study for Monitoring Antimicrobial Resistance Trends*) is an international program started in 2002 involving over 150 hospitals from all over the world. It monitors the *in vitro* susceptibility to antimicrobials of aerobic and anaerobic Gram-negative bacilli isolated from intra-abdominal infections in inpatients and outpatients, focusing on those producing ESBL[4].

Intra-abdominal infections are one of the most common in the healthcare setting[5]. Most occur due to Gram-negative bacilli, such as *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *Enterobacter* spp., and, to a lesser extent, *Pseudomonas aeruginosa* and other non-fermenting gram-negative bacilli[6]. The absence of an early diagnosis and inadequate treatment are suggested to be the main causes of clinical failure and increased morbidity and mortality[7]. The antimicrobial agents currently recommended for the treatment of intra-abdominal infections include several carbapenems and combinations of penicillins with β-lactamase inhibitors depending on the origin of the infection, and extended-spectrum cephalosporins and fluoroquinolones, usually in combination with metronidazole[8,9].

The SMART study provides updated knowledge of local and global resistance rates and early detection of trend changes, supplying significant information for the empirical treatment of intra-abdominal infections and the design of treatment guidelines. This report is a sub-analysis of the SMART study and evaluates the susceptibility patterns of antimicrobials against aerobic and anaerobic gram-negative pathogens isolated from intra-abdominal infections in the period 2002-2010 in 16 Spanish hospitals, with particular focus on EBSL producers.

MATERIAL AND METHODS

Microorganisms and participating sites

All isolates tested were obtained from abdominal samples from patients with a diagnosis of an intra-abdominal infection. To avoid duplicates, one strain per species and patient was included. Each participating center collected 100 non-selected consecutive isolates of aerobic and anaerobic Gram-negative pathogens. During the 9 years of the study (2002 to 2010) a total of 16 hospitals participated (H. Basurto, Bilbao; H. Universitario Marqués de Valdecilla, Santander; H. Universitari Bellvitge, Hospitalet de Llobregat, Barcelona; H. Valle de Hebrón, Barcelona; H. Germán Trías y Pujol, Barcelona; H. Son Espases, Mallorca; H. Clínico Universitario Lozano Blesa, Zaragoza; H. Clínico de Salamanca, Salamanca; H. Universitario y Politécnico La Fe, Valencia; H. Universitario Ramón y Cajal, Madrid; H. Universitario Gregorio Marañón, Madrid; H. Clínico San Carlos, Madrid; H. Universitario Virgen del Rocío, Sevilla; H. Universitario Virgen Macarena, Sevilla; H. Virgen de las Nieves, Granada; H. Carlos Haya, Málaga). Figure 1 shows the distribution of participating centers per year.

The most frequent intra-abdominal sample (more than 50%) was peritoneal fluids, followed by intra-abdominal abscesses (11%) and bile (5%), and, to a lesser extent and in decreasing order, specimens from liver, small bowel, appendix, pancreas, stomach, colon, rectum, etc. Most were obtained during surgery procedures and others from paracentesis and percutaneous aspiration of intra-abdominal abscesses. Isolates from blood, urine, abdominal drainages, superficial wounds, and perirectal abscesses were excluded. The isolates were identified by species at each hospital and sent to a central laboratory (International Health Management Associates, S A., Schaumburg, IL) to confirm identification and establish the susceptibility to antimicrobials of choice in intra-abdominal infections. All results were included in a centralized database. In addition to the source of the sample, patient age was considered. Following the standard criteria of the *Centers for Disease Control and Prevention* (CDC) the organisms were also rated as isolates obtained within 48 hours after hospitalization (community-acquired infection) and isolates obtained after 48 hours of hospital stay (nosocomial infection)[10].

Antimicrobial susceptibility

Antimicrobial susceptibility tests were performed using the broth microdilution method according to the guidelines of the Clinical and Laboratory Standards Institute[11]. Dried MicroScan microdilution panels were used (Siemens Medical Solutions Diagnostics, West Sacramento, CA, U.S.). The antimicrobials analyzed in this study were: piperacillin/tazobactam, ceftriaxone, ceftazidime, cefepime, imipenem, meropenem, ertapenem, amikacin, ciprofloxacin and levofloxacin. Susceptibility to amoxicillin/clavulanic acid was measured with plastic strips containing a gradient of 15 antibiotic concentrations (Etest ®, bioMérieux, Lyon, France). The quality controls strains used were *Escherichia coli* ATCC 25922, *E. coli* ATCC 35218, *Klebsiella pneumoniae* ATCC 700603 (positive ESBL control) and *P. aeruginosa* ATCC 27853. ESBL production in *E. coli*, *Klebsiella* spp. and *Proteus mirabilis* was confirmed according to the CLSI

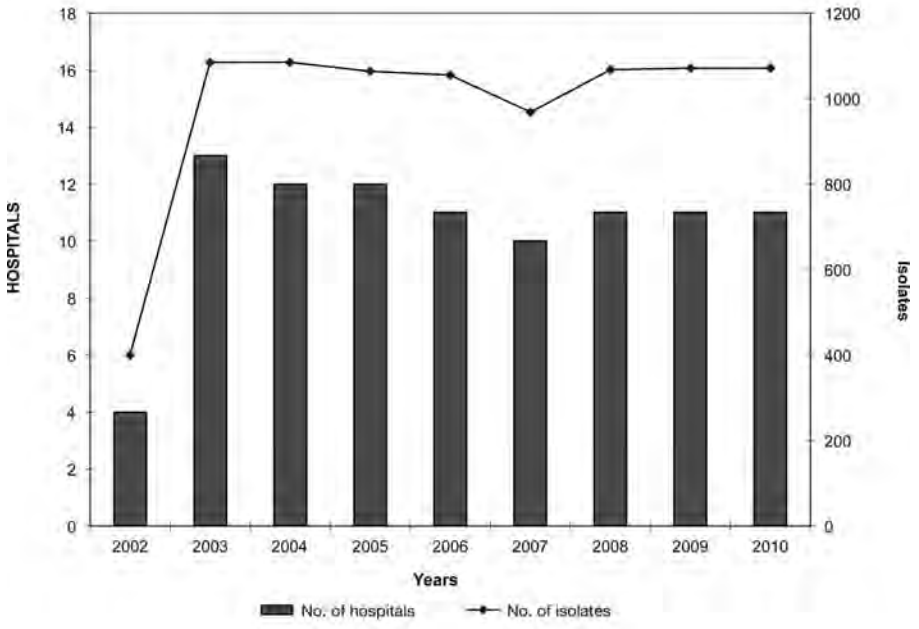


Figure 1 | **Number of participating hospitals and organisms per year shown in intraabominal infection specimens in the SMART study in Spain (2002-2010).**

specifications[12]. For interpreting antibiotic susceptibility, the breakpoints points proposed by the EUCAST in the year 2011 were used[13]. For amoxicilllin- calvulanate, the amoxicillin values from this combination was used as a reference for the application of EUCAST breakpoints.

Statistical analysis

The frequency comparison (incidence between hospital and community isolates) was performed using the chi-squared test (2) taking $P < 0.05$ as statistically significant.

RESULTS

During the study period (2002 to 2010) a total of 8,869 isolates were collected from the Spanish center participants. Figure 1 gives a breakdown of the number of isolates and the number of centers participating by year.

An analysis of all organisms and the entire follow-up period showed that enterobacterial isolates (8,022) accounted for 90.4% of the isolates, with *E. coli* as the most common organism (54.3%), followed by *Klebsiella* spp. (13.8%) and *P. mirabilis* (4.8%). The most common non-fermenting Gram-negative bacilli were *P. aeruginosa* (7.4% of the total isolates). When the origin of the isolates was considered, 60.5% were of nosocomial origin, as compared to 39.5% community-acquired. In 10.4% of the isolates their origin was not specified in the case report forms. Table 1 shows the distribution of the 11 most commonly isolated microorganisms and the community or nosocomial origin. The higher percentage (P <0.01) of *E. coli* isolates in community-acquired intra-abdominal infections (60.9%) as compared to those acquired in the hospital (49.9%) should be noted. In contrast, *P. aeruginosa* was significantly higher (P <0.01) in hospital-acquired infections (8.6% *vs* 5.6%). *Enterobacter cloacae, Enterobacter aerogenes, Citrobacter freundii*, *Morganella morganii* and *Serratia marcescens* (Enterobacteriaceae group with chromosomal inducible AmpC β-lactamases) were also more common in intra-abdominal infections of hospital origin (table 1).

Of all the enterobacterial isolates tested for ESBL (*E. coli*, *Klebsiella* spp. and *Proteus mirabilis*), 489 (7.5%) were producers of these enzymes. The highest frequency was found in *E. coli* (8.7%), followed by *K. pneumoniae* (8.4%), *K. oxytoca* (4.1%) and *P. mirabilis* (1.6%). The incidence over time of ESBL-producing *E coli* and *K. pneumoniae* isolates is shown in figure 2, indicating a relative stability in *E. coli* and an overall reduction in *K. pneumoniae*. In all ESBL-producing organisms, these enzymes clearly occurred more frequently in nosocomial than in community-acquired infections (figure 3). In addition, an age-associated increase was observed in ESBL-producing isolates, reaching a frequency of more than 6% in patients over 60 years of age (figure 4).

Table 1 **Distribution of the most common gram negative organisms collected in intra abdominal infections in Spain in the SMART study (2002-2010).**

Organism	Number of isolates	Community acquisition Number of isolates (%)	Nosocomial acquisition Number of isolates (%)
Escherichia coli	4,824	1,911 (60.9)	2,404 (49.9)
Klebsiella pneumoniae	816	278 (8.9)	444 (9.2)
Klebsiella oxytoca	413	152 (4.8)	214 (4.4)
Proteus mirabilis	428	128 (4.1)	264 (5.5)
Proteus vulgaris	82	26 (0.8)	48 (1.0)
Enterobacter cloacae	525	155 (4.9)	321 (6.7)
Enterobacter aerogenes	156	47 (1.5)	93 (1.9)
Citrobacter freundii	253	74 (2.4)	153 (3.2)
Morganella morganii	231	53 (1.7)	161 (3.3)
Serratia marcescens	80	25 (0.8)	45 (0.9)
Other enterobacteria	214	80 (2.6)	112 (2.3)
Pseudomonas aeruginosa	662	176 (5.6)	415 (8.6)
Other Gram-negative bacilli	185	31 (1.0)	139 (2.9)
TOTAL	8,869[a]	3,136 (39.5)	4,813 (60.5)

[a]in 920 isolates (10.4%) the site of infection specimen was not specified

The antibiotic susceptibility profile of the most common organisms in intra-abdominal infections is shown in table 2. The compounds most active against Enterobacteriaceae were meropenem (susceptibility rates between 94.5% and 100%), ertapenem (89.0-99.7%), imipenem (71.3-100%) and amikacin (94.6-100%). Those which performed worst were the fluoroquinolones, with clearly lower rates of susceptibility. In the case of *E. coli,* about 25% of the isolates were resistant to ciprofloxacin and levofloxacin. Susceptibility to amoxicillin/clavulanic acid in eterobacterial isolates producing chromosomal inducible AmpC β-lactamases (*E. cloacae, E. aerogenes, C. freundii*, *M. morganii* and *S. marcescens*), known to be intrinsically resistant to this antibiotic combination[12], were excluded from the analysis, ranged between 82.4% in *E. coli* and 94.4% in *Proteus vulgaris* (table 2). For piperacillin/tazobactam susceptibility of all the enterobacteria ranged from 63.4% in *E. aerogenes* to 99.3% in *P. mirabilis* (table 2). Piperacillin/tazobactam, ceftazidime, meropenem and amikacin maintained their activity against *P. aeruginosa* in about 80% of the isolates.

When only ESBL-producing *E. coli* and *K. pneumoniae* were taken into consideration and compared to non-ESBL-producers (table 3), meropenem, imipenem and ertapenem activity remained virtually unchanged. A slight decrease was observed in the case of amikacin, but the activity of combinations of penicillins with β-lactamase inhibitors and that of cephalosporins and fluoroquinolones was seen to be highly affected. Loss of susceptibility to amoxicillin/clavulanic acid, piperacillin/tazobactam, ciprofloxacin and levofloxacin was higher in *E. coli,* while in the case of *K. pneumoniae* it was higher for cephalosporins. It must be noted that in ESBL-producing *E. coli.* susceptibility rates for amoxicillin/clavulanic acid were less than 75% of the isolates, and the situation was more problematic for ESBL-producing *K. pneumoniae* in which susceptibility values of 50% were not achieved. In both cases the activity of carbapenems (meropenem, imipenem and ertapenem) exceeded 95%.

When specifically analyzed against isolates of *E. coli* and *K. pneumoniae*, including both ESBL producers and non-producers resistant to amoxicillin/clavulanic acid acid, piperacillin/tazobactam and levofloxacin, ertapenem activity was scarcely modified, with susceptibility values above 95% in all cases (table 4).

DISCUSSION

The increased resistance to broad-spectrum β-lactam antibiotics, including combinations of penicillins with β-lactamase inhibitors and third and fourth generation cephalosporins, have highlighted the need for adapting the treatment guidelines for situations in which these microorganisms may be involved[1,8]. The implementation and ongoing progress of epidemiological surveillance studies help monitor antimicrobial susceptibility and provide data

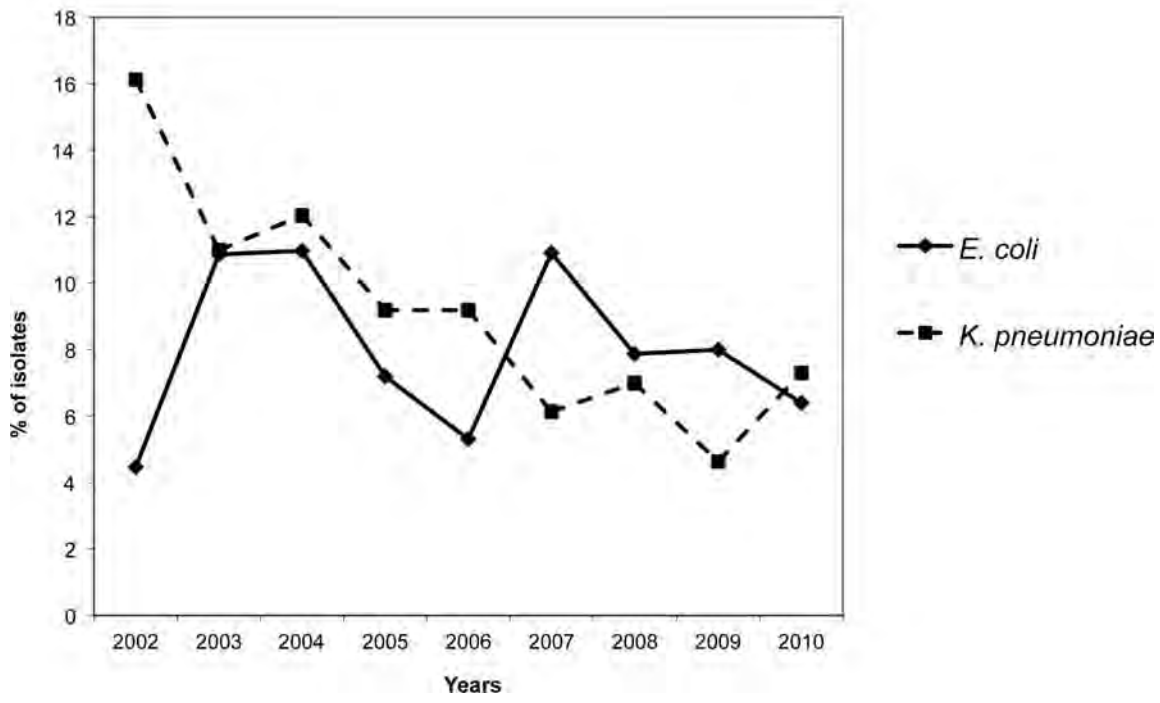
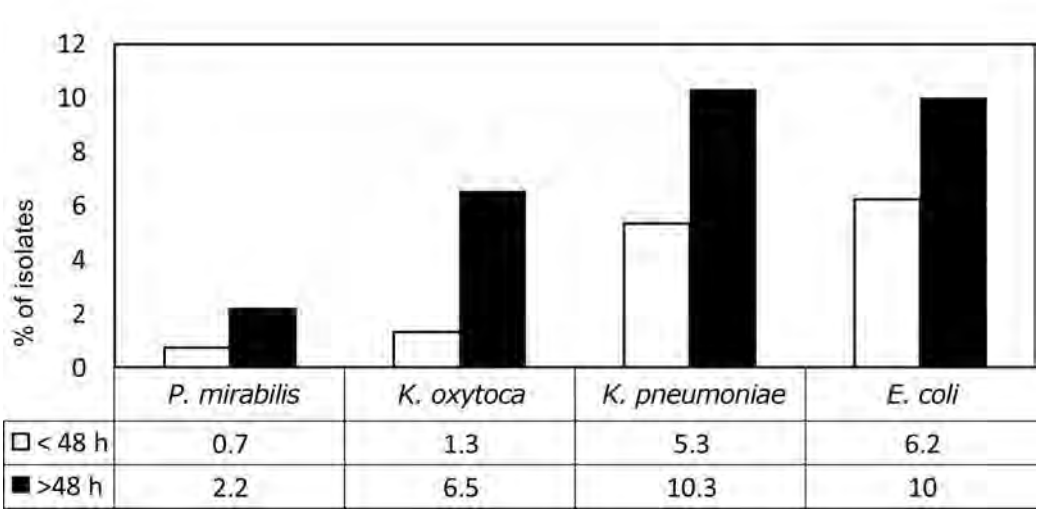


Figure 2 Change over time in the percentage of isolates of *Escherichia coli* and extended spectrum β-lactamase *Klebsiella pneumonia* (ESBL) in the SMART study in Spain (2002-2010).



	P. mirabilis	*K. oxytoca*	*K. pneumoniae*	*E. coli*
□ < 48 h	0.7	1.3	5.3	6.2
■ >48 h	2.2	6.5	10.3	10

Figure 3 Frequency of Enterobacteriaceae with extended spectrum β-lactamases (ESBL) by origin of infection in the SMART study in Spain (2002-2010).

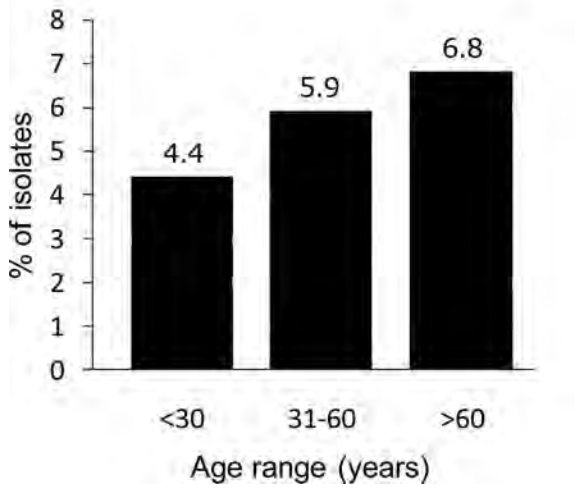


Figure 4 Frequency of Enterobacteriaceae (*Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca* and *Proteus mirabilis*) with extended spectrum β-lactamases (ESBL) by age of the patient in the SMART study in Spain (2002-2010).

for the timely adaptation of empiric treatment guidelines. The SMART study, considered a benchmark in the collection of data on intra-abdominal infections, meets this dual condition[4,14-17]. Its continued progress in Spain since 2002, with the participation of a large number of microbiology departments in University Hospitals and the collection of a significant number of microorganisms has provided a representative analysis of antimicrobial susceptibility profiles in Spain.

In line with other studies[18], the data analyzed indicate the importance of some organisms, such as *E. coli* in both hospital and community-acquired intra-abdominal infections. The greater involvement of *P. aeruginosa* and enterobacterial isolates with chromosomal inducible AmpC β-lactamases is also relevant in hospital-acquired infections. Although clinical success in intra-abdominal infections, where surgical drainage is critical, it is not always directly related to *in vitro* susceptibility, surveillance studies may help to the selection of an appropriate empirical antimicrobial therapy. Inclusion of carbapenems as empirical treatment of choice for intra-abdominal infections[8,9,19] would be supported by the susceptibility data obtained in the SMART study and would question the value of combinations of penicillins with β-lactamase inhibitors (amoxicillin/clavulanic acid and/or piperacillin/tazobactam) and particularly of fluoroquinolones, which are not recommended in Spain.

One of the objectives of the SMART study is to monitor ESBL-producing enterobacteria in intra-abdominal infec-

Table 2 **Activity of different antimicrobials used in intra abdominal infections against the most common microorganisms collected in Spain in the SMART study (2002-2010).**

Microorganisms	Percentage of susceptibility[a]										
	AUG	P/T	CAX	CAZ	CPE	IMP	MERb	ETP	AK	CP	LVX
Escherichia coli	82.4	92.3	91.4	91.1	93.6	99.9	99.8	99.7	98.1	74.7	76.5
Klebsiella pneumoniae	87.4	88.3	93.3	93.0	94.2	99.6	99.5	99.0	98.4	89.3	91.8
Klebisiella oxytoca	87.9	92.4	91.5	97.3	95.6	99.7	100	99.7	99.2	94.4	95.9
Proteus mirabilis	92.4	99.3	96.9	97.9	99.0	87.8	100	99.7	94.6	79.2	90.1
Proteus vulgaris	94.4	98.7	57.3	89.0	97.5	85.3	100	100	98.7	98.7	98.7
Enterobacter cloacae	-[c]	77.3	62.9	63.9	83.1	99.0	100	89.0	99.4	92.5	94.0
Enterobacter aerogenes	-[c]	63.4	49.6	50.3	88.8	94.7	94.5	92.1	98.6	94.1	95.9
Citrobacter freundii	-[c]	84.1	67.4	67.8	90.4	98.8	100	99.2	97.6	92.0	94.2
Morganella morganii	-[c]	96.5	82.1	65.2	97.3	71.3	100	99.1	96.5	81.3	85.8
Serratia marcescens	-[c]	93.5	88.4	93.5	96.1	100	100	98.7	100	92.3	97.3
Other enterobacteria	51.7	88.6	77.7	78.6	94.3	99.0	100	98.1	99.0	92.4	96.1
Pseudomonas aeruginosa	-[c]	77.9	-[c]	80.0	78.7	75.4	83.8	-[c]	82.2	76.5	73.0

[a]EUCAST criteria; [b] meropenem was only studied from 2002 to 2004; [c] This antimicrobial is not considered adequate against the microorganism tested.

AUG: amoxicillin/clavulanic acid; P/T: piperacillin/tazobactam; CAX: ceftriaxone; CAZ: ceftazidime; CPE: cefepime; IMP; imipenem; MER: meropenem: ETP: ertapenem; AK: amikacin; CP: ciprofloxacin; LVX: levofloxacin.

Table 3 **Activity of antimicrobials used in intra-abdominal infections against ESBL producing and non producing organisms in Spain collected in the SMART study (2002-2010).**

Organism	Antibiotics	Non ESBL producer		ESBL producer	
		Number of isolates	% susceptibility[a]	Number of isolates	% susceptibility[a]
Escherichia coli	AUG	2,965	83.3	244	72.1
	P/T	4,427	93.8	395	75.4
	CAX	4,427	97.9	395	19.2
	CAZ	4,427	96.3	395	32.1
	CPE	4,427	99.0	395	32.6
	IMP	4,427	99.9	395	99.7
	MER[b]	1,249	99.8	137	100
	ETP	4,427	99.7	395	98.9
	AK	4,427	98.7	395	91.6
	CP	4,427	77.8	395	40.5
	LVX	4,213	79.6	385	43.3
Klebsiella pneumoniae	AUG	531	90.7	44	47.7
	P/T	747	92.7	68	39.7
	CAX	747	97.8	68	44.1
	CAZ	747	97.5	68	30.8
	CPE	747	98.3	68	48.5
	IMP	747	99.7	68	98.5
	MER[b]	180	100	25	96.0
	ETP	747	99.3	68	95.5
	AK	747	99.0	68	91.1
	CP	747	92.1	68	58.8
	LVX	721	94.1	63	65.0

[a]EUCAST criteria. [b] meropenem was only studied from 2002 to 2004; AUG: amoxicillin/clavulanic acid; P/T: piperacillin/tazobactam;

CAX: ceftriaxone; CAZ: ceftazidime; CPE: cefepime; IMP; imipenem; MER: meropenem: ETP: ertapenem; AK: amikacin; CP: ciprofloxacin; LVX: levofloxacin.

tions. Since they were initially identified in Germany in 1983, there has been an alarming worldwide increase of ESBL-producing enterobacteria, with figures of over 50% in several Asian countries[15]. In line with the results of the EARSS surveillance study, monitoring antimicrobial resistance in invasive isolates, SMART study publications referring to Europe[4,16] report that the percentage of ESBL-producing isolates is higher in Mediterranean countries than in Northern Europe[20,21]. In this study, the results for Spain show a 6.3% rate of ESBL-producing isolates, which rises slightly higher in *E. coli* (8.7%) compared to *K. pneumoniae* (8.4%). Although changes have been observed over the years, the overall trend in *E. coli* did not change, unlike with *K. pneumoniae*, that decreased over time. This could be due to the occurrence of epidemics caused by this type of organism, essentially *K. pneumoniae*, during the period of collection at some of the sites participating in the study, and would explain the swings in frequency observed in some years, biasing the percentages and the global trend. Nevertheless, the overall values are similar to those from other studies monitoring ESBL-producing isolates[17,20].

The study also evidences the higher frequency of ESBL-producing isolates in intra-abdominal infections of hospital origin and in elderly patients. Previous hospital admission and old age have been reported as risk factors for acquisition of infections by ESBL strains[22,23].

Co-resistance is a relevant issue in the design of treatment protocols and the selection of antimicrobials[24]. This analysis reported that carbapenems, including ertapenem, maintained a good activity in ESBL-producing strains resistant to amoxicillin/clavulanic acid, piperacillin/tazobactam or fluoroquinolones. This activity was not affected by the community origin of the infection (data not shown in the tables).

Carbapenems are considered to be the alternative empirical therapy of choice in infections highly suspected to be caused by ESBL-producing enterobacteria and also in those hyperproducing AmpC[25,26]. Despite the emergence of carbapenemases in Spain[27,28], one notable aspect arising from the SMART study is the scarce resistance to carbapenems compared to other antimicrobials, essentially broad-spectrum cephalosporins and combinations of penicillins with β-lactamase inhibitors, so their position as drugs of choice

Table 4 **Activity of ertapenem in isolates resistant to amoxicillin/clavulanic acid, piperacillin/tazobactam, and levofloxacin against ESBL producing and non producing microorganisms collected in the SMART study (2002-2010).**

Organism	BLEE	Antimicrobial (% resistant isolates)	ETP % (number of isolates)		
			Susceptible	Intermediate	Resistant
Escherichia coli	Negative	AUG (16.5)	99.8 (2,959)	0.03 (1)	0.1 (4)
	Positive	AUG (27.1)	98.7 (240)	0.4 (1)	0.8 (2)
	Negative	P/T (6.0)	99.7 (4,417)	0.04 (2)	0.1 (8)
	Positive	P/T (23.7)	98.9 (391)	0.2 (1)	0.7 (3)
	Negative	LVX (20.2)	99.7 (4,203)	0.04 (2)	0.1 (8)
	Positive	LVX (56.1)	98.9 (381)	0.2 (1)	0.7 (3)
Klebsiella pneumoniae	Negative	AUG (8.4)	99.2 (527)	0.1 (1)	0.5 (3)
	Positive	AUG (46.5)	95.3 (41)	-	4.6 (2)
	Negative	P/T (6.6)	99.3 (742)	0.1 (1)	0.5 (4)
	Positive	P/T (55.8)	95.5 (65)	-	4.4 (3)
	Negative	LVX (5.4)	99.3 (716)	0.1 (1)	0.5 (4)
	Positive	LVX (31.7)	95.2 (60)	-	4.7 (3)

ETP: ertapenem; AUG: amoxicillin/clavulanic acid; P/T: piperacillin/tazobactam; LVX: levofloxacin.

remains justified. The selection of the type of carbapenem in intra-abdominal infections would depend on the type of patient, the possible origin of the infection and if *P. aeruginosa* infection was suspected[8,9]. Ertapenem, remarkable for its long half-life, is a good option for the treatment of intra-abdominal infections caused by ESBL-producing and AmpC hyperproducing enterobacteria and in patients not at risk of infection by *P. aeruginosa*[8,9]. In addition, the advantage of its introduction in hospital antibiotic formularies would be the absence of collateral effect or ecological impact on organisms with a naturally low susceptibility to ertapenem such as *P. aeruginosa*[29].

In summary, the microbiological data of the SMART study in Spain support the current therapeutic guidelines in intra-abdominal infections[9] which advocate ertapenem as the empiric treatment of choice for mild-moderate community-acquired infections, even those with unfavorable prognostic factors, including the risk of ESBL-producing enterobacteria.

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CONFLICTS OF INTEREST

Rafael Cantón has collaborated as speaker in educational meetings sponsored by MSD, AstraZéneca and Janssen-Cilag. All other authors declare that they have no conflicts of interest regarding this publication.

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