DESCRIPTIVE ANALYSIS AND UTILIZATION REVIEW OF MEROPENEM IN FIVE UNIVERSITY TEACHING HOSPITALS

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ABSTRACT

A substantial increase in meropenem use was recently observed in the five Québec university teaching hospitals. In 2010, the Therapeutic Drug Management Program was mandated to describe the use of meropenem and to make recommendations to promote optimal use.

METHODS - The study population was identified through the pharmacy databases. All patients who received at least one dose of meropenem between April 1st, 2009 and March 31st, 2010 were retrieved. Medical records were reviewed for indication, dosing, resistance data, comorbidities, concomitant antibiotic use, etc.

RESULTS - 2454 adults and 202 pediatric patients received meropenem during the study period. 1199 (48.7 %) and 170 (84 %) of adult and pediatric prescriptions were respectively written by an infectious diseases physician. Multiple comorbidities were observed in both adults and children (≥ 2 comorbidities in 66 % and 54 %, respectively). More than a third of the patients were in a critical care unit. Most frequent indications in adult and pediatric population were respectively respiratory tract (41 %) and wound infections (50 %). According to product monograph, a higher than recommended dose (eg. 1g q 8 h) was the most frequent observed discrepancy: 91 % of complicated soft tissue infections or UTI in adults, 53 % of complicated soft tissue infections and 100 % of UTI in children. However, this non conformity rate for both groups can be reduced if we use dosing recommendations suggested by other sources.

CONCLUSION - Meropenem was most commonly prescribed for severely ill patients. Poor compliance with dosing recommendations in many diagnoses was observed, with higher dosing generally used. Interventions to correct dosing and to use for appropriate indication would improve the utilization of meropenem as well as reduce costs.

INTRODUCTION

A substantial increase in meropenem use was recently observed in the five Québec university teaching hospitals. In 2010, the Provincial Therapeutic Drug Management Program (PGTM-www.pgtm.qc.ca) was mandated to describe the population who were prescribed meropenem and to precise its indications. The PGTM also conducted an evaluation to assess compliance with the criteria established by each hospital for this antibiotic.

METHODOLOGY

The study population was identified through pharmacy databases for all patients who received at least one dose of meropenem between April 1st, 2009 and March 31st, 2010. Due to the large number of adult patients, a sampling procedure was conducted. The final results presented are taking into consideration each center's weight as per its use and population. All paediatric patients were included. Medical records were reviewed for indication, dosing, resistance data, comorbidities, concomitant antibiotic use, etc.

For the drug use evaluation, criteria were established according to :

- the product monograph for the doses
- each hospital P & T decisions for the indications

Patients undergoing dialysis or other CRRT were excluded from the results of the drug utilization review.

TABLE 1
Patient Characteristics

		ADULT N = 2454 (%)	PAEDIATRIC N=202 (%)
SEXE	Women	1072 (43.7)	102 (50.5)
	Men	1382 (56.3)	100 (49.5)
Mean Age (median) [range]		60.43 (62.0) [18-95]	5.87 (2.37) [0-17.8]
PATIENT LOCALIZATION		%	%
Critical Care Unit *(emergency/intensive care unit)*		41.7	25.3
Medical Unit		17.6	29.7
Surgical Unit		11.9	3.5
Oncology Unit		12.6	21.8
Neonatal Unit		---	17.3
Other		16.2	2.4
NUMBER OF COMORBIDITIES		N (%)	N (%)
0		288 (11.7)	31 (15.3)
1		540 (22.0)	62 (30.7)
2		580 (23.6)	50 (24.8)
3		441 (17.9)	14 (6.9)
4		609 (24.8)	45 (22.3)

FIGURE 1
Most frequent comorbidities (%)

* COPD : chronic obstructive pulmonary disease
* ANC: Absolute Neutrophil Count
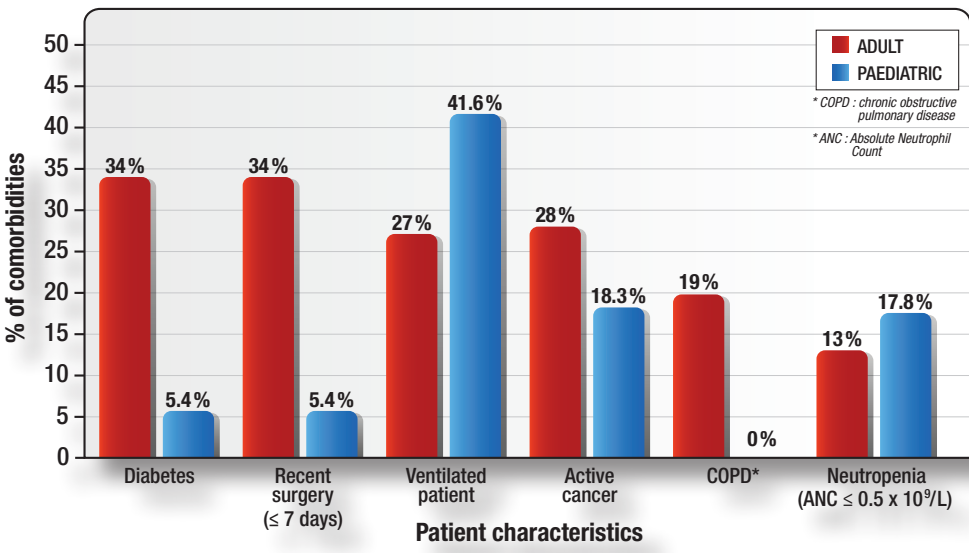
FIGURE 2
Availability of susceptibility/resistance data at initiation of meropenem *(all antibiotic agents)*

None 1463 (56.4%)
Susceptibility data > 7 days 235 (9.1%)
Susceptibility data ≤ 7 days 894 (34.5%)
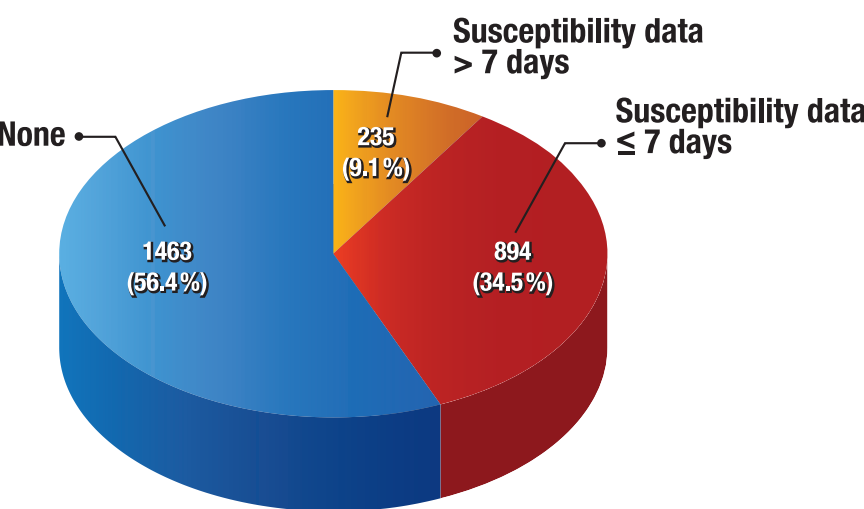
TABLE 2
Indications for meropenem use

NUMBER OF INDICATIONS	ADULT N (%)	PAEDIATRIC N (%)	MOST FREQUENT INDICATIONS	ADULT N (%)	PAEDIATRIC N (%)
0	26 (1.1)	1 (0.5)	RTI	1005 (40.9)	45 (22.3)
1	1922 (78.3)	160 (79.2)	Septicemia	490 (19.9)	67 (33.2)
2	414 (16.9)	31 (15.3)	Intraabdominal	345 (14.0)	32 (15.8)
< 2	92 (3.7)	10 (5)	UTI	303 (12.3)	17 (8.4)
			Skin / osteoarticular	275 (11.2)	11 (5.5)
			CNS	77 (3.1)	24 (11.9)

RTI: respiratory tract infection; UTI: urinary tract infection; CNS: central nervous system

TABLE 3
Antibiotic used in combination with meropenem

	N A	N P	AMINO-GLYCOSIDE A %	AMINO-GLYCOSIDE P %	PENI-CILLIN A %	PENI-CILLIN P %	QUINO-LONE A %	QUINO-LONE P %	TMP-SMX A %	TMP-SMX P %	VANCO A %	VANCO P %	OTHER A %	OTHER P %
RTI	1005	33	8.2	72.7	5.8	9.1	27.6	30.3	4.5	15.2	18.9	12.1	26.5	51.5
Septicemia /bacteriemia	490	67	4.5	65.7	2.4	11.9	19.2	3.0	6.5	7.5	21.2	31.3	29.2	41.8
Intraabdominal	345	32	2.3	37.5	3.2	3.1	15.9	25.0	7.5	9.4	23.8	21.9	35.1	56.3
UTI	303	17	6.9	35.3	2.6	5.9	10.6	0	5.3	0	13.5	11.8	9.6	23.5
Skin / osteoarticular	275	11	3.6	54.5	8.0	0	25.8	9.1	9.8	9.1	28.4	27.3	45.5	9.1
CNS	77	24	1.3	29.2	5.2	4.2	16.9	12.5	0	12.5	100	12.5	0	66.7

A : adult P : paediatric

FIGURE 3
Antibiotic Resistance Description for patients who received meropenem

Ps. aeruginosa

E. coli

S. aureus

Enterococcus
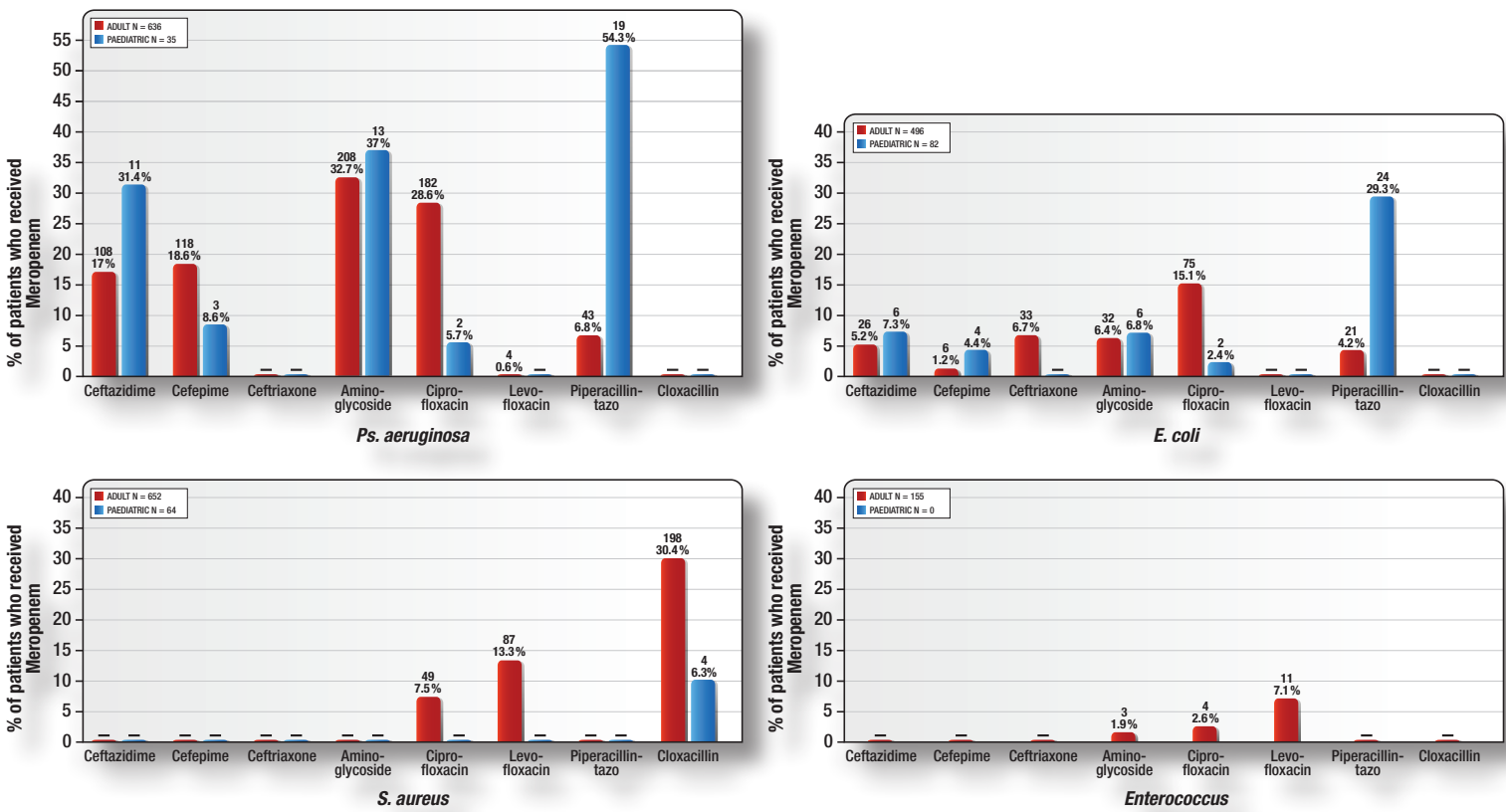
TABLE 4
Meropenem use information

INFORMATION	ADULT	PAEDIATRIC
Prescription by an infectious diseases physician	1199 (48.7 %)	170 (84 %)
Meropenem as initial monotherapy	104 (17 %)	6 (3.6 %)
Outpatient treatment	178 (7.2 %)	12 (5.9 %)
Mean duration of treatment (for all indications)	7.99 days median = 4 days	11.67 days median = 5 days
Reasons* for meropenem discontinuation / modification:		
- Spectrum adjustment	1802 (27.6 %)	281 (28 %)
- Infection resolution	1211 (18.6 %)	250 (24.9 %)
- Susceptibility/resistance	931 (14.3 %)	126 (12.6 %)
- Patient discharge	624 (9.6 %)	54 (5.4 %)
- Treatment failure	376 (5.8 %)	37 (3.7 %)
- Stepdown	420 (5.5 %)	18 (1.8 %)
- Death	229 (3.5 %)	27 (2.7 %)
- Side effect	225 (3.5 %)	14 (1.4 %)
- Other / Unknown	695 (10.7 %)	171 (17.1 %)

*: more than one reason could explain the discontinuation / modification

TABLE 5
Drug utilization review results

	MENINGITIS	NOSOCOMIAL PNEUMONIA / INTRAABDOMINAL INF / BACTERIEMIA	UTI / SKIN INF / CAP / PELVIC INFECTION	OSTEOARTI-CULAR INF / DIABETIC FOOT		MENINGITIS	UTI	SKIN INFECTION / CAP	INTRA-ABDOMINAL INFECTION
Appropriate dose*	2g IV q 8hrs	1g IV q 8hrs OR 500 mg IV q 8hrs	500 mg IV q 8hrs	1g IV q 8hrs	Appropriate dose*	40 mg/kg IV q 8hrs	10 mg/kg IV q 8hrs	10-20 mg/kg IV q 8hrs	20 mg/kg IV q 8hrs
Appropriate dose and frequency	60.7 %	64.4 %	1.4 %	60.7 %	Appropriate dose and frequency	85.7 %	0 %	46.7 %	45.8 %
Inappropriate dose	39.3 %	35.6 %	91.4 %	39.3 %	Inappropriate dose	7.1 %	100 %	53.3 %	50.0 %
Inappropriate frequency	6.4 %	35.6 %	26.2 %	6.4 %	Inappropriate frequency	7.1 %	4.5 %	20.0 %	8.3 %
Inappropriate dose + frequency	6.4 %	35.6 %	19.0 %	6.4 %	Inappropriate dose + frequency	0 %	4.5 %	20.0 %	4.2 %

UTI: urinary tract infection ; CAP: community acquired pneumonia infection
*: according to the monograph; dose adjusted to the renal function was required to be considered conform

CONCLUSION

Meropenem is a widely prescribed antibiotic in the five university teaching hospitals of the province of Québec. A severely ill population received meropenem during the study, as shown by the multiple comorbidities and the important number of deaths. This might explain why meropenem was mainly used in combination therapy. The study clearly demonstrated a poor compliance with dosing recommendations in many diagnoses, with a higher dosage than generally suggested. Inappropriate use of antibiotics and microbial resistance have always been a concern in hospitals. An antimicrobial stewardship program focusing on meropenem indication and dosing could result in significant improvement in both meropenem profile of use and would probably impact drug exependitures as well.

Le PGTm est une initiative des cinq centres hospitaliers universitaires du Québec