HOSPITAL RESISTANCE RATES AND ASSOCIATED ANTIBIOTIC DRUG CONSUMPTION RATES IN A TEACHING HOSPITAL

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BACKGROUND

- Antibiotics are used since 1942 to treat bacterial infections. Their use resulted in great diminution of bacterial infectious mortality during the last century.
- Resistance is defined as the capacity of a microorganism to grow and multiply Their use resulted in great diminution of bacterial infectious mortality.
- The relation between antibiotic consumption and the emergence of resistance was described 30 years ago. The antibiotic misuse is now a public health problem, governmental and learned societies stand for an appropriate use of antibiotics and implementation of antimicrobial stewardship program. Only few antibiotics have been approved over the past few years.
- Despite a global monitoring over the past ten years, relatively few data were published about antibiotic use and emergence of resistance among the paediatric population.
- We focused our study on most identified bacteria and the six types of bacteria which have been identified as global health threats (ESKAPE): *Enteroccocus faecium, Staphyloccocus aureus, Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter species*.

OBJECTIVES

- The objective of the study was to describe the profile of antibiotic consumption and bacterial resistances in a mother-child universitary hospital.

METHODS

- It is a retrospective, descriptive, cross-sectional study conducted over a five year period.

Inclusion criteria

- All pediatric patients

Exclusion criteria

- Patients from Gynecology-Obstetrics and nursery units

Bacterial resistances

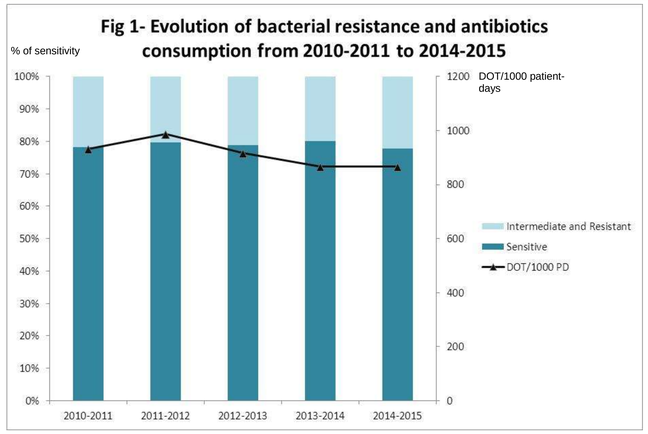
- All results of bacteriological samples from usually sterile biological liquids between april 1st 2010 and march 31st 2015 were included.
- Data were extracted from the laboratory software (Softlab®).
- Resistance rate were calculated for bacteria most found in samples and for bacteria identified as global health threats. Resistance rates between samples made before and after 5 days of hospitalization were calculated too.

Antibiotic conumption

- All antibiotic prescriptions provided by the pharmacy department between april 1st 2010 and march 31st 2015 were included.
- Patient pharmacological files (GespharX®) were used to extract data.
- Ratios of days of therapy/1000 patient-days (DOT/1000PD) were calculated for the five years.
- Presciption from extern clinics were excluded.

RESULTS

Fig 1- Evolution of bacterial resistance and antibiotics consumption from 2010-2011 to 2014-2015



- The global resistance rate (intermediate and resistant tests) was 21.8%, 20.3%, 21.1%, 19.9% and 22.2% from 2010 to 2015 respectively.
- Antibiotic consumption remained stable during the study period.

Table 1- Resistance rates evolution for the types of bacteria most identified (n>100 samples) from 2010-2011 to 2014-2015

Type of bacteria	Resistance rates					
	2010-2011	2011-2012	2012-2013	2013-2014	2014-2015	2015/2010 ratios
Escherichia coli	15.9%	13.8%	14.3%	13.8%	15.7%	0.99
Staphylococcus epidermidis	39.9%	37.4%	38.4%	35.5%	36.8%	0.92
Enterococcus faecalis	29.8%	28.0%	29.7%	24.6%	27.2%	0.91
Coagulase negative *staphylococci*	22.8%	26.7%	26.0%	24.0%	22.8%	1.00
Klebsiella pneumoniae	12.7%	16.4%	14.4%	14.9%	26.6%	**2.09**
Proteus mirabilis	10.5%	11.8%	17.6%	14.3%	17.7%	**1.69**
Pseudomonas aeruginosa	22.8%	21.3%	23.8%	19.6%	19.3%	0.85
Staphylococcus aureus	44.4%	41.2%	42.9%	44.8%	42.8%	0.96
Enterobacter cloacae	5.0 %	10.2%	8.0%	12.6%	14.1%	**2.82**
Klebsiella oxytoca	14.3%	13.7%	11.7%	10.8%	16.4%	1.15
Staphylococcus warneri	6.1%	13.9%	16.2%	21.4%	18.6%	**3.05**
Syaphylococcus hominis	17.3%	23.5%	22.0%	20.3%	20.5%	1.18

Table 2- Resistance rates depending on the date of sampling (less or at least five days after admission)

Date of sampling	Resistance rates				
	2010-2011	2011-2012	2012-2013	2013-2014	2014-2015
Less than five days after admission (n=8580 samples)	17.4%	16.1%	17.4%	17.3%	19.0%
At least five days after admission (n=1720 samples)	**31.0%**	**29.2%**	**31.4%**	**29.9%**	**33.6%**

- Samples made at least five days post-admission had bacterial resistance rates 1.7 to 1.8 fold higher than the samples made less than five after admission.
- Despite a global resistance rate which remained approximately stable, resistance rate of a few types of bacteria increase considerably (i.e *K. pneumoniae, E. cloacae, P. mirabilis*).

Table 3- Evolution of antibiotic consumption (DOT/1000 patient-days) and resistance rates to targeted antibiotics

P. aeruginosa		2011-2012	2012-2013	2013-2014	2014-2015
Fluoroquinolones	% Resistance	➡	⬆	⬇	➡
	Consumption	➡	⬆	⬇	⬆
Carbapenems	% Resistance	⬇	⬆	⬇	⬆
	Consumption	⬆	➡	➡	⬆
Ceftazidim	% Resistance	⬆	⬇	⬇	⬇
	Consumption	➡	➡	⬇	➡
Piperacillin-Tazobactam	% Resistance	⬆	⬇	⬆	⬆
	Consumption	➡	⬆	⬆	➡

E. coli		2011-2012	2012-2013	2013-2014	2014-2015
3rd and 4th generation cephalosporins	% Resistance	⬇	⬆	⬇	⬆
	Consumption	⬆	➡	➡	➡
Fluoroquinolones	% Resistance	➡	⬆	⬇	⬆
	Consumption	➡	⬆	⬇	⬆
Piperacillin-tazobactam	% Resistance	⬇	➡	⬇	⬆
	Consumption	➡	⬆	⬆	➡

K. pneumoniae		2011-2012	2012-2013	2013-2014	2014-2015
3rd and 4th generation cephalosporins	% Resistance	⬆	⬆	⬇	⬆
	Consumption	⬆	➡	➡	➡

⬆ Increase ⬇ Decrease ➡ Stability

- Variation trends evolved in the same way for consumption and resistances to fluoroquinolones (for *P. aeruginosa* and *E. coli*).

DISCUSSION

Antibiotic consumption evolution

- Antibiotic consumption remained stable during the study period (from 2010 to 2015) but the use of broad spectrum antibiotic and new antibiotic increased considerably.
- Suply disruption and practice changes were responsible for most of these increase.

Bacterial resistances evolution

- Global resistance rate did not change from 2010-2011 to 2014-2015, nevertheless for some bacteria, we notice an important increase in their resistance rates over the past five years.

Variation trends of resistance rates depending on antibiotic consumption

- Fluoroquinolone consumption seem to have an influence of bacterial resistance to this antimicrobial class, specially for *P. aeruginosa* and *E. Coli*.

Forces

- To our knowledge, it is the first study in pediatric population in Canada which try to establish correlation between resistance rate and antibiotic use. It is the first study using DOT/1000 patient-days to correlate antibiotic consumption and bacterial resistance.

Orientation of clinical practices

- This exploration will allow us to integrate these data in the antimicrobial stewardship program and rethink about clinical practices.

Limitations

- Despite the fact that DOT/1000 patient-days is more appropriate for pediatric population than Defined Daily Dose/1000 patient-days ratios, this mesure do not take into account the dosage of antimicrobials administered. This is an important bias when we know that an underdosing anti-infectious therapy can lead to an increase of bacterial resistances.

CONCLUSION

- This exploratory study is a first study allowing an evaluation of the evolution of antibiotic consumption and bacterial resistances. Some trends have been released to make further studies more targeted and with additional clinical and biological data. It also allows us to question clinical practices for antibiotic therapies and multi-resistant bacteria treatment.

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