Surveillance of healthcare acquired infections in hospital and community: a retrospective study in Local Healthcare Organization of Rovigo

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ABSTRACT

BACKGROUND: antimicrobial resistance is recognized as one of the greatest threats to human health worldwide. Infections caused by multidrug-resistant bacteria are associated with higher incidences of mortality, morbidity, prolonged hospital stay and increase of costs. Surveillance of alert organism/conditions and bacterial resistance to antimicrobials is a systematic and dynamic system of data collection that analyses and monitors trends of bacterial resistance. This study was conducted to detect antimicrobial susceptibility patterns in order to inform treatment choices and generate hospital-wide baseline data.

METHODS: the Local Healtcare Oganization of Rovigo has started a program of surveillance on antimicrobial resistance in hospital and community. In this work some results of the surveillance of microorganism isolated and related antimicrobial resistance are reported, collected in the period 2009-2010 in Rovigo and Trecenta Hospitals, Territorial Nursing Homes (TNH) and community from patients' blood, urine and respiratory samples.

RESULTS: data show a significant difference in the level of antibiotic resistance between the two Hospitals. High rates of extended-spectrum β-lactamase (ESBL)-producing organisms are detected and carbapenems are the only reliable agents for the treatment of many infections in the Hospital of Trecenta and TNH.

CONCLUSIONS: because ESBL producing bacteria are emerging pathogens in the community, the rational use of available antibiotics or the appropriate antimicrobial prescribing are imperative. Local surveillance is a powerful tool to detect and monitor hospital and community infections and provides information useful as a guide to medical practice, including therapeutics and disease-control activities.

Key words: Antimicrobial resistance; Surveillance; Local data

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INTRODUCTION

In the last decades, the prolonged and dubious antibiotic stewardship has increased the number of resistant microbial strains and, consequently, the risk of treatment failure with a real higher probability of dangerous events in patients. Not suitable therapeutic treatments, inappropriate empirical therapies and indiscriminate antibiotic stewardship even in the veterinary [1, 2] field, resulted in the emergence, spread and circulation of multidrug-resistant organisms (MDROs).

Following the National Health Plan 1998-2000 guidelines, in Local Healthcare Organization (LHO) of Rovigo, we achieved a qualified and well-integrated surveillance system to improve the antibiotic resistance monitoring and the control of healthcare nosocomial infections. Implementation of local guidelines and safe antibiotics stewardship are primary aspects in the reduction of social and economic costs linked to antimicrobial therapy.

In this context, Microbiology Laboratory have a crucial role in early identification of MDROs, sentinel events and in detecting trends of antibiotic resistance. Microbiologist helps clinicians to take decisions on rational treatments based on local epidemiological data [3].

The integration between international studies with local epidemiological data is mandatory, considering that substantial differences have been described by European countries, at national level, from region to region, hospital and hospital and among different departments in the same organization.

Recent data published by the EARS-NET (European Antimicrobial Resistance Surveillance) [4] network regarding Italian environment in the year 2009 show that 36% of strains of *E. coli*, Gram-negative organism mainly involved in hospital infections, are fluoroquinolones resistants. These data report for *Klebsiella pneumoniae* a percentage of resistance higher than 30% for third-generation cephalosporin and for carbapenemes. These antibiotics are frequently used for the treatment of severe infections caused by Gram-negative organisms in hospital, but their effectiveness is undermined by the emergence of new resistance mechanisms as the production of carbapenemase plasmid in bacterial species, such as *E. coli* and *K. pneumoniae* [5].

Even if the percentage of Methicillin-Resistant Staphylococcus Aureus (MRSA) is still high (34%), published data show a decreasing trend with a frequency ranges from 13% to 61%.

Diffusion of antibiotic-resistant *Streptococcus pneumoniae* in community is decreasing as a consequence of the spread of vaccination protocols. In European countries, as well as in the Veneto region, where the vaccine is offered free of charge, we are observing a steady downward trend of resistance to erythromycin and penicillin.

The introduction of new EUCAST guidelines (European Committee on Antimicrobial Susceptibility Testing) for European countries results in a rapid change of breakpoints and, accordingly, in the modification of interpretative criteria for antimicrobial sensitivity and resistance. The result will supply epidemiological data with substantial variations of resistance incidence for some antibiotics [6].

Also in our country we are slowly changing from old American CLSI (Clinical and Laboratory Standards Institute) [7] to new EUCAST guidelines. In this new dynamic scenario, infection control monitoring by detailed surveillance programs appears to be even more necessary both in hospital and at primary care level.

In this retrospective study, we investigated the local epidemiology of the antimicrobial resistance in the Local Healthcare Organization of Rovigo to provide a usefull guide for clinicians initiating the empiric antibiotic therapy.

METHODS

Setting and period

Rovigo LHO covers an area of 998 km^2 in size and 175 000 habitants in population, with a senility rate of 196% (one of the highest in Italy at 31.12.2010) [8]. Two public hospitals are present in this area: the first one, in Medio Polesine region, is called Rovigo Hospital (RH, 436 beds) and the second one, in Alto Polesine region and 30 km far away, is called Trecenta Hospital (TH, 208 beds). In TH there are a Sub Intensive Care Unit and a Hospital Nursing Home (HNH), in which the reintroduction of frail patient in his own family context or in one of territorial nursing homes is facilitate. TH has an elective activity to manage senility patients with multiple pathologies coming from

community or territorial nursing homes located in Alto Polesine region [9].

The study evaluates changes in antimicrobial resistance in the RH, TH, TNH and community during the period January 2009-December 2010.

Surveillance procedures

The Hospital Infection Control Committee (HICC) of Local Healthcare Organization, following the directives of the National Ministry of Health N. 52/1985 and N. 8/1988, has activated a specific program to contrast hospital infections. These directives included: the activation of surveillance programs for the continuous monitoring of sentinel microorganisms/events; the recommendations for an appropriate antibiotic stewardship; the implementation of procedures for the monitoring and management of outbreaks. Laboratory of Microbiology, Hospital Health Director Office, Infections Disease Department, and healthcare workers were all involved in this project. The aims of this program were:

- prompt identification of microorganisms resistant to antimicrobial agents;
- activation of rapid procedures based on scientific proofs, taking into account communication/information issues;
- collection of epidemiological data, set up of control measures and prevention of recurrence of the events;
- avoidance of clinical, epidemiological and legal risks linked to late outbreak identification;
- involvement of health workers in the identification and application of correct measures of prevention and control;
- promotion of an atmosphere of attention and awareness to the problem of Healthcare Associated Infections (HAI) including training courses for staff;
- continuous feedback among departments, Hospital Health Direction Office (HHDO) and HICC.

The first step we made was the creation of microorganism alert list based on microbiological and scientific data [10, 11]. We included:

- Multiresistant Gram-negative microorganisms with a sensibility to one or two classes of antibiotics: *Enterobacteriaceae* resistant to carbapenems, *Pseudomonas aeruginosa* and *Acinetobacter* spp. resistant to colistin, *Stenotrophomonas maltophilia* resistant to sulfamethoxazol-trimethoprim;
- Gram-positive microrganisms (*Staphylococcus* spp. and *Enterococcus* spp.) resistant to glycopeptides;
- *Legionella pneumophila* isolated in culture and/or with urinary antigens test positive;
- *Neisseria meningitidis*.

From our protocol we excluded MRSA and Gram-negative ESBL producers, because for these microorganisms a specific assessment is attivated by each department.

Microbiological methods

Epidemiological reports have been obtained using Mercury-Dianoema software with ALERT system that enables real-time identification of sentinel strains (alert on microorganisms) or sentinel events and situations (alert conditions) with clinical and epidemiological impact.

When alert microorganisms are isolated, HHDO is informed by final or preliminary report faxed by Laboratory of Microbiology. After that several actions occur:

- Notification of sentinel event to department concerned by fax and/or phone, providing also guidelines for event management (Standard precaution and Contact isolation). After this action, one internal mail is sent to Hospital Health Director Office, and Infection Disease Department.
- Check of the department concerned to verify that precautionary measures have been adopted by health workers.
- Use of our own checklist as first tool to check guideline for hospital infection prevention.

In addition to this surveillance activities, reports concerning territorial Nursing Homes and Community for the habitants of Rovigo Local Healthcare Organization area were generated. In the first step, we produced epidemiological data every six months. After that, we divided data from RH and TH to better understand individual local contexts. Due to the quantity of materials, we evaluated only urines, blood cultures and respiratory samples, while few surgical wound samples have been excluded. Bacteria and fungal infections have been identified with automated methods (Vitek2, bioMerieux) and

we have performed antibiotic susceptibility test with a system to determine minimal inhibitory concentration (M.I.C) (Sensititre®) and *breakpoint* values (Vitek2, bioMeriux).

We analyzed individually *P. aeruginosa, S. aureus, Klebsiella* spp., *E.coli, Enterococcus* spp as they showed high epidemiological relevance. Other bacterial strains have been evaluated by phylogenetic group to obtain more consistent statistical data.

Reports were elaborated by HICC and final file is published on our own intranet network.

Statistical analysis

Statistical analysis has been performed using Mercurio®, a commercial software for epidemiologic study, that is the result of the engineering of a research system involving Dianoema S.p.A. The data have been elaborated by Microsoft Excel in order to obtain information about bacteria incidence isolated and antimicrobial resistance.

RESULTS

Between January 2009 and December 2010, 23 991 urine samples, collected from RH, TH, TNH and Community, were examined at Clinical Microbiology Laboratory of Rovigo Hospital (Table 1). Samples positive to the cultural exam were 6 722 (28%). *E.coli* were the microrganism most frequently isolated during the 2010 ranged from 41.6% (TH) to 61% (Community) (Table 1). *Klebsiella spp* from 8.5% (TNH) to 9.4% (Community) and *Proteus mirabilis* from 3.7% (Community) to 21.7% (TNH).

The incidence level of *E.coli*, the principle cause of urinary tract infections, is prevalent in the hospitals and it is in increasing in TNH (+7%).

A strong presence of ESBLs producers strains has been detected in TH and TNH. The percentage of *Klebsiella* spp. and *Proteus mirabilis* strains isolated in TH is over 50%, while those found in TNH is over 60%. This percentage decreases when *Klebsiella* spp. and *Proteus mirabilis* strains are isolated in RH (from 30% to 37.5%).

Data on antibiotic resistance in *E. coli* and *Klebsiella* spp. isolated from all materials are listed in Table 2. Data shows that antimicrobial resistance increased in RH: third-generation cephalosporins (25.5%), fluoroquinolones (36.7%) and sulfamethoxazol-trimethoprim (36.1%). No carbapenemes resistant strains were detected in 2010. In TH, *E.coli* strains showed resistance percentages higher than

TABLE 1

TRENDS (2009-2010) IN THE INCIDENCE OF *E.COLI, KLEBSIELLA SPP, P.MIRABILIS* AND ESBLS PRODUCERS ISOLATED FROM URINE IN RH, TH, TNH AND COMMUNITY

YEARS	RH			TH			TNH			COMMUNITY		
	INCIDENCE		%ESBLS	INCIDENCE		%ESBLS	INCIDENCE		%ESBLS	INCIDENCE		%ESBLS
	N	%		N	%		N	%		N	%	
E. COLI												
2009	278	44.7	43.5	192	41.1	34.9	70	44.9	51.4	1 394	58.1	6.9
2010	299	43.5	23.5	236	41.6	41.5	67	51.9	41.8	1 242	61.3	7.2
KLEBSIELLA SPP.												
2009	72	11.6	34.4	49	10.5	57.1	18	11.5	67.7	214	8.9	11.2
2010	60	8.7	30.0	51	9.0	54.9	11	8.5	63.6	191	9.4	17.3
PROTEUS MIRABILIS												
2009	24	3.9	16.7	23	4.9	52.2	26	16.7	50.0	98	4.1	18.9
2010	32	4.7	37.5	52	9.2	53.8	28	21.7	67.8	74	3.7	29.7
TOTAL NUMBER OF ISOLATES												
YEARS	RH			TH			LTCR			COMMUNITY		
2009	622			467			156			2 397		
2010	686			567			129			2 026		

in RH and national levels: third-generation cephalosporins (45.5%), fluoroquinolones (60%) and sulfamethoxazol-trimethoprim (36.1%). These data confirm the possibility of variation among hospitals located in the same town and in similar departments. However, the detection of carbapenemes resistant strains have required the activation of surveillance protocols in TH.

Even if a decrease of resistance has been observed in Hospital Nursing Home and Territorial Nursing Homes compared to 2009, these values are still higher than the average observed in hospital environments. The percentage (>70%) of enterobacteriaceae resistant to fluoroquinolones found is alarming.

Tables 3 and 4 list the differences for antibiotic-resistances observed in *S. aureus* and *in P. aeruginosa* isolated in Rovigo and TH. Data obtained for *S. aureus* strains isolated in RH showed similar values to those published by EARS-NET. They also confirmed the decrease of MRSA strains (-13.4%) and the increase of fluoroquinolones (+6.6%) and gentamicin (+4.8%) resistance. Results found in TH contrast those observed in RH. The percentage of MRSA increased from 47.8% to 65.4%, even if the total number of isolated strain observed decreased.

The data obtained for *P. aeruginosa* strains isolated in RH showed an increase resistance to several antibiotics: carbapenemes (+8.1%), fluoroquinolones (16.7%) and gentamicin (6.4%). The percentages found in TH for these antibiotics are higher than those found in Rovigo, with the exception of piperacillin/tazobactam (which were at the same level), carbapenemes (which decreased by 27%) and ciprofloxacin (which increased by 54%).

The impact of the most frequent microorganism isolated in blood cultures was also analyzed (Table. 5). During this study, a high increase of Gram-negative in both hospitals (Rovigo, 5.8% and Trecenta 9.1%) was observed. The result in TH showed that the percentage of isolation of *E. coli* ESBL producers was 60%, a level that makes the use of beta-lactams problematic.

The percentage of isolation of *P. aeruginosa* decreased by more than 2% in Rovigo and

TABLE 2

TRENDS (2009-2010) IN PERCENTAGE OF ANTIBIOTIC RESISTANCE OF *E. COLI* AND *KLEBSIELLA SPP.* ISOLATED FROM RH, TH AND TNH

Antibiotic	RH		TH		TNH	
	E.coli	*Kleb. spp*	*E.coli*	*Kleb. spp*	*E.coli*	*Kleb.spp*
Ceftazidime						
2009	22.5%	26.8%	39.6%	60%	51.8%	68.4%
2010	25.5%	25%	45.5%	49.4%	47.6%	63.6%
Cefotaxime						
2009	22.5%	26.8%	39.6%	60%	51.8%	68.4%
2010	25.5%	25%	45.5%	49.4%	47.6%	63.6%
Ciprofloxacin						
2009	31.8%	33.8%	54.9%	69.5%	80.2%	84.2%
2010	36.7%	24.1%	60.3%	50.7%	78%	72.7%
Gentamicin						
2009	19%	17.6%	31%	44.7%	50.6%	68.4%
2010	16.2%	13.1%	34.7%	48.1%	34.1%	63.6%
Carbapenemes						
2009	0.5%	0.7%	0.0%	2.3%	2.5%	0%
2010	0%	0%	1%	1.3%	0%	0%
Sulfamethoxazol-trimethoprim						
2009	33.7%	28.1%	42.5%	50.6%	48.1%	57.9%
2010	36.1%	23.2%	46.1%	40.3%	18.8%	36.4%

TABLE 3

TRENDS (2009-2010) OF ANTIBIOTIC RESISTANCE OF *S. AUREUS* ISOLATED FROM RH, TH, TNH

Antibiotic	RH	TH	TNH
Oxacillin			
2009	32.4%	47.8%	71.4%
2010	19%	65.4%	100%
Gentamicin			
2009	23.8%	42%	42.9%
2010	28.6%	45.4%	66.7%

TABLE 4

TRENDS (2009-2010) OF ANTIBIOTIC RESISTANCE OF *P. AERUGINOSA* ISOLATED FROM RH, TH, TNH

Antibiotic	RH	TH	TNH
Piperacillin/Tazobactam			
2009	26.1%	30.0%	30%
2010	21.9%	30.5%	25%
Ciprofloxacin			
2009	26.1%	51.5%	40%
2010	42.8%	54%	62.5%
Gentamicin			
2009	15.8%	37.7%	20%
2010	22.2%	33.6%	37.5%
Carbapenemes			
2009	18.9%	36.9%	10%
2010	27%	31.5%	37.5%

TH while the incidence of coagulase-negative staphylococci was stable at 33% with a reduction of 2.7% in Rovigo and 6.4% in TH. A lot of coagulase-negative microorganisms isolated in single bottle from blood cultures are classified as contaminants during the sampling phase because they are often present in the skin of patients. The decrease observed could be due to the use of aseptic techniques during sampling by operators that received specific training courses regarding this issue. *Candida* spp. was found to be higher (+5.1%) in TH than in Rovigo and there was a significant increase with respect to the previous year (+3.5%).

Nine case of sentinel events have been observed in 2010. Seven of these events have been observed in TH. Microorganisms isolated from patient were: *A. baumannii*, MDR (3 isolates from bronchial washing, 2 from sputum, 1 from peritoneal fluid), one strain MDR *E. coli* (blood culture), one *E. faecalis* resistant to vancomycin (blood culture), one MDR *P. aeruginosa* (bronchial washing).

For all nine cases, procedure programs of containment interventions were activated as described above.

DISCUSSION

The epidemiological data of 2010 compared with 2009 highlight some critical issues concerning the appropriateness and quality of sampling, the widespread dissemination of epidemiological data, clinical awareness of adherence to therapeutic treatments on the basis of local data and new interpretative criteria proposed by EUCAST. The incidences of microorganisms isolated from urine specimens are stable and consistent with the literature data. New strains of *E. coli* and *Klebsiella spp.* resistant to carbapenemes, most frequently isolated, require special attention and continuous monitoring to limit the spread. In fact, carbapenemes are used for the Gram negative infections mainly for ESBL producer strains, belonging to CTX-M [12] group and showing strong hydrolytic activity against cefotaxime and ceftazidime.

In TH and Territorial Nursing Homes, ESBL producers are frequently isolated also in blood culture, therefore a carbapenemes-base therapy could be less effective. The high resistance detected can be explained by the high elderly population. These patients showed higher risk of infection due to a reduced immune defenses, presence of disadvantageous physiological factors (age, disease chronic pathologies), prolonged antibiotic treatment and use of invasive medical devices [13]. Epidemiological local data and antimicrobial stewardship polices allow the clinician to better assess which terapy to administer in order to avoid the emergence of carbapenem-resistant strains [14].

An appropriate approach to blood culture collection has resulted in a decreased number of coagulase-negative staphylococci isolated in both Hospitals and may contribute to a significant share decrease of samples with contamination. In order to improve the results, health workers were trained to explain microbiological guidelines for blood culture management and sample collection.

Epidemiological data highlighted the increased incidence of Gram-negative bacteria.

In particular, an increase of *E. coli* and third-generation cephalosporins was detected in both hospitals. This observation reduced the use of third-generation cephalosporins in the therapies administered. The treatment of *E. coli* strains resistant to fluoroquinolones suggest a policy of "molecules saving". Treatments with fluoroquinolones should be limited to severe infections. The administration of last generation antibiotics, such as glycopeptides and carbapenems, can be justified in Intensive Care Unit (ICU), in patients at high risk or when there are no effective treatment options. ESBL producer strains have been isolated not only in the hospitals but also in the community: 7.2% *E.coli*, 17.3% *Klebsiella* spp. and 29.7% *P. mirabilis.*

The percentage of *E. coli* and *Klebsiella* spp. fluoroquinolones-resistant (>70%) makes this family of antibiotics almost useless for the treatment of infections in hospitalized patients in TNH. The surveillance system adopted by Rovigo LHO was born as a direct consequence of the spread of the principles of empirical medicine and the introduction of process improvement and quality assurance in healthcare facilities. This system was essential in the prompt management of "sentinel events", in the control of infection clusters and in the possibility of calculating the standard measures applied.

The study has several noteworthy limitations: first, inherent limitations regarding the methodological aspects of retrospective studies should be considered; second, the duration of the study period may not be long enough to see the changes in antimicrobial resistance and the results may not be generalizable to other health institutions in Veneto.

Although our study has afore-mentioned limitations, the probability of outbreaks was found to be higher in TH. This result was mostly due to the type of patient admitted (mostly elderly), who tend to have a history of chronic pathologies, prolonged antibiotic treatments and in some case are affected by MDROs strains. The procedures activated in these cases have been successful because no outbreaks have been detected.

CONCLUSIONS

The Epidemiological surveillance study has allowed monitoring of local hospital environments, helped to highlight the differences between hospitals, TNH and point-of-care and underlined the main problems of antibiotic resistance.

The results obtained provide an up-dated picture of epidemiological framework, improving new discussions for the monitoring strategies with an evidence-based approach. Even if this model is now applied only in few departments, it could be implemented in other areas. Epidemiological observations represent an effective reference tool for clinicians (hospital and general practitioners) to manage treatment decisions based on local data. General practitioners have been informed regarding the antibiotic resistance findings in the Rovigo area, in order to limit the prescription of specific antibiotics when resistance exceeds a certain threshold.

The problem concerning antibiotic resistance is due to the in-appropriate use of antibiotics [15] that can select MDR strains also at community level. The diffusion of information, including precaution measures, the identification and isolation of infected patients by MDROs are essential tools for the control of outbreaks [16]. In this context, the HICC has a determining role in the prevention and management of hospital infections.

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