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Strategies to control antibiotic resistance: results from a survey in Italian children's hospitals

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Parole chiave: Antimicrobial stewardship, infezioni correlate all'assistenza, bambini, indagine, antibiotico-resistenza

Abstract

Background. *Antimicrobial stewardship programs and comprehensive infection control programs represent the main strategies to limit the emergence and transmission of multi-drug resistant bacteria in hospital settings. The purpose of this study was to describe strategies implemented in Italian children's hospitals for controlling antibiotic resistance.*
Study design. *Cross sectional multicenter study.*
Methods. *Four tertiary care Italian children's hospitals were invited to participate in a survey aimed at collecting information on activities implemented as of December 2015 using a self-administered online questionnaire. The questionnaire was divided in three sections focalizing on: i) policies for prevention and control of hospital-acquired infection, ii) prevention and control of multi-drug resistant bacteria, and iii) antibiotic prescribing policies and Antimicrobial stewardship programs. Questionnaires were compiled between May and July 2016.*
Results. *All hospitals had multidisciplinary infection control committee, procedures on hand hygiene, isolation measures, disinfection/sterilization, waste disposal and prevention on infections associated to invasive procedures. All sites screened patients for multi-drug resistant bacteria colonization in selected units, and adopted contact precautions for colonized patients. Screening during hospitalization, or in case of infections in the same ward were not universally implemented. All hospitals had policies on surgical prophylaxis, while policies on medical prophylaxis and treatment of bacterial infections varied among sites. Two sites recommended to review the appropriateness of antibiotic prescribing after 48-72 hours and one recommended de-escalation therapy.*

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Conclusions. *This study highlighted several areas of improvement, such as actions for screening patients in case of occurrence of multi-drug resistant bacteria, antimicrobial stewardship programs and implementation of policies targeting antibiotic prescriptions for therapeutic purposes and medical prophylaxis.*

Introduction

Antibiotic-resistant pathogens constitute an important and growing threat to public health (1); in fact, more than half a million deaths per year are estimated as attributable to antibiotic resistance (2).

Inappropriate use of antibiotics is the main risk factor for the emergence and spread of multidrug resistant (MDR) microorganisms, particularly in the hospital setting, where antibiotic pressure is found at its highest levels (3). Antimicrobial stewardship and comprehensive infection control programs have contributed to limit the emergence and transmission of antimicrobial-resistant bacteria (4).

Antibiotics are among the drugs most commonly prescribed to children, and are often used to treat common conditions generally caused by viral agents, against which antibiotics are mostly ineffective (5). Several studies have reported overuse of broad spectrum antibiotics and excessively prolonged surgical antibiotic prophylaxis in hospitalized neonates and children (6, 7). Recommendations for antimicrobial stewardship programs (ASPs) specific to pediatrics have been authored (8, 9) and several studies have shown that ASP programs in pediatric institutions had favorably affected antibiotic use (10-13).

Italy is a country with high antibiotic consumption and high prevalence of antimicrobial resistant bacteria, including carbapenem-resistant Enterobacteriaceae (CRE) and Methicillin-resistant Staphylococcus aureus (MRSA) (14, 15).

Studies investigating infection control programs and ASPs in hospitals highlighted wide variations by geographical area and type of hospital (16-19). Few data on actions implemented in children's hospitals have been published up to now (20, 21). In 2014, the Center for Diseases Control of the Italian Ministry of Health funded the Project "Good Practices for surveillance and control of antibiotic-resistance" which was aimed to: a) identify the "best practices" for surveillance and control of antibiotic-resistance, and b) harmonize and share the collected practices with other contexts (22). As part of this national project, we conducted a survey to describe strategies implemented in Italian children's hospital to control antibiotic resistance.

Methods

Study design and setting

This survey was conducted between May and July 2016 and involved four Italian children's hospitals, i.e. Ospedale Infantile Regina Margherita (Turin, Piedmont), Ospedale dei Bambini di Brescia (Brescia, Lombardy), Meyer Children's Hospital (Florence, Tuscany) and Bambino Gesù Children's Hospital (Rome, Latium). These hospitals were selected to participate in the study because they are stand-alone tertiary care children's hospitals located in Regions participating in the above reported national Project.

Survey instrument

We developed a web-based multiple-choice questionnaire, which explored actions recommended to control MDR bacteria in hospital settings (4, 23-27).

The questionnaire included information on hospital characteristics and three further sections. The first one investigated policies for prevention and control of healthcare associated infections (HAI), including infection control committee, hand hygiene, isolation measures, disinfection and sterilization, waste disposal, prevention of infections associated with invasive procedures [i.e. central line-associated bloodstream infections (CLABSI), ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections (CUTI), surgical site infections (SSI)], and surveillance of HAI. The second section concerned policies for prevention and control of MDR bacteria, including screening of CRE or MRSA carriers, adoption of contact precautions, and MRSA decolonization. The third section collected information on antibiotic prescribing policies and implementation of ASPs (e.g. multidisciplinary team, antibiotic prescription guidelines, appropriateness review of antibiotic prescriptions after 48-72 hours, de-escalation therapy, pre-authorization requirements and audit of antibiotic use, antibiotic consumption indicators).

All the collected information referred to the practices implemented as of December 2015. Data were analyzed using Microsoft Excel 2013.

Results

Characteristics of respondents

Characteristics of participating hospitals are shown in Table 1. All hospitals had pediatric and neonatal intensive care, onco-hematology and pediatric surgery units. The hospital total number of inpatient beds ranged from 214 to 607. The annual number of inpatients admissions and surgery procedures varied from 5,661 to 27,336 and from 2,682 to 35,192, respectively.

Policies for HAI prevention and control

A multidisciplinary infection control committee (ICC) was in place in all the participating sites, and always included an infectious disease physician, an epidemiologist, an infection control nurse and a clinical microbiologist. Other professionals participating to ICC varied by site and included pharmacists (3 sites out of 4), physicians from clinical wards (2 sites), quality and safety managers (2 sites), nurses from clinical wards (1 site) and occupational health physicians (1 site). ICC met quarterly in two sites, monthly in one site, and annually or in case of critical events in the remaining site.

All hospitals had policies on hand hygiene, isolation measures, disinfection and sterilization, waste disposal, prevention of

Table 1 - Characteristics of participating children's hospitals, 2015

	Hospital 1	Hospital 2	Hospital 3	Hospital 4
Total number of beds	277	245	607	214
Number of beds by ward type				
Pediatric Intensive Care Unit	10	15	30	5
Neonatal Intensive Care Unit	16	22	22	34
Neonatal pathology	175	0	15	50
Oncohematology	42	30	33	8
Surgery	48	74	187	21
Number of inpatient admissions	5,661	8,898	27,336	8,805
Number of surgical procedures	2,682	7,572	35,192	4,065

Table 2 - Policies for HAI prevention and control by participating Hospitals, 2015

	Hospital 1	Hospital 2	Hospital 3	Hospital 4
Hand Hygiene	X	X	X	X
Isolation measures	X	X	X	X
Disinfection/Sterilization	X	X	X	X
Waste disposal (including biological waste)	X	X	X	X
CLABSI prevention	X	X	X	X
VAP prevention	X		X	X
CUTI prevention	X		X	X
SSI prevention	X	X	X	X

CLABSI: central line-associated bloodstream infections; VAP: ventilator-associated pneumonia; CUTI: catheter-associated urinary tract infections: SSI: surgical site infections

CLABSI and SSI. Policies on prevention of VAP and CUTI were implemented in three sites (Table 2).

Two sites conducted HAI point prevalence surveys annually, and one site every two years; the remaining site conducted prevalence survey of SSI every three years. Three sites also carried on surveillance of HAI incidence. HAI surveillance data were posted on the hospital intranet (3 sites), or e-mailed to physicians and nurses responsible of wards (1 site).

Policies for prevention and control of MDR bacteria

To screen for CRE or MRSA colonization, all hospitals performed rectal and nasal swabs in patients hospitalized in intensive care units and other high-risk units (e.g. transplant units, onco-hematology units), on admission and discharge.

During hospitalization in these units, patients continued to be screened for CRE on a regular basis in three sites, and for MRSA in two sites. In case of occurrence of infections due to MDR, three sites had policies for screening all patients hospitalized in the same ward. Two sites performed mupirocin decolonization of MRSA nasal carriers (Table 3).

All hospitals adopted contact precautions for patients identified as CRE or MRSA positive; these included antiseptic hand hygiene, use of gloves, gowns, single rooms or cohort, and dedicated patient equipment. Adoption of contact precautions was actively verified by the ICC team. In three sites, the adoption of contact precautions was notified on the patient room door and in clinical records. One site implemented a structured hand-over process to communicate information on contact precautions whenever a CRE or MRSA positive patient was transferred to a different ward. In two sites patients and their caregivers received written information regarding precautions to be adopted after discharge.

Antibiotic prescribing policies and implementation of antimicrobial stewardship programs

A multidisciplinary antimicrobial stewardship team was established in three sites (Table 4), and involved an infectious disease physician, an epidemiologist, a pharmacist and a microbiologist. Guidelines on antibiotic prescriptions were available in all sites; all hospitals implemented guidelines on surgical antibiotic prophylaxis, while implementation of recommendations regarding medical prophylaxis and antibiotic use for therapeutical purposes varied by hospital.

Table 3 - Policies regarding screening of carriers of CRE (**A**) and MRSA (**B**) by participating Hospitals, 2015

	Hospital 1	Hospital 2	Hospital 3	Hospital 4
Screening of carriers (rectal swabs) at admission/discharge	A/B	A/B	A/B	A/B
Intensive Care Units	A/B	A/B	A/B	A/B
Other high risk Units*	A/B	A/B	A/B	A/B
Screening of carriers during hospitalization	A/B		A	A/B
Screening of carriers in case of occurrence of CRE infections		A/B	A/B	A/B
Mupirocin decolonization in carriers		B	B	

* Onco-hematology, pneumology, cardiac surgery, transplant, bone marrow transplant ward, medical and surgical neonatology, surgery were reported as high risk Units for CRE. Hematopoietic stem-cell transplant center, onco-hematology, bone marrow transplant ward, cardiology were reported as high risk Units for MRSA

Antibiotic prescriptions were reviewed after 48-72 hours in two hospitals; one hospital had also policies on de-escalation therapy.

Formulary restriction and preauthorization requirements were adopted in three sites for specific antibiotic molecules as carbapenems (3 sites), linezolid, tygeciclin and daptomycin

Table 4 - Antibiotic prescribing policies and antimicrobial stewardship programs (ASP) by participating hospitals, 2015

	Hospital 1	Hospital 2	Hospital 3	Hospital 4
ASP team	X		X	X
Antibiotic prescription guidelines	X	X	X	X
Pneumonia	X			X
Urinary tract infections	X			X
Skin infections				X
Sepsis	X			X
Surgical prophylaxis	X	X	X	X
Medical prophylaxis			X	X
Appropriateness review of antibiotic prescriptions		X	X	
Recommandations on de-escalation therapy			X	
Pre-authorization requirements	X	X	X	
carbapenems	X	X	X	
glycopeptides				
linezolid		X	X	
tigecycline		X	X	
colistin				
daptomycin		X	X	
Other molecules (e.g. third generation cephalosporins, clindamycin.)	X			
Audit of antibiotic use	X		X	X

(2 sites), third generation cephalosporins and clindamycin (1 site). Prospective audits of antibiotic use were conducted in three sites.

Three sites out of four monitored antibiotic consumption. Antibiotic use was mainly expressed in terms of point prevalence of prescriptions (2 sites), use-associated costs (3 sites) and defined daily dose (1 site). Days of therapy (DOT) and length-of-therapy (LOT) had not been adopted as indicators of antibiotic consumption. None of the participating hospitals had tools for computer based prescribing.

Discussion and Conclusions

Results from this survey show variability in strategies to control antibiotic resistance in hospitalized children. Despite all sites participating to this study have multidisciplinary ICC that include essential professional figures (i.e. infectious disease specialist, hospital epidemiologist, nurse and clinical microbiologist) (28), pharmacists have been shown to be crucial to improve appropriateness of antibiotic prescriptions (4, 29), but they are not universally involved in ICCs. Procedures on hand hygiene, isolation measures and disinfection/sterilization are available in all the participating sites, and all of them also monitor hand hygiene adherence. Methods used to collect data on hand hygiene adherence were not investigated in the present study; however, this issue should be further addressed since compliance to hand hygiene results fluctuate with the method used for monitoring (30).

Data collection on susceptible profiles of microorganism isolated from patients admitted to the hospitals is important to provide timely antimicrobial resistance (AMR) data for policy decisions and to analyse temporal trends of AMR (15). Similarly, detection of CRE/MRSA carriers is crucial to implement contact precautions aimed at limiting in-hospital transmission of multidrug resistant bacteria. According to our results, policies on screening of MDR carriers do also differ by hospital. Intensive care, onco-hematology and transplant units were most frequently considered as high-risk units for MRSA/CRE screening, since patients are at high risk of serious MRSA/CRE infections and high proportion of MRSA/CRE infections among colonized patients have been documented (25, 31). Other differences in type of units considered at high risk and selected for routine screening of CRE/MRSA carriers may be due to local hospital epidemiology of MRSA/CRE (25, 26).

However, all hospitals should actively search for carriers in a ward, whenever a case of CRE/MRSA occur (32). We also found variability in hospital policies concerning nasal decontamination in MRSA carriers (33). Recommendation on MRSA decontamination were not universally shared; however, several national and international guidelines suggested to perform nasal decontamination of all patient MRSA-positive (32, 34) and in particular of those with a higher risk of developing infections (25, 27, 35).

Major concern is related to the implementation of antimicrobial stewardship programs. In particular, only 2 sites reviewed antibiotic therapy after 48-72 hours and only one had procedures focusing on de-escalation therapy, which are recommended by IDSA guidelines (4). Whilst all sites have surgical antibiotic prophylaxis guidelines, the degree of variability in guidelines regarding medical prophylaxis and antibiotic treatments is substantial and could represent a leading factor for appropriate choice of antibiotic molecules, combination therapies and duration of administration (13, 36). IDSA guidelines strongly recommended the implementation of local antimicrobial guidelines since clinical pathways were proved to be useful for the improvement of several diseases management (37).

Reliable statistics on consumption of antibiotics are useful to hospitals for performing internal assessments (such as consumption trends over time) and making comparisons with others (38). Three sites reported to have established metrics for the quantification of antibiotic consumption. Defined Daily Dose was used in one site even if this methodology is not applicable to the pediatric population (39); the other two sites monitored costs associated to antibiotic consumption. Metrics that are considered to be more specific for pediatric population (e.g. DOT and/or LOT) (40) should be implemented to obtain reliable data for monitoring antibiotic consumption in hospitalized children. To this regard, the use of tools for computer based prescribing should be promoted.

This study has some limitations. Local policies were assumed to be based on international and national recommendations, though the survey did not investigate which were the evidence based guidelines used as references. Infection control activities and ASPs implementation may have been overestimated, given that data collection was based on self-administered questionnaire completed by those responsible for these actions (16). To this regard, results obtained from this survey should be complemented with process and outcomes indicators such as consumption data of alcohol-based hand rub, antibiotic consumption, incidence of HAI and infections due to MDR bacteria. Moreover, this study involved tertiary care stand alone children's hospitals in Regions participating to a national project focused on antimicrobial resistance; thus we cannot assume that our results are representative of the policies implemented in other Italian hospitals taking care of children.

In conclusion, this survey showed that MDR infection control policies and ASPs have been implemented, although areas of improvements have been highlighted. Performing such surveys over time could possibly help in understanding quality improvements and to share best practices among different organizations.

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Competing interests

None declared

Ethical approval

Not required. This is a survey only aimed at describing strategies implemented in the participating hospitals for controlling antibiotic resistance. No demographic or clinical data of hospitalized patients were collected and/or analyzed.

Riassunto

Strategie per il controllo dell'antibiotico resistenza: risultati di un'indagine condotta in ospedali pediatrici italiani

Introduzione. I programmi di Antimicrobial Stewardship e le azioni per il controllo delle infezioni ospedaliere rappresentano le principali strategie per limitare l'emergenza e la trasmissione di batteri multiresistenti nelle strutture ospedaliere. L'obiettivo di questo studio era descrivere le buone pratiche in atto negli ospedali pediatrici italiani per il controllo dell'antibiotico-resistenza.

Disegno dello studio. Indagine trasversale conoscitiva multicentrica.

Metodi. Quattro ospedali pediatrici italiani sono stati invitati a partecipare ad un'indagine conoscitiva che prevedeva la compilazione di un questionario on-line composto da tre sezioni riguardanti: i) le politiche per la prevenzione e il controllo delle infezioni acquisite in ospedale, ii) la prevenzione e controllo dei batteri multiresistenti e iii) politiche di prescrizione di antibiotici e Antimicrobial Stewardship. I questionari sono stati compilati tra maggio e luglio 2016 e facevano riferimento alle attività implementate nell'anno 2015.

Risultati. Tutti gli ospedali avevano istituito un comitato multidisciplinare per il controllo delle infezioni e redatto procedure per l'igiene delle mani, le misure di isolamento, la disinfezione/sterilizzazione, lo smaltimento dei rifiuti e la prevenzione delle infezioni associate a procedure invasive. In tutti gli ospedali erano

presenti procedure per lo screening dei portatori di batteri multiresistenti al momento del ricovero dei pazienti in Unità Operative ad alto rischio. In caso di infezioni o colonizzazioni da batteri multiresistenti, tutti i centri adottavano precauzioni da contatto. L'attività di screening dei pazienti durante il ricovero in ospedale, o in caso di infezioni insorte nello stesso reparto di degenza, non era stata implementata in maniera universale. Tutti gli ospedali avevano adottato politiche sulla profilassi chirurgica, mentre la disponibilità di procedure sulla profilassi medica e sul trattamento delle infezioni batteriche variava tra i diversi centri. In due ospedali esisteva una procedura per la verifica dell'appropriatezza prescrittiva dopo 48-72 ore e uno dei due prevedeva raccomandazioni sulla de-escalation therapy.

Conclusioni. Questo studio ha evidenziato diverse aree di miglioramento, tra cui la necessità di implementare: 1) azioni per lo screening dei pazienti in caso di infezioni da batteri multiresistenti nello stesso reparto di degenza, 2) Antimicrobial Stewardship e 3) politiche sulla prescrizione antibiotica per fini terapeutici e per la profilassi medica.

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