ORIGINAL ARTICLE

Hospital discharge in patients at risk of surgical site infection: antimicrobial stewardship at Ferrara University Hospital, Italy

P. ANTONIOLI[1], A. FORMAGLIO[2], D. GAMBERONI[2], L. BERTONI[2], P. PERRONE[2], A. STEFANATI[3], M. LIBANORE[4], R. CULTRERA[5], G. GABUTTI[3]

[1] Department of Hospital Hygiene & Healthcare Associated Infection Risk Management, Coordination of Clinical Health Promotion Activities, Hospital Health Medical Management, Ferrara University Hospital, Ferrara, Italy; [2] Postgraduate School of Hygiene and Preventive Medicine, University of Ferrara, Italy; [3] Section of Public Health Medicine, Department of Medical Sciences, University of Ferrara, Italy; [4] Hospital Infectious Diseases Clinic, Ferrara University Hospital, Ferrara, Italy; [5] University Infectious Diseases Clinic, Ferrara University Hospital, Ferrara, Italy

Keywords

Antimicrobial stewardship • Surgical patients • Hospital discharge • Surgical site infections

Summary

Introduction. *The appropriate use of antibiotics is a global priority in order to avoid antibiotic resistance. Up to 50% of antibiotics usage in hospital is inappropriate (e.g. prolonged surgical prophylaxis, "defensive medicine" approach). In 2015, at the Ferrara University Hospital, an antimicrobial stewardship intervention to reduce antimicrobial prescription at the time of hospital discharge in patients at risk of surgical site infection was implemented. This programme included: update meetings for health professionals, focused meetings for critical wards, reviews of some surgical prophylaxis protocols, recommendations to reduce broad-spectrum antimicrobials use, and planning of an audit. The purpose of this study has been to evaluate the effect of this antimicrobial stewardship programme.*

Methods. *To evaluate the effect of this intervention, a study has been carried out including inpatients in surveillance for surgical site infection who had surgery during the last quarter of 2014 (pre-intervention group; 461 patients) and of 2015 (post-intervention group; 532 patients).*

Results. *The proportion of patients with prescription of at least one antimicrobial at discharge decreased from 33% to 24.4% ($p = 0.002$). The most prescribed categories of antimicrobials in both groups were the combination of penicillins with beta-lactamase inhibitors (with prescription rate reduced from 21.9% to 18%; $p = 0.13$) and fluoroquinolones (from 8.2% to 3.2%; $p < 0.001$).*

Conclusions. *This statistically significant reduction in antimicrobial prescription after the intervention was registered without a change in surgical site infections rate (from 3.5% to 3.2%; $p = 0.08$). Therefore, this intervention was effective in reducing the antimicrobial prescription at discharge, without affecting patients' safety.*

Introduction

The rapid worldwide antibiotic-resistant bacteria spread is affecting the efficacy of antibiotics [1, 2]. Antibiotic resistance mainly results from the excessive and inappropriate use of antibiotics [1, 3]. The consumption of antibiotics is globally increasing every year, creating the preconditions of a global public health emergency [4].

Antibiotic resistance causes an increase in morbidity and mortality as well as an increase in hospitalizations and costs [5, 6]. In Europe, infections sustained by antimicrobial resistant germs cause about 25,000 deaths every year and a cost of at least 1.5 billion euros [6, 7].

Appropriate use of antibiotics can help to counteract bacteria-resistance development and to preserve drug's efficacy for the use in the future [8]. Since a long time, the international scientific community has underlined the need to hinder this phenomenon and to sustain the proper use of antibiotics, that is their targeted, rational and moderate use [9]. Despite these international guidelines, it is estimated that about 20-50% of antibiotics usage in acute-care hospitals is either unnecessary or inappropriate [10]. This phenomenon unnecessarily exposes patients to potential side effects of antimicrobial therapy [11].

Italy is among the European countries with the highest levels of antibiotic resistance and with the highest use of antibiotics both in the community and in the hospital setting [6, 7, 12].

In the hospital setting, about 40-50% of all antibiotic prescriptions involves peri-operative antibiotic prophylaxis [13], which is one of the tools to reduce the incidence of surgical site infections (SSI) [14].

According to guidelines in use and to scientific evidence, surgical prophylaxis should be limited to perioperative period, be given immediately prior to the onset of surgery and not extended beyond 24 hours from the surgical procedure [13, 15]. However, in many cases antibiotic prophylaxis is prolonged in the post-operative period, in the attempt to reduce the incidence of SSI [14, 15]. This

misuse of antibiotics is not justified, as it is ineffective in further reducing the incidence of SSI, can cause an increase in antibiotic resistance, and can predispose to serious infections [13-15].
This phenomenon may be accompanied by an inappropriate or excessive prescription for antibiotics at hospital discharge, related to a "defensive medicine" behavior [16].
Several studies demonstrate that hospital-based programs dedicated to enhance antimicrobials' use, generally known as antimicrobial stewardship programs, can both reduce hospital acquired infections and multi-drug resistant microorganisms, limiting in addition adverse events resulting from antimicrobials use [17].
Several methods of antimicrobial stewardship can be implemented in order to counteract this attitude (e.g. audit and feedback, continuing education, recommendations, etc.) [18], even if there is no unanimous consensus on the impact of different interventions [19].
The purpose of this study has been to evaluate the effect of an antimicrobial stewardship intervention focused on the reduction of antimicrobial prescription at the time of hospital discharge in patients at risk of SSI involved in a surveillance programme at the Ferrara University Hospital.

Methods

Setting

Ferrara University Hospital is an Italian tertiary public acute care hospital with 637 ordinary and 84 day-hospital beds, 24,023 regular admissions (excluding healthy new-borns), 8,022 admissions in day-hospital and 10,055 surgical operations per year (data referring to 2016).

Antimicrobial stewardship intervention

With reference to existing data, demonstrating the opportunity to optimize antimicrobial prescription at discharge, particularly in surgical patients, in 2015 Ferrara University Hospital implemented a multidisciplinary antimicrobial stewardship intervention including five main components: three update meetings for health professionals, focused meetings for critical wards, reviews of some surgical prophylaxis protocols, recommendations to reduce broad-spectrum antimicrobials use, and planning of an audit.
The three update meetings focused on the most emerging infections in our hospital (infections due to *Clostridium difficile*, pneumonia, sepsis) and on responsible antimicrobial use. These meetings involved medical and nursing personnel and were held by a team, called "Operative Group for the responsible use of antimicrobials", composed of an infectious disease specialist, a microbiologist, a specialist in hygiene and preventive medicine (responsible for hospital infection control), and a nurse specialized in infection control. During each meeting the epidemiological characteristics, risk factors and hospital guidelines for diagnosis and therapy were discussed, with particular attention to the appropriate use of antimicrobials during the whole hospital stay, discharge included. In particular it was asked for the reduction of fluoroquinolones use, that were found to be overused in the past years if compared to regional data (e.g. 23.9 vs 14.4 DDD/100 inpatient days in 2013) [20].
Furthermore, the team performed focused meetings with health workers of the surgical units that showed the highest prescription of antimicrobials on discharge in 2014, in order to find out specific solutions.
Then, a review of some perioperative chemoprophylaxis protocols was made.
Finally, was highlighted the indication to follow the institution's guidelines to reduce the prescription for some types of antimicrobials (in particular broad-spectrum ones) and to indicate the motivation for the antimicrobial prescription in the discharge letter.
During these interventions, the surgical units staff was informed that in the future would have been performed an audit in order to check the situation about antimicrobial prescription at discharge.

Inclusion and exclusion criteria

In order to determine the impact of the antimicrobial stewardship intervention, a study including surgical inpatients involved in the Italian national surgical site infection surveillance programme (SNICh) [21] had been performed.
We chose this group of subjects as these patients have a short hospital stay and a higher risk of developing SSIs, being therefore potentially exposed to a prolonged antimicrobial prophylaxis or to an inappropriate prescription at discharge. The study involved all inpatients undergoing an operative procedure included in the SNICh surveillance program during the last quarter of 2014 (pre-intervention group) and the last quarter of 2015 (post-intervention group).
In this study, surgical inpatients in SNICh surveillance admitted in surgical units that did not use the digital discharge letter (otolaryngology, gynaecology, obstetrics, and ophthalmology wards) or patients died during the hospital stay were excluded.

Data collection

The same method to collect data for both periods was used. Demographic, clinical and surgical characteristics of patients were extracted from computerized register of surgical operations. Information on the antimicrobials prescribed at discharge and the characteristics of the post-operative course were extracted from the digital discharge letters stored in institution's data warehouse.
Data were recorded in anonymous form on an electronic worksheet for processing. For each patient the information considered were the following: age, gender, and duration of hospital stay (days); American Society of Anesthesiologists (ASA) score [22]; type of surgery (elective or urgent-emergency surgery); operative procedures, surgical wound contamination class and pros-

thetic implant material classified or definite according to the SNICh protocol [21]; duration of operative procedure (minutes); characteristics of the post-operative clinical course described in the digital discharge letter (regular or complicated); characteristics of antimicrobials prescribed at hospital discharge (number and typology of active principle, classified according to the Anatomical Therapeutic Chemical classification - ATC [23]) and characteristics of SSI (according to the SNICh protocol [21]), when applicable.
Data collection related to the two groups was completed in December 2015 and 2016, respectively.

Objectives

The primary purpose of this study was to assess if a statistically significant change in antimicrobial prescription behaviour at discharge occurred after the stewardship intervention. Secondarily, it was checked if a change in SSIs rate among the studied groups occurred.

Statistical analysis

Pearson's chi-square test, Fisher's exact test, and t-test were used to perform comparisons between the periods, as appropriate. *P* value < 0.05 was considered statistically significant. All analyses were performed using MedCalc Version 17.6.

Results

The study included 993 surgical patients: 461 before the intervention of antimicrobial stewardship (pre-intervention group) and 532 after the intervention (post-intervention group). There was no statistically significant difference between the two groups in baseline demographic characteristics (Tab. I). Concerning the surgical characteristics of patients (Tab. II), in the post-intervention group there was a statistically significant increase in patients undergoing breast surgery, probably due to the reorganization of general surgery ward, which took place in 2015, and led to the creation of a breast surgery dedicated ward.
Overall, the proportion of surgical patients with prescription of antimicrobials at discharge decreased significantly, from 33% in the pre-intervention group to 24.4% in the post-intervention group ($p = 0.002$).
A statistically significant decrease in the prescription of antimicrobials occurred in (Tab. I and Tab. II): female gender (42% pre-intervention vs 27.8% post-intervention; $p < 0.001$); patients with ASA score II (38.5% vs 22.2%; $p < 0.001$); urgent-emergency surgery (48.4% vs 24%; $p < 0.001$); breast surgery (94.1% vs 47.5%; $p < 0.001$), gallbladder surgery (44.2% vs 10.8%; $p < 0.001$), and kidney surgery (63.6% vs 18.2%; $p = 0.03$); clean-contaminated class of surgical wound (33.3% vs 19.5%; $p = 0.02$); patients operated without prosthetic material implant (30.5% vs 20.6%; $p = 0.002$); surgery patients with post-operative course described as regular (33.6% vs 24.4%; $p = 0.005$).
Regarding the characteristics of antimicrobials (Tab. III), the most prescribed Anatomical Therapeutic Chemical categories in both periods were the combinations of penicillins with beta-lactamase inhibitors, in large part amoxicillin and enzyme inhibitors, prescribed in 21.9% of subjects belonging to the pre-intervention group and in 18% of patients in the post-intervention group. Al-

Tab. I. Demographic and clinical characteristics of patients.

Variable	Pre-intervention Group			Post-intervention Group			*P* value (Pts AM)
	No. Pts (n = 461)	No. Pts AM (n = 152)	Pts AM%	No. Pts (n = 532)	No. Pts AM (n = 130)	Pts AM%	
Age, mean *(SD)*	60.1 *(20.8)*	58.9 *(19.3)*	-	60.0 *(19.6)*	59.4 *(19.0)*	-	0.83
Female	226	95	42.0	284	79	27.8	< 0.001
Male	235	57	24.3	248	51	20.6	0.33
Hospital length of stay, mean days *(SD)*	8.9 *(11.2)*	7.8 *(9.5)*	-	7.8 *(9.5)*	6.4 *(6.5)*	-	0.15
ASA score:							
I	29	9	31.0	44	12	27.3	0.73
II	187	72	38.5	212	47	22.2	< 0.001
III	184	54	29.3	221	60	27.1	0.62
IV	48	14	29.2	35	5	14.3	0.11
Missing record	13	3	23.1	20	6	30.0	1.0
Post-operative clinical course:							
Regular	363	122	33.6	401	98	24.4	0.005
Complicated	98	30	30.6	131	32	24.4	0.30
Pts who developed a SSI	16	9	56.3	17	4	23.5	0.08

Pts = patients; Pts AM = patients with at least one antimicrobial prescription at discharge; SD = standard deviation; ASA = American Society of Anesthesiologists; SSI = Surgical Site Infection.

Tab. II. Surgical characteristics of patients.

Variable	Pre-intervention Group			Post-intervention Group			*P* value (Pts AM)
	No. Pts (n = 461)	No. Pts AM (n = 152)	Pts AM%	No. Pts (n = 532)	No. Pts AM (n = 130)	Pts AM%	
Surgical procedures:							
Elective surgery	370	108	29.2	403	99	24.6	0.15
Urgent or emergency surgery	91	44	48.4	129	31	24.0	< 0.001
Operative procedure:							
Breast surgery	51	48	94.1	101	48	47.5	< 0.001
Herniorrhaphy	62	9	14.5	75	13	17.3	0.66
Gallbladder surgery	52	23	44.2	74	8	10.8	< 0.001
Colon surgery	52	11	21.2	73	8	11.0	0.12
Laminectomy	54	0	0	41	2	4.9	0.18
Hip prosthesis	31	5	16.1	22	3	13.6	1.0
Thoracic surgery	23	5	21.7	25	10	40.0	0.18
Craniotomy	22	0	0	21	3	14.3	0.11
Kidney surgery	22	14	63.6	11	2	18.2	0.03
Spinal fusion	14	1	7.1	14	3	21.4	0.60
Other	78	36	46.2	75	30	40.0	0.44
Prosthetic material implant:							
Yes	120	48	40.0	133	48	36.1	0.52
No	341	104	30.5	399	82	20.6	0.002
Duration of operative procedure, mean minutes (*SD*)	244 *(193)*	249 *(206)*	-	235 *(141)*	255 *(179)*	-	0.79
Surgical Wound Classification:							
Clean	243	81	33.3	306	82	26.8	0.10
Clean-Contaminated	87	29	33.3	118	23	19.5	0.02
Contaminated	18	6	33.3	24	8	33.3	1.0
Dirty-Infected	16	7	43.8	19	4	21.1	0.27
Missing record	97	29	29.9	65	13	20.0	0.16

Pts = patients; Pts AM = patients with at least one antimicrobial prescription at discharge; SD = standard deviation.

Tab. III. Characteristics of antimicrobials prescribed at hospital discharge (absolute value and percentage of patients with prescription of antimicrobial).

ATC category	Pre-intervention Group No. Pts (%) (n = 461)		Post-intervention Group No. Pts (%) (n = 532)		*P* value
Combinations of penicillins, incl. beta-lactamase inhibitors	101	(21.9)	96	(18.0)	0.13
Fluoroquinolones	38	(8.2)	17	(3.2)	< 0.001
Imidazole derivatives	9	(2.0)	6	(1.1)	0.29
Third-generation cephalosporins	2	(0.4)	11	(2.1)	0.03
Macrolides	2	(0.4)	5	(0.9)	0.46
Other	10	(2.2)	9	(1.7)	0.58

ATC = Anatomical Therapeutic Chemical; Pts = patients.

though, this reduction was not statistically significant ($p = 0.13$). Differently, a statistically significant difference was recorded in the prescription of fluoroquinolones (decreasing from 8.2% to 3.2% comparing pre- and post-intervention group, respectively; $p < 0.001$) and in the prescription of third-generation cephalosporin (increasing from 0.4% to 2.1%; $p = 0.03$).

The indication for antimicrobial prescription on discharge (e.g. ongoing therapy in discharge) was recorded in the digital discharge letters for 9.9% pre-intervention and 24.6% of patients post-intervention ($p < 0.001$). Finally (Tab. I), the proportion of patients who developed an SSI during the SNICh surveillance period (within 30 days after the operative procedure, for patients operated

without prosthetic material implant, and within 1 year for procedures with prosthetic material implant) [21] did not significantly change comparing the two groups (3.5% pre-intervention vs 3.2% post-intervention; $p = 0.08$).

Discussion

The need of our antimicrobial stewardship intervention originated from the analysis of antimicrobial prescription data of the last quarter of 2014 (Tabs I, II and III), higher than the regional mean. It could be speculated that this over prescription originated from an unjustified attitude in prolonging the surgical prophylaxis over the limit suggested by national guidelines [13] or from a "defensive medicine" behavior for the aim of reducing the risk of SSI.

For this reason, Ferrara University Hospital's "Operative Group for the responsible use of antimicrobials" implemented a multidisciplinary intervention in order to reduce this excessive antimicrobial prescription at discharge, without affecting patients' safety.

The comparison between pre- and post-intervention groups showed a statistically significant decrease (-8.6%; $p = 0.002$) in antimicrobial prescription at discharge. However, we did not observe a change in SSIs rate among the studied groups (from 3.5% to 3.2%; $p = 0.08$).

The change in prescription was particularly significant in breast surgery (Tab. II), that was, indeed, one of the most critical wards in the first year of data collection, probably due to poor compliance to the local surgical chemoprophylaxis guidelines. Other statistically significant reductions in antimicrobial prescription at discharge occurred in urgent-emergency surgery, in patients without a prosthetic implant and in patients with postoperative course described as regular. Probably these reductions represent an attempt to limit unnecessary prescriptions, according to the recommendations about the appropriate use of antimicrobials.

Concerning the type of used antimicrobial, there was a statistically significant reduction in prescription of fluoroquinolones, as suggested during the update meetings. Conversely, prescription of combinations of penicillins with beta-lactamase inhibitors, in large part amoxicillin and enzyme inhibitors, continued to be critical. Moreover, an inexplicable increase in the prescription of third-generation cephalosporin was recorded, even if the absolute value remained limited.

In both groups, the indication for antimicrobial prescription on discharge was explicitly reported in the minority of digital discharge letters. However, the presence of explicit motivation significantly increased, comparing pre- and post-intervention groups, reflecting the indications given at the time of the intervention.

One of the main limitations of this study is represented by the short period of examination (last quarter of the years in study), because it could be not representative of the whole year and/or could not detect potential long-term changes due to the intervention. Another important limitation is that the number of some categories of operative procedures are not homogeneous in the two years in study (e.g. breast surgery).

Conclusions

This study seems to demonstrate that multidisciplinary interventions of antimicrobial stewardship are effective in influencing excessive prescription of these drugs at discharge, without affecting patients' safety. These results confirm, as other studies have demonstrated [17, 24, 25], that antimicrobial stewardship programs are effective in reducing and improving antibiotic prescription. Therefore, these programs are an important part of good practices to be maintained for an efficient infection risk management.

Acknowledgements

GG received grants from GlaxoSmithKline Biologicals SA, Sanofi Pasteur MSD, Novartis, Crucell/Janssen, Seqirus, Sanofi Pasteur, Merck Italy, Pfizer and PaxVax for being consultant or taking part in advisory board, expert meetings, being a speaker or an organizer of congresses/conferences and acting as investigator in clinical trials. No competing financial interests exist for the other authors.

Authors' contributions

All Authors have made a substantial contribution to the conception, design, analysis and interpretation of data, drafting the article and revising it critically for intellectual content; all Authors approve the final version submitted to the *Journal of Preventive Medicine and Hygiene*.

References

[1] Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P T. 2015;40:277-83.

[2] World Health Organization. Antibacterial agents in clinical development: an analysis of the antibacterial clinical development pipeline, including tuberculosis. Geneva: World Health Organization; 2017. Available at: www.who.int/iris/bitstream/handle/10665/258965/WHO-EMP-IAU-2017.11-eng.pdf. Accessed on 07/06/2018.

[3] Institute of Medicine (US) Forum on Emerging Infections; Knobler SL, Lemon SM, Najafi M, Burroughs T, Editors. The Resistance Phenomenon in Microbes and Infectious Disease Vectors: Implications for Human Health and Strategies for Containment: Workshop Summary. Washington (DC): National Academies Press (US); 2003. pp. 130-139. doi: 10.17226/10651.

[4] Elias C, Moja L, Mertz D, Loeb M, Forte G, Magrini N. Guideline recommendations and antimicrobial resistance: the need for a change. BMJ Open 2017;7:e016264. doi: 10.1136/bmjopen-2017-016264.

[5] Smith RA, M'ikanatha NM, Read AF. Antibiotic resistance: a

primer and call to action. Health Commun 2015;30:309-14. doi: 10.1080/10410236.

[6] Directorate-General for Health and Food Safety (European Commission), NIVEL, University of Antwerp. Antimicrobial resistance and causes of non-prudent use of antibiotics in human medicine in the EU. Luxembourg: Publications Office of the European Union; 2017. Available at: www.ec.europa.eu/health/amr/sites/amr/files/amr_arna_report_20170717_en.pdf. Accessed on 07/06/2018.

[7] European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2017. Available at: www.ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/antimicrobial-resistance-europe-2015.pdf. Accessed on 07/06/2018.

[8] European Centre for Disease Prevention and Control. European Antibiotic Awareness Day 2017. 2017. Available at: www.ecdc.europa.eu/en/news-events/european-antibiotic-awareness-day-2017. Accessed on 07/06/2018.

[9] Pantosti A, Del Grosso M. Giornata europea degli antibiotici: uso responsabile per il controllo dell'antibiotico-resistenza [European Antibiotics Day: responsible use for the antibiotic-resistance control]. Rome: Istituto Superiore di Sanità; 2009. Italian. Available at: http://old.iss.it/binary/publ/cont/0932web.pdf. Accessed on 07/06/2018.

[10] Schuts EC, Hulscher MEJL, Mouton JW, Verduin CM, Stuart JWTC, Overdiek HWPM, van der Linden PD, Natsch S, Hertogh CMPM, Wolfs TFW, Schouten JA, Kullberg BJ, Prins JM. Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. Lancet Infect Dis 2016;16:847-56. doi: 10.1016/S1473-3099(16)00065-7.

[11] Lushniak BD. Antibiotic resistance: a public health crisis. Public Health Rep 2014;129:314-6. doi: 10.1177/003335491412900402.

[12] European Centre for Disease Prevention and Control. Summary of the latest data on antibiotic consumption in the European Union, November 2016. Stockholm: ECDC; 2016. Available at: www.ecdc.europa.eu/sites/portal/files/documents/antibiotics-ESAC-Net%20Summary%202016_0.pdf. Accessed on 07/06/2018.

[13] Sistema nazionale per le linee guida. Linea Guida: Antibioticoprofilassi perioperatoria nell'adulto [Guideline: perioperative antibiotic prophylaxis in adults]. Document 17 Sep 2008. Milan: Zadig; update Sep 2011. Italian. Available at: www.anmdo.org/wp-content/uploads/2016/10/Linee-guida-Antibioticoprofilassi-perioperatoria-nelladulto.pdf. Accessed on 07/06/2018.

[14] De Chiara S, Chiumello D, Nicolini R, Vigorelli M, Cesana B, Bottino N, Giurati G, Caspani ML, Gattinoni L. Prolongation of antibiotic prophylaxis after clean and clean-contaminated surgery and surgical site infection. Minerva Anestesiol 2010;76:413-9.

[15] Coppolino S, Federico F. Terapia antibiotica in pazienti dimessi da un reparto di Chirurgia Generale: considerazioni sull'appropriatezza prescrittiva in ospedale e sul territorio [Antibiotic therapy in patients discharged from a General Surgery department: considerations on the prescriptive appropriateness in the hospital and in the community]. Bollettino SIFO 2011;57:89-93. Italian.

[16] Messano GA, Cancrini F, Marsella LT. Antibiotic resistance and defensive medicine, a modern challenge for an old problem: the case of Ureaplasma urealyticum. Ig Sanita Pubbl 2014;70:295-304.

[17] Conway EL, Sellick JA, Horey A, Fodero K, Ott MC, Krajewski MP, Mergenhagen KA. Decreased mortality in patients prescribed vancomycin after implementation of antimicrobial stewardship program. Am J Infect Control 2017;45:1194-7. doi: 10.1016/j.ajic.2017.06.012.

[18] Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, Gould IM, Ramsay CR, Michie S. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev 2017;2:CD003543. doi: 10.1002/14651858.

[19] Dik JW, Hendrix R, Poelman R, Niesters HG, Postma MJ, Sinha B, Friedrich AW. Measuring the impact of antimicrobial stewardship programs. Expert Rev Anti Infect Ther 2016;14:569-75. doi: 10.1080/14787210.2016.1178064.

[20] Gagliotti C, Buttazzi R, Pan A, Ambretti S, Capatti C, Carretto E, Pedna MF, Sarti M, Venturelli C, Moro ML. Sorveglianza dell'antibioticoresistenza e uso di antibiotici sistemici in Emilia-Romagna. Rapporto 2013 [Surveillance of antibiotic resistance and use of systemic antibiotics in Emilia-Romagna. 2013 Report]. Bologna: Agenzia sanitaria e sociale regionale - Regione Emilia-Romagna; 2014. Italian. Available at: https://assr.regione.emilia-romagna.it/it/servizi/pubblicazioni/rapporti-documenti/sorveglianza-antibioticoresistenza-rapporto-2013. Accessed on 07/06/2018.

[21] Centro nazionale per la prevenzione e il controllo delle malattie (CCM). Sistema nazionale sorveglianza delle infezioni del sito chirurgico (SNICh) - Protocollo [National surveillance system of surgical site infections (SNICh) - Protocol]. Bologna: Agenzia sanitaria e sociale regionale - Regione Emilia-Romagna; 2011. Italian. Available at: http://assr.regione.emilia-romagna.it/it/servizi/pubblicazioni/rapporti-documenti/protocollo-snich-aggiornamento-dic2011. Accessed on 07/06/2018.

[22] Owens WD, Felts JA, Spitznagel EL Jr. ASA physical status classifications: a study of consistency of ratings. Anesthesiology 1978;49:239-43.

[23] WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment 2014. Oslo, Norway: WHO Collaborating Centre for Drug Statistics Methodology; 2013. Available at: http://sifac.it/wp-content/uploads/2013/12/dice1838.pdf. Accessed on 07/06/2018.

[24] Yogo N, Shihadeh K, Young H, Calcaterra SL, Knepper BC, Burman WJ, Mehler PS, Jenkins TC. Intervention to reduce broad-spectrum antibiotics and treatment durations prescribed at the time of hospital discharge: a novel stewardship approach. Infect Control Hosp Epidemiol 2017;38:534-41. doi: 10.1017/ice.2017.10.

[25] Giacobbe DR, Del Bono V, Mikulska M, Gustinetti G, Marchese A, Mina F, Signori A, Orsi A, Rudello F, Alicino C, Bonalumi B, Morando A, Icardi G, Beltramini S, Viscoli C; San Martino Antimicrobial Stewardship Group. Impact of a mixed educational and semi-restrictive antimicrobial stewardship project in a large teaching hospital in Northern Italy. Infection 2017;45:849-56. doi: 10.1007/s15010-017-1063-7.

■ Received on May 7, 2018. Accepted on May 27, 2018.

■ Correspondence: Giovanni Gabutti, Section of Public Health Medicine, Department of Medical Sciences, University of Ferrara, via Fossato di Mortara 64/b, 44121 Ferrara, Italy - Tel. +39 0532 455568 - Fax +39 0532 205066 - E-mail: giovanni.gabutti@unife.it