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.
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 characteris-

tics, 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 (otorhinolaryngology, 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-

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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. Secondly, 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. \( P < 0.05 \) 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 \((42\% \text{ pre-intervention vs } 27.8\% \text{ post-intervention}; \ p < 0.001)\); patients with ASA score II \((38.5\% \text{ vs } 22.2\%; \ p < 0.001)\); urgent-emergency surgery \((48.4\% \text{ vs } 24\%; \ p < 0.001)\); breast surgery \((94.1\% \text{ vs } 47.5\%; \ p < 0.001)\), gallbladder surgery \((44.2\% \text{ vs } 10.8\%; \ p < 0.001)\), and kidney surgery \((63.6\% \text{ vs } 18.2\%; \ p = 0.03)\); clean-contaminated class of surgical wound \((33.3\% \text{ vs } 19.5\%; \ p = 0.02)\); patients operated without prosthetic material implant \((30.5\% \text{ vs } 20.6\%; \ p = 0.002)\); surgery patients with post-operative course described as regular \((33.6\% \text{ vs } 24.4\%; \ p = 0.005)\).

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-

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**Tab. I.** Demographic and clinical characteristics of patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-intervention Group</th>
<th>Post-intervention Group</th>
<th>( P ) value (Pts AM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Pts (n = 461)</td>
<td>No. Pts AM (n = 152)</td>
<td>Pts AM%</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>60.1 (20.8)</td>
<td>58.9 (19.3)</td>
<td>-</td>
</tr>
<tr>
<td>Female</td>
<td>226 95</td>
<td>42.0</td>
<td>-</td>
</tr>
<tr>
<td>Male</td>
<td>235 57</td>
<td>24.3</td>
<td>-</td>
</tr>
<tr>
<td>Hospital length of stay, mean days (SD)</td>
<td>8.9 (11.2)</td>
<td>7.8 (9.5)</td>
<td>-</td>
</tr>
<tr>
<td>ASA score:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>29 9</td>
<td>31.0</td>
<td>44</td>
</tr>
<tr>
<td>II</td>
<td>187 72</td>
<td>38.5</td>
<td>212</td>
</tr>
<tr>
<td>III</td>
<td>184 54</td>
<td>29.3</td>
<td>221</td>
</tr>
<tr>
<td>IV</td>
<td>48 14</td>
<td>29.2</td>
<td>35</td>
</tr>
<tr>
<td>Missing record</td>
<td>13 3</td>
<td>25.1</td>
<td>20</td>
</tr>
<tr>
<td>Post-operative clinical course:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>363 122</td>
<td>33.6</td>
<td>401</td>
</tr>
<tr>
<td>Complicated</td>
<td>98 30</td>
<td>30.6</td>
<td>131</td>
</tr>
<tr>
<td>Pts who developed a SSI</td>
<td>16 9</td>
<td>56.3</td>
<td>17</td>
</tr>
</tbody>
</table>

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.
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 SSI 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.

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**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*.

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