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Reducing the duration of antibiotic therapy in surgical patients through a specific nationwide antimicrobial stewardship program. A prospective, interventional cohort study

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ABSTRACT

Background: Guidelines recommend 5–7 days of antibiotic treatment in patients with surgical infection and adequate source control. This nationwide stewardship intervention aimed to reduce the duration of treatments in surgical patients to <7 days.
Methods: Prospective cohort study evaluating surgical patients receiving antibiotics ≥7 days in 32 hospitals. Indication for treatment, quality of source control, type of recommendations issued, and adherence to the recommendations were analysed. Temporal trends in the percentages of patients with treatment >7 days were evaluated using a linear regression model and Pearson's correlation coefficients.
Results: A total of 32 499 patients were included. Of these, 13.7% had treatments ≥7 days. In all, 3912 stewardship interventions were performed, primarily in general surgery (90.7%) and urology (8.1%). The main types of infection were intra-abdominal (73.4%), skin/soft tissues (9.8%) and urinary (9.2%). The septic focus was considered controlled in 59.9% of cases. Out of 5458 antibiotic prescriptions, the most frequently analysed drugs were piperacillin/tazobactam (21.7%), metronidazole (11.2%), amoxicillin/clavulanate (10.3%), meropenem (10.7%), ceftriaxone (9.3%) and ciprofloxacin (6.7%). The main recommendations issued were: treatment discontinuation (35.0%), maintenance (40.0%) or de-escalation (15.5%), and the overall adherence rate was 91.5%. With adequate source control, the most frequent recommendation was to terminate treatment (51.2%). Throughout the study period, a significant decrease in the percentage of prolonged treatments was observed (Pc=-0.69;$P < 0.001$).

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Conclusions: This stewardship programme reduced the duration of treatments in surgical departments. Preference was given to general surgery services, intra-abdominal infection, and beta-lactam antibiotics, including carbapenems. Adherence to the issued recommendations was high.

1. Introduction

In 2015, the World Health Assembly published a global work plan for the prevention of antimicrobial resistance (AMR), which established the optimisation of the use of antibiotics among its major policy objectives [1].

The inappropriate or excessive use of antimicrobials is a decisive factor in the emergence of antibiotic-resistant pathogens [2], and it has been observed that the use of 30% of antibiotics in Western acute hospitals is considered to be incorrect [3]. Although the implementation of antimicrobial stewardship programmes (ASPs) has increased over the past decades [4], few have been specifically designed for use in surgical specialities or conducted under the leadership of surgeons [5]. Given that surgeons are actively involved in prescribing antibiotics, they should play a major role in the development and leadership of ASPs in surgical departments [6].

In intra-abdominal infections, antibiotic administration has been reported to be inadequate in as many as 74% of cases, with most breaches being due to excessive treatment duration [7]. In our region, a rise in antimicrobial consumption has been reported over the last decade, mainly linked to infections of the urinary tract or the abdomen. Mean durations of 7.6 days for empirical treatment and 11.4 days for targeted treatment have been recorded [8].

To our knowledge, no ASPs specially designed to shorten treatment duration in surgical patients have been described. This prospective, interventional cohort study was designed to reduce the duration of antimicrobial treatment in surgical departments, and to assess the feasibility of implementing an ASP at multicentre level, leveraging a national surveillance programme for healthcare-associated infections. Secondary objectives were to decrease the consumption of carbapenems and other agents with a specific ecological effect.

2. Materials and methods

Multicentre, prospective, interventional cohort study to analyse the effect of an ASP in the surgical setting.

2.1. Setting and patients

The VINCat infection control and antimicrobial stewardship programme has been in place in Catalonia (Spain) since 2006. The programme, deployed in a population of 7.7 million, performs prospective active surveillance of nosocomial infections at acute-care hospitals in both public and private sectors (for a detailed description, see Gudiol et al [9]). The programme includes an ASP module in which data on annual antibiotic consumption are monitored and used for benchmarking. In addition, ASP interventions have been conducted. The 7VINCut programme was designed to shorten the duration of antibiotic therapy in adult patients admitted to surgical departments.

Conducted between January 2019 and December 2021, this study used prospectively recorded data leveraging the VINCat infection surveillance network. Secondary goals were to decrease the prescription of carbapenems in Surgical Departments and that of other antimicrobials with an ecological burden (amoxicillin/clavulanate, piperacillin-tazobactam, and third and fourth generation cephalosporins and quinolones). Data from 32 hospitals participating in the network were included in the analysis.

All patients aged 18 years or older admitted to the General Surgery Service and undergoing systemic antibiotic treatments lasting for 7 days or more were included. At hospitals with a General Surgery Service with fewer than 40 beds, additional surgical services were added to obtain a sample comprising at least this number. Antibiotics prescribed for surgical prophylaxis were excluded. Because of the nature of the infections treated at Orthopaedics and Vascular Surgery departments, which often require long-term treatments, cases with diseases specific to these services (osteomyelitis, diabetic foot, etc.), but admitted in a General Surgery Service, were excluded.

2.2. Intervention

The intervention started with the dissemination of the project protocol to all hospitals participating in the network, and the organisation of a training workshop for surgical and antibiotic stewardship teams. In this multidisciplinary project, hospitals were invited to create a dedicated surgical ASP team comprising 3–5 individuals, incorporating surgeons, pharmacists, microbiologists, nurses, and infectious disease specialists.

The interventional ASP relied on an audit and feedback strategy to issue recommendations for shortening the duration of antibiotic treatment regimens and reducing the use of targeted drugs.

All patients hospitalised in the selected departments were prospectively analysed once a week. ASP teams identified patients whose antibiotic treatment lasted more than seven days using a computer-aided system. The team met to discuss the appropriateness of each antibiotic treatment, issuing a recommendation in the electronic medical record. The intervention was performed only once for each patient unless they had a new focus of infection. The recommendations proposed for longer-term treatments were: withdraw, maintain, de-escalate, broaden spectrum, change route of administration, optimise dose, or no recommendation. These recommendations were discussed in surgery departments and implemented if considered necessary. After 48 hours, a member of the ASP team reviewed the adherence to the recommendations in the electronic medical record.

Although the programme focused on the duration of antibiotic therapy, the stewardship teams added some recommendations with regard to the microbiological appropriateness of the treatments and also with regard to the use of broad-spectrum antibiotics, especially carbapenems.

Antibiotic prescriptions evaluated were both empirical and broad-spectrum, pathogen-targeted regimens. When available, the microbiological results were reviewed before the ASP recommendations were made.

The main endpoint assessed was the proportion of patients out of all those admitted to the surgical services who underwent more than seven days of antimicrobials. Other variables included: category of infection for which the antimicrobial treatment was prescribed, quality of infection source control (good, uncertain, poor),

broad-spectrum antibiotics, type of recommendations, and the proportion of adherence to the recommendations. The ASP teams assessed the quality of septic focus control based on the surgeon's operative notes and the patient's initial evolution. In addition, they took into account the drugs' microbiological adequacy, the doses administered, and the route of administration.

2.3. Ethics and statistics

The study was approved by the hospital's Research Ethics Committee General Universitari de Granollers (code 20222042). The requirement for informed consent document was waived. The project was registered with ClinicalTrials.gov Identifier NCT05813821 and was reported in accordance with the STROCSS 2021 criteria [10].

The data were stored in a computerised database and analysed using the IBM SPSS programme (v. 21.0, Chicago, IL). The evolution of the percentage of new patients undergoing prolonged antibiotic treatment related to the total number of patients on antibiotic treatment was evaluated by simple linear regression. The linear relationship was tested by ANOVA tests, and Pearson's correlation coefficients (Pc) were obtained. Values of $P \leq 0.05$ were considered statistically significant. A two-tailed distribution was assumed for all p values.

3. Results

The number of hospitals participating in the intervention rose from 26 in 2019 to 32 in 2021 (accounting respectively for 54.9% and 59.3% of the total number of surgical stays in the network). Between 2019 and 2021, 32 499 patients undergoing antibiotic treatment in surgical services were included, of whom 4439 (13.7%) were treated for a period longer than 7 days.

The prescriptions of 3912 patients were analysed (88.1% of the target population of patients with prolonged treatments: 1268 in 2019; 1032 in 2020, and 1612 in 2021). Most of the patients studied were admitted to the General and Digestive Surgery Department (90.7%) or the Urology Department (8.1%).

The main source of infection requiring prolonged antibiotic treatment was the abdomen (73.4%), followed by skin and soft tissue (9.8%) and urinary tract (9.2%).

3.1. Recommendations issued by the ASP teams

Overall, maintaining the prescribed treatment was the most frequent recommendation, followed by discontinuing treatment (Table 1). However, this proportion evolved over the course of the study period; while in 2019 the majority recommendation was to discontinue treatment, in 2021 it was to maintain treatment (Fig. 1).

From a total of 3912 patients, ASP teams analysed 5458 antibiotic prescriptions. The most frequent antibiotics subject to stewardship intervention were: piperacillin/tazobactam (21.7%), metronidazole (11.2%), meropenem (10.7%), amoxicillin-clavulanic acid (10.3%), ceftriaxone (9.3%) and ciprofloxacin (6.7%). The antimicrobials analysed differed according to the focus of infection under treatment, the most common being piperacillin/tazobactam for intra-abdominal and respiratory infections, amoxicillin/clavulanic acid for skin and soft tissue infections, and ceftriaxone for urinary tract infections (Table 2). Of the 5458 prescriptions exceeding 7 days of treatment, 3730 (68.3%) were for antibiotics with a high ecological effect (Table 3).

Table 1
Types of recommendations issued by the ASP teams and rates of adherence.

Recommendation	Intervention n (%)	Adherence to the recommendation n (%)[a]
Maintain	1563 (40%)	1532 (98%)
Withdraw	1369 (35%)	1168 (85.3%)
De-escalate	606 (15.5%)	544 (89.8%)
Broaden spectrum	192 (4.9%)	179 (93.2%)
Change route	182 (4.7%)	158 (86.8%)
Total	3912 (100%)	3581 (91.5%)

[a] % accepted for each type of recommendation

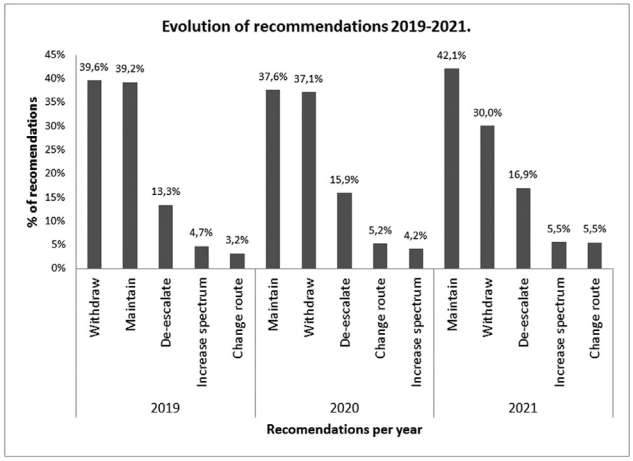

Fig. 1. Evolution of recommendations issued by the antibiotic stewardship teams.

3.2. Adherence to recommendations

In all, 91.5% of the recommendations made by the ASP teams were accepted by the attending surgeons. However, their acceptance differed depending on the type of recommendation, the antibiotic prescribed, and the quality of the septic source. The advice to maintain treatment was accepted in 98.0%, while the suggestion to discontinue treatment had an adherence rate of 85.3% (Table 1). Table 3 shows compliance with the advice in each of the main antimicrobial groups according to the type of recommendation issued.

The quality of septic source control was reported in 93.4% of the stewardship interventions. It was considered good in 59.9% of cases and uncertain or poor in 37.1%. Based on this assessment, the recommendations of the ASP teams differed: in cases in which the infectious focus was controlled, the advice was to stop treatment in 51.2% of the interventions, but when the control was incorrect or uncertain, the most frequent recommendation was to maintain treatment (Table 4).

3.3. Evolution of the percentage of patients on antibiotic treatment ≥ 7 days

The percentage of new patients with prolonged treatments was 15.1% (SD 1.53) during the first six months of 2019 and fell progressively to 11.4% (SD 1.86) during the last six months of the intervention. This proportion decreased significantly over the course of the stewardship programme (Pc= -0.69; $P < 0.001$) (Fig. 2).

4. Discussion

Previous studies have shown that shortening antibiotic treatment in intra-abdominal infections does not worsen clinical outcomes, as long as control of the infection source is adequate [11–13]. Clinical parameters such as fever and white blood cell count and biological markers such as procalcitonin have been used to shorten the duration of treatment [14–16], while short, fixed treatments have also been tested and have achieved comparable results to longer schedules until clinical resolution. [17].

Table 2
Main antibiotics prescribed depending on the location of the infection.

Antibiotic	Intra-abdominal Infection 4105 (75.2%)	Urinary tract infection 410 (7.5%)	Skin and soft tissue infection 532 (9.7%)	Respiratory infection 187 (3.4%)	Other infections[a] 224 (4.1%)
Piperacillin/tazobactam	1007 (24.5%)	32 (7.8%)	75 (14.1%)	51 (27.3%)	21 (9.4%)
Metronidazole	545 (13.3%)		40 (7.5%)		20 (8.9%)
Meropenem	477 (11.6%)	40 (9.8%)	40 (7.5%)	15 (8.0%)	
Amoxicillin/clavulanate	376 (9.2%)	35 (8.5%)	89 (16.7%)	35 (18.7%)	27 (12.1%)
Ceftriaxone	366 (8.9%)	84 (20.5%)			20 (8.9%)
Ciprofloxacin		62 (15.5%)	65 (12.2%)	8 (4.3%)	
Levofloxacin				11 (5.9%)	
Vancomycin					19 (8.5%)

[a] Cardio-vascular (36), Fever of unknown origin (26), Gastro-intestinal (20), Gynaecological/obstetric (19), Bone and joints (18) and Head/neck (14).

Table 3
Adherence to recommendations in accordance with the quality of septic source control.

Antibiotic	Interventions n (%)		Adherence to recommendation n (%)[a]	
Penicillins with beta-lactamase inhibitor	1748	46.9%	1590	91.0%
Maintain	694	39.7%	680	98.0%
Withdraw	637	36.4%	534	83.8%
De-escalate	267	15.3%	236	88.4%
Increase spectrum	73	4.2%	70	95.9%
Change route	77	4.4%	70	90.9%
Carbapenems	880	23.6%	817	92.8%
Maintain	352	40.0%	343	97.4%
Withdraw	229	26.0%	200	87.3%
De-escalate	251	28.5%	230	87.3%
Increase spectrum	30	3.4%	27	90%
Change route	18	2%	17	94.4%
3rd and 4th generation cephalosporins	684	18.3%	619	90.5%
Maintain	259	37.9%	254	98.1%
Withdraw	268	39.2%	229	85.4%
De-escalate	55	8.0%	50	90.9%
Increase spectrum	46	6.7%	42	91.3%
Change route	56	8.2%	44	78.6%
Quinolones	418	11.2%	380	90.5%
Maintain	179	42.8%	176	98.3%
Withdraw	149	35.6%	126	84.6%
De-escalate	27	6.5%	22	81.5%
Increase spectrum	35	8.4%	32	91.4%
Change route	28	6.7%	24	85.7%
Total	3730	100%	3406	91.3%

[a] % accepted for each type of recommendation.

Table 4
Adherence to the recommendations according to the antibiotics analysed.

Source control / Recommendation	Interventions N (%)		Adherence to recommendation N (%)[a]	
Good source control	2189	59.9%	1968	89.9%
Maintain	548	25%	534	97.4%
Withdraw	1121	51.2%	961	85.7%
De-escalate	326	14.9%	299	91.7%
Broaden spectrum	69	3.2%	64	92.8%
Change route	125	5.7%	110	88%
Uncertain source control	463	12.7%	439	94.8%
Maintain	298	64.4%	290	97.3%
Withdraw	28	6%	24	85.7%
De-escalate	84	18.1%	74	88.1%
Broaden spectrum	41	8.9%	40	97.6%
Change route	12	2.6%	11	91.7%
Poor source control	1002	27.4%	941	93.9%
Maintain	604	60.3%	596	98.7%
Withdraw	108	10.8%	91	84.3%
De-escalate	176	17.6%	153	86.9%
Broaden spectrum	71	7.1%	66	93.0%
Change route	43	4.3%	35	81.4%
Total	3654		3348	91.6%

[a] % accepted for each type of recommendation.

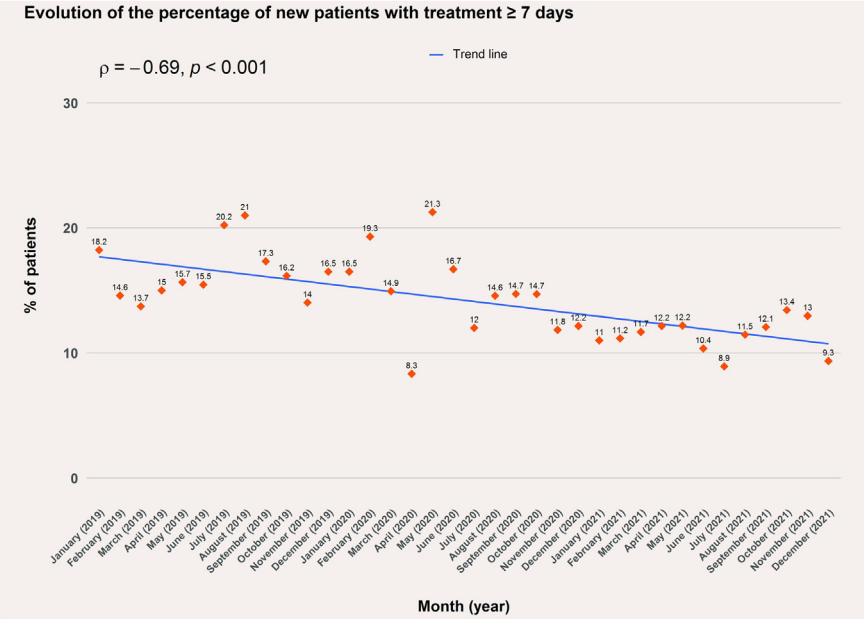

Fig. 2. Evolution of the percentage of new patients with treatment ≥7 days out of the total number of patients with antibiotic treatment admitted to the surgical services participating in the intervention.

Taken together, these data suggest that long-term therapy does not decrease the complications of intra-abdominal infections and that antimicrobials can be safely withdrawn within four days of adequate control of the focus. In fact, more prolonged antimicrobial regimens for intra-abdominal infection have been reported to increase mortality [18].

State-of-the-art guidelines for intra-abdominal infection [19–22] advocate antimicrobial treatment lasting 5–7 days in complicated cases, the precise length depending on intraoperative findings, quality of focus control, and improvement of postoperative signs and symptoms. These guidelines also support the termination of antibiotic therapy with oral administration of the drug in patients who are already tolerating an oral diet [23].

ASPs have been described as comprehensive packages of activities designed to use antimicrobials in a responsible manner [24], and a large body of data supports their value for optimising antibiotic prescription practices [5,25,26]. ASP teams habitually comprise experienced multidisciplinary specialists with the requisite training in prescribing and monitoring the use of antimicrobials – i.e., infectious disease specialists, clinical microbiologists, and pharmacists [24], while some programmes recommend the inclusion of a clinician with surgical skills if possible [27]. It has been proposed that surgeons should be included in ASPs deployed in surgical departments [6], but there are few reports of the use of ASPs in the surgical setting [5,6,23].

Little is known about the implementation of multi-centre ASP programmes in large groups of hospitals. It might be argued that ASPs are more difficult to introduce at a multi-centre level [28]. An important outcome of the present study was the finding that an ASP intervention can be successfully implemented in a large number of acute-care hospitals in a very limited time. The key to the success appears to have been taking advantage of the structure of a well-established health-associated infection surveillance programme which already had a hospital-based antibiotic stewardship section. The organisation of the network and the previous experience of the infection control and stewardship teams made it possible to carry out this specific intervention for surgical services.

This intervention achieved a significant reduction in the percentage of patients with an antimicrobial treatment duration ≥7 days in surgical services. As expected, the infections that required prolonged treatment were mainly peritonitis or hepatobiliary infections, and in these cases adequate source control was obtained in fewer than half of the cases. When short courses of antibiotics are to be administered for surgical sepsis, adequate source control is essential [17,18,26,29]; this explains the low percentage of correct source control recorded in this subgroup of patients with prolonged treatment.

The present study demonstrates that a prospective audit in combination with a motivational intervention and provider feedback can reduce the length of antimicrobials in surgery, likely due to the establishment of good practices in the surgical services. There was probably more room for improvement at the beginning of the study, when the most frequent recommendation issued by the ASP teams was to 'withdraw' antimicrobial treatment; however, this changed to 'maintain' during the last months of the study, as the ASPs teams felt that the treatments were justified. Possibly there was a learning process at work here that improved prescriptive praxis.

It should be noted that the time period of the study includes the COVID-19 epidemic, an event that radically changed the profile of patients presenting at emergency surgery departments [30–33]. Although during that time suboptimal outcomes in surgical patients have been reported, the 7VINCut intervention maintained its effect over time and no increase in the duration of antibiotic treatment regimens was detected.

Given that the acceptance of ASP interventions has been reported to be lower among surgical specialists than among other medical professionals [34,35], the Global Alliance for Optimising the Rational Use of Antibiotics for Intra-abdominal Infections has proposed that antimicrobial stewardship and education programmes be headed by surgical leaders in order to improve prescribing practices [29]. Surgeons' commitment to ASPs will likely be pivotal to the latter's success [5,36].

Certain authors have found that guidelines to reduce antibiotic exposure, ASPs aimed at reducing the use of carbapenems, and advices to reduce or withdraw prescriptions are associated with lower compliance rates. [34,35]. This does not seem to have been the case in our study, as there was a high percentage of agreement

on the advice to reduce treatments, and compliance with the recommendations for carbapenems did not differ from that recorded for the other antibiotics.

Contributors to better adherence include the presence of the ASP physician in rounds, verbal counselling [35] and telephone-based communication [34]. In the present study, the recommendations were written in the electronic medical record and were subsequently discussed by the surgeons at their clinical meeting.

The effectiveness of ASPs depends on cooperation between healthcare professionals in a given institution. In this setting, surgeons with a special interest in surgical infection should be actively engaged in infection-related improvement programmes in surgical units. ASPs designed and implemented by multidisciplinary teams that include surgeons can achieve optimal adherence [37].

4.1. Limitations of the study

The first part of the study coincided the period of the COVID-19 pandemic, a circumstance that entailed a major reduction in admissions to surgical services. Secondly, because of the methodology used, it was not possible to correlate improved prescribing habits with a decrease in antibiotic consumption or its effect on AMR. However, given the large cohort of patients included, these results may well be applicable to other settings, and probably reflect the real effect of non-restrictive stewardship programmes in surgery.

4.2. Conclusions

The 7VINCut stewardship programme achieved a reduction in antibiotic treatments lasting over 7 days. The inclusion of surgeons in multidisciplinary teams seem to help to improve the management of antibiotics at surgical services.

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Competing Interests: The authors declare no conflict of interest.

Ethical Approval: The study was conducted according to the guidelines of the Declaration of Helsinki. Data extraction was approved by the VINCat Technical Committee on 01 August 2022. The study was approved by the Clinical Research Ethics Committee of Hospital General de Granollers, with code 20222042. The need for informed consent and for the provision of an information sheet were waived by the Research Ethics Committee because of the nature of the study, in which data were routinely collected as part of the quality improvement programmes in place in the hospitals; due to the use of anonymous clinical data in the analysis, and because their extraction for the study was covered by the general admission consent provided by the patient.

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Data Availability Statement: Restrictions apply to the availability of these data, which belong to a national database and are not publicly available. Data was obtained from VINCat and are only available with the permission of the VINCat Technical Committee.

Appendix

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