

Appendix 1. Antimicrobial Stewardship Program intervention details.

The hospital ASP (*Programa de Optimización del uso de Antimicrobianos Sant Joan de Déu, PROA-SJD*) was first implemented in January 2017. The PROA-SJD core team was composed of a full-time paediatric infectious diseases specialist, and other part-time physicians including a paediatric intensive care specialist, clinical pharmacists, a microbiologist, a hospital epidemiology and infection control physician and a nurse. Support was received from the computer, statistics and hospital management teams.

The main ASP strategy was postprescription review with feedback (PPRF). All systemic antimicrobials (intravenous, intramuscular or oral route) were included in ASP evaluation. An electronic form (see **Table** below) was included in the patients' electronic clinical chart to inform the prescribers as to whether the antimicrobial prescription was considered 'optimal' or 'non-optimal'. For a prescription to be considered 'optimal', all the following criteria had to be met: 1) the administration of the antimicrobial was appropriate considering the diagnosis, the antimicrobial spectrum, our own reference guidelines, adapted to local epidemiology, and also accounting for patient allergies and comorbidities; 2) the drug was given through the right route, and at the right dose and with the right schedule; and 3) the expected and/or actual duration of the antimicrobial treatment were appropriate. Otherwise, prescriptions were categorized as 'non-optimal' and recommendations to discontinue or to modify therapy were provided not only in the ASP electronic form, but also face-to-face during clinical rounds or by phone in specific cases. Surgical teams received electronic and face-to-face recommendations every working day, while the rest of the departments received ASP recommendations weekly or twice a week. Besides the day-to-day recommendations of the ASP team (in which certain groups of patients

were prioritized), monthly quality point-prevalence surveys (PPS) were performed following same criteria. During this PPS, all antimicrobial prescriptions of patients admitted at 8 am on the day of the survey were evaluated. Acceptance of ASP recommendations was at the prescribers' discretion.

No preprescription authorization was implemented, but prescription filters for selected antimicrobials (meropenem, linezolid, teicoplanin, colistin, liposomal amphotericin B, itraconazole, voriconazole, posaconazole, micafungin, gancyclovir, cidofovir, valgancyclovir and foscarnet) were incorporated in the e-prescription system, making it necessary for the prescriber to specify the indication.

In parallel with PPRF, an antimicrobial resistance awareness campaign based on posters and informative capsules was conducted, and a pocket hospital guide on antimicrobial prescription was distributed. In order to simplify the prescription process and to assure the right dosing and duration, some pre-set protocols with automatic calculation of dosing according to patient weight for the most common procedures or diagnoses were included in the e-prescription program. In addition, the ASP team organized monthly or quarterly meetings to discuss protocols and specific aspects of AU with the different medical and surgical teams and to share antimicrobial QP data.

Table. Items that were included in the patients' electronic clinical chart that were evaluated during postprescription review and feedback

Item	Electronic clinical chart field
1 Time of prescription	Date and hour
2 Time of ASP evaluation	Date
3 Department in charge	Dropdown list of medical and surgical hospital departments
4 Antimicrobial prescribed	Dropdown list of antimicrobials included in the hospital e-formulary
5 Administration route	Intravenous, intramuscular or oral
6 Intention of treatment	Prophylaxis (medical or surgical), empiric treatment or targeted treatment
7 Diagnostic	Main diagnostic leading to the antimicrobial prescription from a dropdown list of diagnoses based on Global-PPS, ECDC and EPINE-PPSs
8 Microbiological results	Culture or molecular results, when available, from a dropdown list of microorganisms and susceptibility patterns based on ECDC and EPINE-PPSs
9 Reason for treatment	Community-acquired infection, healthcare-associated infection or risk of infection in immunosuppressed patient
10 Indication for any antimicrobial prescription	Yes or no
11 Antimicrobial spectrum	'Optimal', narrower or wider than recommended
12 First choice according to local guidelines	Yes, no or no local guideline available
13 Dosing and interval between doses	'Optimal', lower/shorter or higher/longer than recommended
14 Prescription duration	'Optimal', shorter or longer than recommended, or not specified
15 De-escalation	Adequately done, indicated and pending, not indicated yet-reconsider in 24-72h, not indicated
16 Sequential treatment	Adequately done, indicated and pending, not indicated yet-reconsider in 24-72h, not indicated
17 Classification of the prescription	'Optimal' (according to optimal responses in all items 10-14) or 'non-optimal'
18 Recommendations	Open field

References

- Goossens H, Nathwani D. Global-PPS: Global Point Prevalence Survey of Antimicrobial Consumption and Resistance 2017 (Protocol-version September 2016). <http://www.global-pps.com/documents/>
- European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals – protocol version 5.3. Stockholm: ECDC; 2016. <https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/PPS-HAI-antimicrobial-use-EU-acute-care-hospitals-V5-3.pdf>
- EPINE-PPS: Point Prevalence Survey of the Spanish Study of the Prevalence of Nosocomial Infections (Codebook. Version 9.0, March 2016). [http://www.sempsph.com/media/com_jnews/upload/EPINE-EPPS%202016%20Protocolo%20\(v9.0\).pdf](http://www.sempsph.com/media/com_jnews/upload/EPINE-EPPS%202016%20Protocolo%20(v9.0).pdf)

Supplementary Table 1. Distribution of antimicrobial use in PICU by drug expressed in days-of-therapy over 100 days present (DOT/100DP). Details on drugs with less than 1 DOT/100DP are not given.

Antimicrobial drug	DOT/100DP (%)	Antimicrobial drug	DOT/100DP (%)
Antibacterials	1061.2 (88.5)	Cefoxitin	3.5 (0.3)
Cefazolin	183.6 (15.3)	Cloxacillin	3.2 (0.3)
Amoxicillin-clavulanate	127.6 (10.6)	Cefuroxime	1.9 (0.2)
Vancomycin	126.2 (10.5)	Cefuroxime-axetil	1.4 (0.1)
Cefotaxime	102.1 (8.5)	Cefepime	1.1 (0.1)
Piperacillin-tazobactam	93.7 (7.8)	Other	6.0 (0.6)
Meropenem	73.5 (6.1)	Antifungals	68.6 (5.7)
Ciprofloxacin	56.5 (4.7)	Amphotericin b (liposomal)	21.2 (1.8)
Cotrimoxazole	39.4 (3.3)	Fluconazole	19.3 (1.6)
Linezolid	38.6 (3.2)	Micafungin	18.5 (1.5)
Azithromycin	33.7 (2.8)	Voriconazole	7.6 (0.6)
Metronidazole	28.2 (2.3)	Posaconazole	1.8 (0.1)
Ampicillin	26.0 (2.2)	Other	0.4 (<0.1)
Amikacin	22.2 (1.8)	Antivirals	69.4 (5.8)
Ceftriaxone	20.3 (1.7)	Acyclovir	30.8 (2.6)
Ceftazidime	18.7 (1.6)	Valganciclovir	19.2 (1.6)
Amoxicillin	13.7 (1.1)	Oseltamivir	7.6 (0.6)
Teicoplanin	12.1 (1.0)	Ganciclovir	7.4 (0.2)
Clindamycin	10.6 (0.9)	Foscarnet	2.7 (0.2)
Gentamicin	7.7 (0.6)	Ribavirin	1.2 (0.1)
Clarithromycin	5.5 (0.5)	Other	0.5 (<0.1)
Penicillin G (sodic)	5.3 (0.4)	All antimicrobials	1199.2 (100)

Supplementary Table 2. Demographic and clinical data of the 95 patients admitted in the PICU that received antimicrobials (n=168) and that were evaluated during the 12 monthly point-prevalence surveys during 2019. Data expressed as number (%) or median (IQR).

Characteristic	
Sex (male)	49 (51.6)
Age (years)	2.6 (0.6-6.0)
Reason for PICU admission	
Surgery (without infection)	29 (30.5)
Sepsis	26 (27.3)
Community-acquired pneumonia	17 (17.9)
Meningitis or ventriculitis	6 (6.3)
Hospital-acquired pneumonia	3 (3.2)
Other infections	14 (14.8)
Number of prescribed antimicrobials	
One	60 (63.2)
Two	17 (17.9)
Three	8 (8.4)
Four or more	10 (10.5)
Prescribed antimicrobials (therapeutic/prophylactic intention)	
All antimicrobials	168 (133/35)
Amoxicillin-clavulanate	32 (28/4)
Cefazolin	20 (3/17)
Vancomycin	19 (17/2)
Cefotaxime	15 (13/2)
Piperacillin-tazobactam	11 (11/0)
Meropenem	10 (10/0)
Ciprofloxacin	8 (8/0)
Acyclovir	7 (5/2)
Cotrimoxazole	6 (1/5)
Linezolid	6 (5/1)
Metronidazole	6 (6/0)
Ceftriaxone	4 (4/0)
Amikacin	4 (4/0)
Other drugs	20 (18/2)