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The PIRASOA programme: ecological impact of an antimicrobial stewardship programme based on educational interviews in primary care of the public health system of Andalusia, Spain

Germán Peñalva Moreno^{*1}, Rocio Fernandez-Urrusuno², Manuel Camara³, Manuel M. Aguilar⁴, Juan C. Dominguez-Camacho⁵, Francisco Bernal⁶, Ignacio Pajares⁵, Rocio Hernandez-Soto², Lucia Carrion⁷, Inmaculada Vazquez-Cruz³, María del Carmen Domínguez Jiménez⁸, Carmen Serrano⁹, Ana Dominguez-Castano¹⁰, Marina De Cueto¹¹, Jose Antonio Lepe¹², Aranzazu Irastorza¹³, Jose Miguel Cisneros Herreros¹⁴

¹*Hospital Universitario Virgen del Rocío; Clinical Unit of Infectious Diseases, Microbiology and Preventive Medicine*

²*Servicio Andaluz de Salud; Distrito Sanitario Aljarafe-Sevilla Norte*

³*Servicio Andaluz de Salud; Ags de Osuna*

⁴*Servicio Andaluz de Salud; Distrito Sanitario Huelva Condado Campiña*

⁵*Servicio Andaluz de Salud; Distrito Sanitario Sevilla*

⁶*Servicio Andaluz de Salud; Distrito Sanitario Huelva Costa*

⁷*Servicio Andaluz de Salud; Distrito Sanitario Huelva*

⁸*Hospital de La Merced; Microbiology*

⁹*Hospital San Juan de Dios del Aljarafe*

¹⁰*Complejo Hospitalario Universitario de Huelva*

¹¹*Hospital Universitario Virgen Macarena Y Virgen del Rocío; Enfermedades Infecciosas, Microbiología Y Medicina Preventiva*

¹²Hospital Virgen del Rocio

¹³Servicio Andaluz de Salud

¹⁴Hospital Virgen del Rocio; Infectious Disease, Microbiology and Preventive Medicine; Infectious Diseases

Background: The implementation of Antimicrobial Stewardship Programmes (ASP) in Primary Care (PC) is aimed to improve the appropriateness of the therapy, to diminish antibiotic pressure by lowering the overall consumption and by using narrow spectrum antibiotics as much as possible and, consequently, to reduce antimicrobial resistances. The ecological impact of the ASP in PC is not well known. Our aim was to assess the ecological impact of the PIRASOA programme (Institutional Programme for the Prevention, Control of Healthcare-Associated Infections and Appropriate Use of Antimicrobials) ASP for Primary Care by evaluating the incidence of ESBL *Escherichia coli* in the community and its possible relationship with changes of the prescription profile.

Material/methods: Design: A quasi-experimental study, before and during the intervention. Setting: Four Primary Care Health Districts, with 213 primary care centres and 1,093 physicians assisting a population of 1,939,295 inhabitants. Study period: January 2012 to June 2016, 18 quarterly time series, eight before and ten after the intervention. Beginning of the intervention: January 2014. Two study variables: 1) Difference between consumption rates of amoxicillin/clavulanate versus amoxicillin, as well as ciprofloxacin versus fosfomicin/trometamol, measured as Daily Defined Dose per 1,000 Health Insurance Cards and day (DHD). 2) Incidence Density (ID) of ESBL *E. coli* in the community, measured as number of positive urine cultures episodes to ESBL *E. coli* per 1,000 Health Insurance Cards and day. Statistical analysis: Joinpoint Regression to study the ID time-series and Mann-Whitney U test to study the consumption differences before and after starting the programme.

Results: The differences between amoxicillin/clavulanate and ciprofloxacin versus amoxicillin and fosfomicin respectively are substantially marked from the beginning of the programme, and they decrease more intensely during the intervention period with statistical significance ($p < 0.01$). Differences of amoxicillin/clavulanate versus amoxicillin: pre-intervention period, Me=5.17 DHD (IQR: 4.50-5.40) versus Me=1.49 DHD (IQR: 0.63-2.35) during the intervention. Differences of ciprofloxacin versus fosfomicin: pre-intervention period, Me=1.08 (IQR: 1.04-1.21) versus Me=0.78 (IQR: 0.69-0.93) during the intervention. The ID of ESBL *E. coli* in the community shows a statistically significant change at the eighth quarter (CI 95% 6-10; $p < 0.05$), shifting from a previous increasing trend with a quarterly average change (QAC) of +2.91% ($p = 0.009$) to an intense reduction of -10.5% QAC during the first year after the beginning of the intervention ($p = 0.3$). One year after beginning the intervention, the ID of ESBL *E. coli* maintains a declining trend of -1.92% QAC ($p = 0.09$) for the rest of the time-series period.

Conclusions:

- 1.- The PIRASOA programme ASP for PC has had a positive ecological impact, reducing the ID of ESBL *E. coli* in the community.
- 2.- And it has changed the prescription profile by decreasing antibiotics with a higher ecological impact: amoxicillin/clavulanate and ciprofloxacin, while increasing those with narrow spectrum: amoxicillin and fosfomicin/trometamol.