Antimicrobial Resistance and COVID-19

Resistência aos Antimicrobianos e COVID-19

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Antimicrobial resistance (AMR) was declared by the World Health Organization (WHO) as one of the top ten public health threats to humanity, calling for an urgent multisectoral action to achieve the sustainable development g,oals.[1] AMR requires a joint interdisciplinary and multi-institutional approach to mitigate its consequences, as it intersects human and animal health, food and the environment.[2-4] The burden of AMR is well known: avoidable deaths and disability, and high financial costs for the countries all over the World.[5] Every year AMR is responsible for 33 000 deaths and for €1.5 billion in healthcare costs and productivity losses, only in Europe.[6] If nothing changes, WHO estimates pointed out to the dramatic number of 10 million deaths related to AMR by 2050.[4]

Nevertheless, an unexpected pandemic has reached the World since the beginning of 2020, forcing not only to change lifestyle but also to reshape namely the healthcare sector. Theoretically, a bidirectional interaction is expected to occur between AMR and COVID-19, which balance and impacts remains uncertain.[7] Can we be facing a changing game?

The overuse/misuse of antibiotics is one of the main drivers for AMR emergence.[1,4,5] In a literature review with meta-analysis that included 24 studies, Langford *et al,* have found that co-infection was only reported in 3.5% (95%CI: 0.4-6.7%) and secondary infection in 14.3% (95%CI: 9.6-18.9%) of COVID-19 patients. However, over 70% of patients have received antibiotics, the vast majority broad-spectrum agents.[8] Based on the main findings of this study, we can conclude that the overall proportion of COVID-19 patients with concurrent bacterial infections was low, but the usage of antibiotics was disproportionately high, which can be a substantial drive for AMR and reduce antibiotic effectivity. We must remember that, in the beginning of the pandemic, antimicrobials have been used for their presumed effect on SARS-CoV-2, which was not confirmed. Furthermore, given the overlap of symptoms and laboratory results, it has been difficult to establish a fast differential diagnosis between viral and bacterial pneumonia, which also leads to inappropriate empiric antibiotic use. In patients with severe COVID-19 disease, the potential concern of co-infections or secondary infections, namely with multi-resistant pathogens, can induce clinicians to unnecessary prescribe last resort antimicrobials, which can contribute for ineffectiveness of their action. A prolonged COVID-19 crisis can lead to an antibiotic production increase and a consequent acceleration of its concentration in the environment, with selective pressure for AMR in water and soil. This can potentially rise the prevalence of resistant antimicrobials within the animal-food supply chain and consequently impacts human health.[7]

On the other hand, the social distancing, travel restrictions and additional infection control measures instituted to prevent SARS-CoV-2 spread could also limit the transmission of

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resistant pathogens. AMR reduction expectations cannot be linear due to several reasons[7]: i) raised probability of nosocomial infection due to prolonged hospitalizations of COVID-19 patients; ii) fragilities of stewardship activities during the pandemic due to resources constraints; iii) infection control breaks related to staff shortages due or self-isolation; iv) deployment of staff less prepared; v) enhanced opportunities of household transmission.

During this pandemic era, the global research agenda has been focused on the SARS-CoV-2 infection,[9] slowing down the research in other areas, such as AMR and its monitoring. More than ever, it is crucial to understand the direct and indirect impacts of COVID-19 on AMR, throughout reliable quantitative data which is determinant to adapt and improve health policies to the new generated needs of the pandemic. Efforts based on a concerted strategy and agenda are required at local, national and international levels. Until then, it is crucial to reinforce antibiotic stewardship programs and infection control measures around the World.

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