

**Antimicrobial stewardship program in COVID-19 era: Ruin of the reign?**

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**Abstract:**

COVID-19 is the most important matter in the medical field worldwide in 2020. Although COVID-19 is a viral disease, the threshold to antibiotic prescription for COVID-19 patients is low, partly because of WHO recommendations and previous experiences from influenza, despite the lack of strong evidence of co-infection or superimposed bacterial infection in COVID-19 patients. Antibiotic stewardship program (ASP) could play an important role in this period, otherwise, we will face a crisis of superbugs in the early future.

**Keywords:** COVID-19, Antibiotic stewardship program (ASP), Superbugs

**Introduction**

The COVID-19 pandemic has disturbed health care systems worldwide, parallel to the dramatic increase in antibiotic consumption and consequently a rise in antibiotic resistance. (1) If we neglect this potential threat during the COVID-19 crisis, then we will face a superbugs disaster later.

An antibiotic stewardship program (ASP) works towards an improvement of antibiotic prescription. ASP can play a significant role in the COVID-19 era (2,3). According to some experts, ASP even could be kicked off in the emergency department (ED). (4) However, optimizing antibiotic prescription in the ED is challenging, mainly because of the high workload and the stressful environment. In our opinion, the most logical place for ASP in the hospital is the intensive care unit (ICU) because of the burden of broad-spectrum antibiotic prescription in the ICU. (5)

Although the cornerstone of antimicrobial stewardship is post-prescription feedback to providers, the ASP team can develop local antibiotic treatment protocols and monitor drug supply or shortage as well. (6) The disturbance of routine works hinders antimicrobial stewardship programs within hospitals. More requests for infectious disease consultation in COVID-19 wards will put stewardship teams under a work overload, leading to loss of their concentration for appropriate antimicrobial therapy and even sometimes breaking the ASP rules.

Generally, antimicrobials are being used in several ways: (7)

1- They partner re-purposed medications for the treatment of COVID-19, as is happening with the combination of azithromycin and hydroxychloroquine. (8)

2- Empiric or targeted treatment of probable bacterial co-infections (mainly community-acquired) or superimposed (mainly hospital-acquired) of the pulmonary system, especially in severe cases of COVID-19.

The World Health Organization and other official authorities recommend the use of antibiotics for severe COVID-19. (9-12) However, even in classic cases of COVID-19, the threshold of antibiotic prescription by physicians is low. This behavior stems from the approach to superimposed bacterial infection in patients with influenza. (13,14), More broad-spectrum antibiotic consumption means more staff workload, cost, difficulty in supply and rise of resistance without obvious benefits, especially in ICU settings. (15)

According to recently published studies, the rate of bacterial superinfection in COVID-19 is low. (16,17) Monitoring of inflammatory markers such as C-reactive protein (CRP) and procalcitonin (PCT) might be beneficial. (18)

Antibiotic therapy if started, should be re-evaluated after a maximum of 72 hours, then decided about its

discontinuation or continuation with the de-escalation method or oral switch therapy as much as possible. (19,20) In the majority of cases, the duration should not exceed 5 days (21). One confounder factor in this field is cytokine release syndrome (CRS), which can simulate bacterial sepsis, leading to prolonged unnecessary antibiotic therapy. (22)

Our suggestion is monotherapy with  $\beta$ -lactams as the first option (e.g. amoxicillin and clavulanic acid or third-generation cephalosporins). Macrolides and quinolones due to risk of QTc prolongation, several antibiotic-drug interactions and unnecessary routine atypical coverage are better avoided (23).

In any respiratory deterioration during hospitalization, superimposed bacterial infection should be investigated aggressively and if confirmed, a 7- 8-day antibiotic course is generally advised. Other differential diagnoses include, CRS, myocarditis and pulmonary emboli.

For patients in intensive care units requiring mechanical ventilation, empirical treatment of ventilator-associated pneumonia (VAP) must be started based on local antimicrobial resistance data, and treatment should be adapted according to the microbial culture results. (24)

To support the reinforcement of the stewardship program during the COVID-19 pandemic, the ASP team should develop local evidence-based guidelines for antibiotic prescription in COVID-19 patients with great consideration of broad-spectrum antibiotics (carbapenems, piperacillin-tazobactam, quinolones and vancomycin). (25)

In conclusion, the COVID-19 pandemic has put a heavy pressure on all healthcare professionals, especially infectious disease physicians. An antimicrobial stewardship program is the cornerstone of a successful response in view of antibiotic prescription in patients with COVID-19. We recommend that antibiotic stewardship programs be continued during the COVID-19 crisis.

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