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Rapid Antibiotics Guideline for Treatment and Management of COVID-19 Pneumonia with Bacterial Co-infection

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Abstract:

Background: There are many patients having serious or critical illness will require hospital admission due to SARS-CoV-2 pneumonia. While antibiotics are ineffective for treatment of viral infections, they are prescribed in patients with suspected or documented SARS-CoV-2 for a variety of reasons. This raises concerns of antibiotic overuse or receiving unnecessary antibiotics and increase antimicrobial resistance (AMR).

Objective: The authors would like to develop a rapid antibiotic guideline for the treatment of patients with SARS-CoV-2 who have coinfections. These recommendations are intended to ensure the better antibiotic management of suspected or confirmed bacterial pneumonia in adults during the SARS-CoV-2 pandemic.

Methods: We used MEDLINE, OVID Epub and EMBASE searches complemented with extensive use of Web engine to identify guidelines on empirical treatment of community and hospital-acquired pneumonia in the last 10 years.

Results: We could develop antibiotic prescribing recommendation for patients with suspected community-acquired pneumonia, that has developed before or within 48 hours and patients with suspected hospital acquired pneumonia at more than 48 hours of admission.

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Conclusion: Patients who develop SARS-CoV-2 pneumonia can have guideline for antibiotic prescription in case of suspected secondary superimposed bacterial infection.

Keywords: COVID-19 infection, Pneumonia, Antibiotics

Introduction

The SARS-CoV-2 cases were first reported from Wuhan, China in early December 2019, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1,2]. Within a span of months, SARS-CoV-2 has become pandemic spreading across countries with the number of cases and deaths rising daily[2-9]. Although most infected individuals exhibit a mild illness, and some have serious or critical illness will require hospital admission due to SARS-CoV-2 pneumonia[2-8]. Approximately 10% will require ICU care, including invasive ventilation due to acute respiratory distress syndrome (ARDS)[2-8]. While higher mortality among elderly individuals and those with comorbidities, such as chronic lung disease, cardiovascular disease, hypertension, and diabetes[2-8].

While antibiotics are ineffective for treatment of viral infections, they are prescribed in patients with suspected or documented SARS-CoV-2 for a variety of reasons[6,10]. This raises concerns of antibiotic overuse or receiving unnecessary antibiotics and increase antimicrobial resistance (AMR). First, agents are being explored in clinical trials as potential direct therapies for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), such as azithromycin[6,10]. Second, antimicrobials are commonly prescribed for the management of presumptive or confirmed bacterial co-infection directly related to SARS-CoV-2 pneumonia[6,10]. During influenza pandemics bacterial co-infection in patients has been reported to be as high as 20–30% and is associated with a severity of illness, prolong hospital or ICU admission, and increased risk of mortality[6,10,11]. Current evidence suggests that prevalence, incidence and characteristics of bacterial infection in patients with SARS-CoV-2 is low, but prescribing rates and use of broad-spectrum antimicrobial agents is increased[6,10,11].

Given the rapid global spread of SARS-CoV-2, limited guidelines advocate the use of empirical antibiotics for patients with severe SARS-CoV-2 based on data and literature from past influenza pandemics[6,10,11]. This raises concerns of antibiotic overuse or receiving unnecessary antibiotics and increase antimicrobial resistance (AMR). In a retrospective cohort analysis of 191 patients from two hospitals in Wuhan, 95% of patients were treated with antibiotics and 21% were treated with antivirals[7]. However, a retrospective case series of 393 SARS-CoV-2 patients in New York revealed that only 5.6% of patients had bacteremia and none of them received antibiotics during treatment[6,8,10,11].

As it can be difficult to differentiate SARS-CoV-2 from bacterial pneumonia and increase the risk of patients without bacterial infections are receiving unnecessary antibiotics. Therefore, we have recognized the necessity of developing a rapid antibiotic guideline for the treatment of patients with SARS-CoV-2 who have coinfections. These recommendations are intended to ensure the better antibiotic management of suspected or confirmed bacterial pneumonia in adults during the SARS-CoV-2 pandemic. This includes people presenting to hospital with moderate to severe community-acquired pneumonia and people who develop pneumonia while in hospital.

Development process of treatment guidelines

We used methodologically rigorous process for evaluating the best available evidence, clinical syndrome specific guidance and providing treatment recommendations. In addition, we used MEDLINE, OVID Epub and EMBASE searches complemented with extensive use of Web engine to identify guidelines on empirical treatment of community and hospital-acquired pneumonia in the last 10 years. This is to be ensured that our guidelines are rational and best available evidence for antimicrobials. The search was structured to include SARS-CoV-2 terms, viral pneumonia and bacterial infection was defined as an acute infection including either (a) co-infection on presentation, or (b) secondary infection emerging during the course of illness or hospital stay. We assessed the extent to which recommendations considered resistance, in addition to efficacy and safety, when recommending antibiotics. This guideline was developed using the GRADE approach for evidence assessment. In addition, the methodological approach was modified according to the Guidelines International Network/ McMaster checklist for the development of rapid recommendations.

Table 1 Antibiotics Recommendations for SARS-CoV-2 infected adult (Age >18) with suspected community-acquired pneumonia

Empirical treatment	**Antibiotics and dosage** (oral doses are for immediate-release medicines)
Oral antibiotics for moderate or severe pneumonia	Options include: Doxycycline: 200 mg on first day, then 100 mg once a day Co-amoxiclav: 500 mg/125 mg three times a day with Clarithromycin: 500 mg twice a day In severe pneumonia, and if the other options are unsuitable: Levofloxacin: 500 mg once or twice a day *consider the safety issues with fluoroquinolones
Intravenous antibiotics for moderate or severe pneumonia	Options include: Co-amoxiclav: 1.2 g three times a day with Clarithromycin: 500 mg twice a day Cefuroxime: 750 mg three or four times a day (increased to 1.5 g three times a day if infection is severe) with Clarithromycin: 500 mg twice a day In severe pneumonia, and if the other options are unsuitable: Levofloxacin: 500 mg once or twice a day *consider the safety issues with fluoroquinolones

Table 2 Antibiotics Recommendations for suspected hospital-acquired pneumonia in adults with SARS-CoV-2 (Age >18)

Empirical treatment	**Antibiotics and dosage** (oral doses are for immediate-release medicines)
Oral antibiotics for non-severe pneumonia when there is not a higher risk of resistance	Options include: Doxycycline: 200 mg on first day, then 100 mg once a day Co-amoxiclav: 500 mg/125 mg three times a day Co-trimoxazole: 960 mg twice a day (see the BNF for information on monitoring of patient parameters) If the other options are unsuitable: Levofloxacin: 500 mg once or twice a day (consider the safety issues with fluoroquinolones)
Intravenous antibiotics for severe pneumonia; for example, symptoms or signs of sepsis or ventilator-associated pneumonia or when there is a higher risk of resistance	Options include: Piperacillin with tazobactam: 4.5 g three times a day, increased to 4.5 g four times a day if infection is severe Ceftazidime: 2 g three times a day If the other options are unsuitable: Levofloxacin: 500 mg once or twice a day (use a higher dosage if infection is severe; consider the safety issues with fluoroquinolones)
Antibiotic to be added if meticillin-resistant *Staphylococcus aureus* infection is suspected or confirmed; dual therapy with an intravenous antibiotic listed above	Vancomycin: 15 mg/kg to 20 mg/kg two or three times a day intravenously, adjusted according to serum vancomycin concentration. Maximum 2 g per dose. Teicoplanin: Initially 6 mg/kg every 12 hours for 3 doses intravenously, then 6 mg/kg once a day (see the BNF for information on patient parameter and therapeutic drug monitoring) Linezolid: 600 mg twice a day orally or intravenously (with specialist advice only; see the BNF for information on monitoring of patient parameters)

Discussion

As antibiotics save lives, most antibiotic treatments for pneumonia depend on the empirical method[6]. Adequate antibiotics treatment is crucial during SARS-CoV-2 pandemic to prevent secondary bacterial infections[6,10,11]. However, the appropriate use of antibiotics for the treatment of pneumonia is the key to addressing the issues of antimicrobial resistance while ensuring access to lifesaving antibiotics[6,10,11]. But defining what appropriate means remains problematic given the ongoing substantial challenges in diagnosing SARS-CoV-2 pneumonias. In the case of SARS-CoV-2, better understanding and predicting disease severity, which can help guide treatment and management decisions, are essential to effectively combatting pandemic[6,10,11]. Since the distribution of causative bacteria and antibiotic resistance vary between countries, it is necessary to develop an appropriate antibiotic treatment guideline based on epidemiological data and literature.

To guide decision making about antibiotics, use antibiotic prescribing recommendation Table 1 for patients with suspected community-acquired pneumonia, that has developed before or within 48 hours of admission. However, antibiotic prescribing recommendation Table 2 for patients with suspected hospital acquired pneumonia that develops 48 hours or more after admission and that was not incubating at admission. For both recommendations, when choosing antibiotics, also take account of local antimicrobial resistance data and other factors such as their availability, toxicity, and previous history of allergies. If the patient can take oral medicines and their condition is not severe enough to need intravenous antibiotics, oral antibiotics were recommended. However, importantly review all antibiotics at 24 to 48 hours or as soon as bacteria culture sensitivity results are available and switch to a narrower spectrum antibiotic when appropriate. Also, if the pneumonia is due to SARS-CoV-2 only and there is no evidence of bacterial infection, discontinued the antibiotic treatments[6,10,11]. Moreover, if antibiotics are continued, administered them for a total of 5 days, then discontinued them unless there is a clear bacteria culture test is positive.

For intravenous antibiotic recommended to reviewed within 48 hours and consider about switching to oral antibiotics if the patient progress prominent. In specific populations, such as hepatic impairment, renal impairment, pregnancy, and breastfeeding, and when administering intravenous antibiotics followed the guidelines for appropriate use and dosing[6,10,11]. It is necessary to consult a local microbiologist for alternative options in case of complications. If patients have history of penicillin allergy, avoid using co-amoxiclav and use cefuroxime with caution. For fluoroquinolones, it is necessary to followed the appropriate guidelines because of very rare reports of disabling and potentially long-lasting or irreversible side effects affecting musculoskeletal and nervous systems[6,10,11]. Discontinued the treatments if signs of a serious adverse reaction, such as tendonitis, prescribing with special caution for people over age 60 years and avoiding coadministration with corticosteroid.

The recommendations in this guideline are based on evidence from the best available clinical studies with patient important endpoints. Our recommendations highlight the important need to focus on antibiotic prescribing in patient with SARS-CoV-2, and to ensure that antibiotic stewardship programs are well positioned to improve prescribing and minimizing the antibiotic resistance.

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Conflicts of interest and competing financial interests

No author declares any potential conflict of interest or competing financial or non-financial interest in relation to the manuscript.

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