Official journal of the Spanish Society of Chemotherapy

Update in infection diseases 2020

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What happened to infectious diseases and anti-infective therapy in 2020 beyond COVID-19?

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Revista Española de Quimioterapia
doi:10.37201/req/s01.02.2021

ABSTRACT

The year 2020 was the year of infectious diseases with the arrival of SARS-CoV-2, which represented a profound change in the world we knew. However, we present a brief description of some of the top infectious diseases articles from 2020 not related with SARS-CoV-2. We reviewed a selection of the most important and relevant achievements in diagnosis and therapy related to bacteremia, nosocomial pneumonia, skin and soft tissue infections, infections by *Clostridioides difficile*, mycobacterial infections and invasive fungal infections. This year entailed a significant step forward in the indisputable value of the health care stewardship programs.

Keywords: Infectious diseases non-COVID, antimicrobial therapy, nosocomial infections

The year 2020 was the year of infectious diseases with the arrival of SARS-CoV-2, which represented a profound change in the world we knew. However, we present a brief description of some of the top infectious diseases articles from 2020 not related with SARS-CoV-2.

BACTEREMIA

Sepsis is life-threatening organ dysfunction, it is considered a major cause of health loss, but data for the global burden of sepsis are limited. In the study of Rudd *et al.*, data about global sepsis incidence and mortality from 1990 to 2017 are analysed. In 2017, an estimated 48.9 million incident cases of sepsis were recorded worldwide and 11 million sepsis-related deaths were reported, representing 19.7% of all global deaths. Age-standardised sepsis incidence fell by 37.0% and mortality decreased by 52.8% from 1990 to 2017. However, sepsis incidence and mortality varied substantially across regions, with the highest burden in sub-Saharan Africa, Oceania, South Asia, East Asia, and Southeast Asia [1].

Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia is associated with mortality of more than 20% so the use of appropriate treatment is under continuous study. In the study of Tong *et al.*, participants of 27 hospitals with MRSA bacteremia were randomized to standard therapy (intravenous vancomycin or daptomycin) plus an antistaphylococcal β-lactam (intravenous flucloxacillin, cloxacillin, or cefazolin) or standard therapy alone. They conclude that addition of an antistaphylococcal β-lactam to standard antibiotic therapy with vancomycin or daptomycin did not result in significant improvement in the primary composite end of mortality, persistent bacteremia, relapse, or treatment failure [2].

Pujol *et al.* designed a multicentre trial to test the hypothesis that daptomycin plus fosfomycin achieves higher treatment success than daptomycin alone in hospitalized adults with MRSA bacteremia and native valve endocarditis. Daptomycin plus fosfomycin provided a 12% higher rate of treatment success than daptomycin alone, but this difference did not reach statistical significance and it was more often associated with adverse events. They suggest that this antibiotic combination could be more effective in younger patients and those with more severe disease [3].

NOSOCOMIAL PNEUMONIA

The relatively high incidence, rising rates of antimicrobial resistance, and suboptimal clinical outcomes of patients with nosocomial pneumonia provide the impetus to optimize the use of existing antibiotics. Meropenem is a licensed agent for the treatment of nosocomial pneumonia. The pharmacodynamics is optimized with the use of prolonged infusions, especially continuous infusion (CI).

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In the study of Benitez-Cano *et al*., critically ill patients with nosocomial pneumonia were enrolled to received 1 g/8 h or 2 g/8 h by CI (8 h infusion). Although, the administration of meropenem by CI improves drug exposure in the epithelial lining fluid, only the highest dose of meropenem allowed achieving an optimal probability of target attainment (PTA) for all isolates with a MIC < 4 mg/L. However, in intermediate strains (MIC between 2 and 8 mg/L), the meropenem dose by CI needed to achieve an optimal PTA would have to be as high as 8 g/8 h, a dose that is four times higher than the highest approved meropenem dose [4].

SKIN AND SOFT TISSUE INFECTIONS

Skin and soft tissue infections are a common chief complaint in the Emergency Department. Research has shown that clinical examination alone can be unreliable in distinguishing between cellulitis and abscesses, a distinction that is important because each one require different treatments. Point-of-care ultrasonography has been demonstrated as a good tool to improve the diagnostic accuracy for these skin and soft tissue infections [5].

In patients with diabetic foot osteomyelitis who underwent surgical debridement, the duration of systemic antibiotic treatment with a short antibiotic regimen (3 weeks) compared with a long regimen (6 weeks) is associated with non-inferior results for clinical remission and adverse events [6].

Rates of cardiac implantable electronic device (CIED) related infections have increased and been associated with increased morbidity, mortality and financial burden on healthcare systems. The utilization of an antibiotic envelope at the time of device implantation or upgrade reduces major CIED infections, especially if used in patients to be at higher risk for infection [7].

Clostridioides difficile

Clostridioides difficile has been a significant enteric pathogen of humans. Previously, it was thought that *C. difficile* was primarily a hospital-acquired infection; however, with the emergence of community-associated cases, and whole-genome sequencing suggesting the majority of the hospital *C. difficile* infection (CDI) cases are genetically distinct from one another, there is compelling evidence that sources/reservoirs of *C. difficile* outside hospitals play a significant role in the transmission of CDI [8].

Regarding CDI treatment, a systematic review of the literature and network meta-analysis, compare the relative effectiveness of vancomycin (VCM), metronidazole (MTZ) and fidaxomicin (FDX). The meta-analysis suggests that FDX and VCM, but not MTZ, are effective first-line treatments for CDI, and that FDX may be more effective at preventing CDI recurrence than VCM [9].

NON-TUBERCULOUS MYCOBACTERIA

Non-tuberculous mycobacteria (NTM) represent over 190 species and subspecies, some of which can produce disease in humans of all ages and can affect both pulmonary and extrapulmonary sites. In the guideline of Daley *et al*., a revision of the treatment of pulmonary disease in adults (without cystic fibrosis or human immunodeficiency virus infection) caused by the most common NTM pathogens such as *Mycobacterium avium* complex, *Mycobacterium kansasii*, *Mycobacterium xenopi* and *Mycobacterium abscessus* was done [10].

FUNGAL INFECTIONS

Aspergillus fumigatus sensu lato encompasses a number of difficult-to-distinguish species, the highest percentage being *A. fumigatus sensu stricto* and the so-called cryptic species accounting for 10–15% of the isolates. Cryptic species commonly show intrinsic resistance to amphotericin B and azoles. In contrast, *A. fumigatus sensu stricto* isolates may acquire resistance following azole exposure. Tackling resistance is a challenge since azole-resistant patients present up to 31% higher mortality than azole-susceptible cases.

In the study of Escribano *et a*l., 30 hospitals from Spain and the Spanish Mycology Reference Laboratory (SMRL) were enrolled. Eight hundred and forty-seven isolates [*A. fumigatus sensu stricto* (*n* = 828) and cryptic species (*n* = 19)] were included. Only cryptic species were amphotericin B resistant. *A. fumigatus* clinical isolates proved that 7.4% of isolates were azole resistant. Resistance was commonly found in cryptic species or in isolates carrying TR_{34}-L98H *cyp51A* gene substitutions, the latter restricted to some cities located in the northern and mediterranean areas of Spain [11].

Candida auris is a recently emerging nosocomial pathogen, which was initially described in Japan in 2009 and then reported in over 30 countries worldwide afterwards. *C. auris* is usually resistant to several drugs, such as fluconazole, voriconazole, and amphotericin B.

In the study of Chen *et al.,* a systematic review and meta-analysis was done. More than 4733 cases of *C. auris* were reported in over 33 countries, with more cases in South Africa, United States of America, India, Spain, United Kingdom, South Korea, Colombia and Pakistan. *C. auris* exhibited a decrease in case count after 2016. Resistance to fluconazole, amphotericin B, caspofungin, micafungin and anidulafungin in *C. auris* were 91, 12, 12.1, 0.8 and 1.1%. The overall mortality of *C. auris* infection was 39%.

In recent years, the global public health community has increasingly recognized the importance of antimicrobial stewardship (AMS). However, the subject of antifungal stewardship (AFS) has received less attention. While the principles of AMS guidelines likely apply to stewarding of antifungal agents, there are additional considerations unique to AFS. AFS activities are outlined in Table 1 [12].

Table 1 **Essential, achievable, and aspirational antifungal stewardship activities. Adapted from [12].**

Stewardship Activity Level	Description
Essential	Development of institutional treatment pathways or bundles for antifungal prophylaxis and empiric therapy
	Development of targeted education programs for appropriate diagnosis and treatment
	Antifungal prescription review for drug-drug interactions
	Handshake rounds or postprescription review and feedback
	Intravenous to oral transition program
	Local surveillance and reporting of IFD to prescribers
Achievable	Rapid non-culture-based diagnostic tests for *Candida* and *Aspergillus* spp communicated to AFS team/clinicians
	Provide timely antifungal susceptibility testing results provided and communicated in a timely manner to AFS team/clinicians
	Specific comments to guide therapy and antifungal dosing recommendations are provided on microbiology reports
	Cumulative antifungal susceptibility reports reported to prescribers
	Timely TDM reported to AFS team and clinicians
	Review of autopsy reports and patient outcomes systematically to assess for undiagnosed IFDs and/or underutilization of antifungal agents
Aspirational	Participate in regional or national surveillance systems
	Individualized patient risk assessment (eg, institutional risk model, genetic risk factor screening)
	Optimize use of point-of-care microbiological tests, when available
	Utilize personalized TDM-dose adaptation (such as Bayesian methods) for antifungal therapy
	Incorporate advanced radiologic approaches for invasive aspergillosis (CT pulmonary angiography, FDG PET/CT)

AFS: antifungal stewardship; CT: computad tomography; FDG PET/CT: fluorodeoxy glucose positron emission tomography/computed tomography; TDM: therapeutic drug monitoring.

CONFLICT OF INTEREST

The authors declare no conflicts of interest

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