Type: Invited Presentation

Final Abstract Number: 05.004
Session: Antifungal Prophylaxis or Treatment - Why, when and what?
Date: Thursday, March 3, 2016
Time: 10:15-12:15
Room: Hall 6

New options for prevention and treatment of invasive fungal infections

R. Duarte

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Abstract: (no abstract received from presenter)

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Type: Invited Presentation

Final Abstract Number: 06.001
Session: HIV - Management of Opportunistic Infections in Low-and-Middle-Income Countries
Date: Thursday, March 3, 2016
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Room: G.01-03

Tuberculosis/HIV co-infection

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Abstract: Tuberculosis (TB) is the only opportunistic infection, which is transmissible to the healthy immunocompetent host. HIV is the most important known risk factor that promotes progression to active TB in people with *Mycobacterium tuberculosis* infection. The lifetime risk of tuberculosis in immunocompetent persons is 5% to 10%, but in HIV positive patients, there is a 5% to 15% annual risk of developing active TB disease. During the past two decades, TB has become the major opportunistic infection complicating the HIV epidemic worldwide, especially in Asia and Africa.

India has one of the world's highest burdens of both TB (~2.1 million cases annually) and HIV infection (2.3 million prevalent cases). While TB occurs in all socioeconomic strata and ethnic groups, prevalence rates have been clearly linked to poverty. It has been estimated that undernutrition, HIV, smoking and diabetes are all strong risk factors for TB. Maternal TB in an HIV-infected woman is a risk factor for transmission of HIV to the infant and is associated with premature delivery or low-birth weight and with higher maternal and infant mortality.

Patients with advanced immunodeficiency are at high risk for acquisition of Rifampicin resistance when treated with twice-weekly or thrice-weekly regimens. This is possibly due to malabsorption and low blood levels of anti-TB drugs. Cure rates with standard anti-TB treatment regimens average 86%, but outcomes in HIV-infected individuals are worse than uninfected patients. Though most HIV-infected patients respond well to anti-tuberculosis treatment (ATT) initially, there is a significant risk of developing other opportunistic infections as well as recurrent TB, leading to increased mortality. Timely initiation of antiretroviral therapy (ART) has been shown to reduce mortality and improve long-term outcome of these patients. Several trials have now shown that early initiation of ART (within the first few weeks of ATT) reduces mortality and improves TB outcomes. The choice of ART regimen is governed by the drug-drug interactions between anti-TB and antiretroviral drugs: rifampicin is an inducer of the cytochrome p450 enzyme system, which metabolizes NNRTI drugs nevirapine and efavirenz. The metabolism of the latter is less affected by rifampicin and hence efavirenz is the NNRTI of choice when combined with ATT.

The 4 "I" policy for addressing co-infection of TB and HIV includes intensified case finding, infection control, isoniazid preventive chemotherapy and integration of TB and HIV services within antenatal, PMTCT, family planning and immunization services. Since HIV has become a chronic, manageable condition, the challenge ahead is to provide services to patients in an integrated manner and strengthen health systems so that long-term care can be effectively provided. Research priorities include improved and more sensitive point of care diagnostics for TB, shorter and more effective TB treatment regimens with minimum drug interactions with antiretroviral drugs and a better TB vaccine that is safe and effective in HIV-infected populations.

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Cryptococcal meningitis and beyond - Management of select opportunistic infections in Sub-Saharan Africa

G. Meintjes

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Abstract: In sub-Saharan Africa, despite successful scale-up of ART programmes, opportunistic infections remain a frequent cause of morbidity, hospitalization and death. Factors that contributed to this are delays to HIV diagnosis, late engagement in ART care, difficulties with ART adherence and many patients not remaining engaged in care. Although tuberculosis is the most frequent HIV co-infection in the region, other opportunistic infections also result in considerable morbidity and mortality.

The main focus of this presentation will be cryptococcal meningitis. National surveillance data from South Africa show that 6000-8000 cases of cryptococcosis have been diagnosed annually over the last decade. Case fatality rates remain extremely high, with around two-thirds of patients dying or being lost to follow-up in routine clinical settings and one-third in clinical trial settings. In terms of management, a randomized controlled trial conducted in Vietnam demonstrated that the induction antifungal therapy associated with the best survival was a combination of amphotericin B with flucytosine for 2 weeks. Flucytosine access is limited in sub-Saharan African countries, but this is being addressed by advocacy initiatives. Sertraline has anti-cryptococcal activity and is currently being evaluated as an addition to combination therapy. Over 60% of patients have raised intracranial pressure; this is managed with serial therapeutic lumbar punctures. Unlike TB, very early ART has been shown to increase mortality in patients with cryptococcal meningitis: in the Cryptococcal Optimal ART Timing

(COAT) trial those participants who started ART 1-2 weeks after cryptococcal diagnosis had a 73% higher mortality rate compared with those started 5-6 weeks after diagnosis. Immune reconstitution inflammatory syndrome (IRIS) is reported in 20% of patients with cryptococcal meningitis starting ART; management of this condition will be discussed.

Among all patients with CD4 counts < 100 presenting for HIV care in sub-Saharan Africa 2-20% are found to have cryptococcal antigenaemia even though most do not have clinical features of meningitis at the time. Observational data and findings of a cluster-randomised trial suggest that pre-emptive fluconazole for such antigenaemic patients may prevent meningitis and death. The optimal dose and duration of fluconazole for this indication needs to be defined.

Other important opportunistic disease contributing to HIV-related mortality in the region (pneumocystis pneumonia, Karposi's sarcoma and chronic gastro-enteritis) will be discussed, but this presentation will not address HIV-associated tuberculosis.

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Challenges in the management of opportunistic infections: Focus on Southeast Asia

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Abstract: Late presenters into HIV care remain common in South East Asia. In an analysis of more than 3700 patients in an Asian observational cohort, more than 72% were late presenters ie presenting into HIV care for the first time with CD4 of < 200 cells/mm^3 or with an AIDS defining illness. Consequently physicians in South East Asia continue to manage patients who present with a myriad of opportunistic infections including toxoplasmosis, CMV infection, disseminated fungal infections and tuberculosis. Advanced HIV infection also leads to an increased risk for immune reconstitution syndrome which may present as a diagnostic and or therapeutic challenge in these patients.

Apart from late presentation, substance use disorder and coinfections with hepatitis B and C are also relatively common in the region and can lead to additional challenges in the management of opportunistic infections and provision of antiretroviral therapy. Drug-drug interaction and hepatotoxicity are amongst the difficulties that may be encountered in these patients.

A further important consideration when managing patients with opportunistic infections is the optimal timing for the initiation of antiretroviral therapy. In recent years several large clinical trials have been performed to address this issue especially in relation to tuberculosis. These and data from observational studies would suggest that early initiation of antiretroviral therapy in the setting of active opportunistic infections confer survival benefits with the exception of tuberculous meningitis and cryptococcal meningitis.

Despite the advances that have been made in antiretroviral therapy and a global call for early and immediate initiation of treatment on diagnosis, a large majority of patients continue to present with late stage disease with opportunistic infections. Physicians in South East Asia and other low and middle income countries need to continue be equipped with the ability to diagnose and manage these infections effectively.

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The challenge of opportunistic infections: Focus on South America

J. Torres

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Abstract: Some opportunistic diseases are either exclusive or more commonly observed in South American AIDS patients than in those from different parts of the world. Interactions between HIV and endemic parasitic and other locally prevalent pathogens occur frequently in South America. However, knowledge about the impact of these interactions has been accumulating only recently.

HIV infection may alter the natural history of tropical diseases in different ways. Diagnosis and treatment may be altered and an increased pathogen burden may augment morbidity and mortality. The impact that tropical diseases have on the course of HIV infection may also be deleterious. Many intercurrent infections increase the HIV viral load enhancing the progression of HIV disease and the risk of transmission of HIV to non-infected individuals. Similarly, chronic immunomodulation by pathogens, such as helminths and protozoa, may considerably accelerate the natural history of HIV infection.

Characteristics of coinfection in the region with HIV and some emblematic endemic pathologies, such as paracoccidioidomycosis, histoplasmosis, Chagas' disease, visceral leishmaniasis, strongyloidiasis and HTLV1, as well as some unique challenges posed by them, are reviewed in detail.

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Mers-CoV: From camels to humans

Z. Memish

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Abstract: The Middle East respiratory syndrome coronavirus (MERS-CoV) is a novel enzootic beta coronavirus that was first described in September 2012. The clinical spectrum of MERS-CoV infection in humans ranges from an asymptomatic or mild respiratory illness to severe pneumonia and multi-organ failure; overall