Perspective

Antiviral therapy in current clinical practice: Respiratory virus infections

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Abstract

Respiratory virus infections have a huge impact on healthcare settings and the public health sector of any country. Management of seasonal respiratory virus outbreaks and surveillance of emerging and re-emerging respiratory viruses requires a strategic plan and the establishment of adequate diagnostic facilities, vaccination programmes, infection control measures and therapeutic options. In addition, the management of respiratory virus infections in immune-compromised individuals requires special attention in a healthcare system. Countries with limited resources need to focus on establishing cost-effective services to manage such a wide range of healthcare needs related to respiratory virus infections.

Healthcare systems face a major challenge in managing common respiratory tract virus infections among patients from risk groups, as these viruses can cause severe disease. Guidelines provide defined categories of patients from risk groups, and how to manage their respiratory virus infections with specific antiviral medications.[1,2] Antiviral medication may include antiviral drugs and monoclonal antibodies, both of which play a major role in safeguarding the lives of patients in risk groups from respiratory virus infections.

Seasonal influenza A & B viruses can cause severe disease among very young children, the elderly, pregnant women, and people with obesity, diabetes, chronic organ disease or immune suppression.[1] Oseltamivir is the main antiviral agent recommended in guidelines to manage seasonal influenza virus infections among patients from these risk groups.[1] In addition, zanamivir is also considered (most often as a second-line therapeutic option) based on the severity of the disease, the type/subtype of Influenza virus circulating at the time, and the status of the patient's immune system.[1] The guidelines recommend that antiviral therapy should be started within 36 to 48 hours of the onset of symptoms, but clinicians can consider treatment even in late presentations based on the clinical indications.[1] An influenza virus surveillance system with adequate testing

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facilities is required for the rational use of these antiviral drugs. Empirical antiviral treatment can be considered for influenza-like illness in patients from risk-groups when virus circulation is reported by national or regional influenza surveillance systems. Such surveillance systems need to have facilities to carry out Influenza virus typing, subtyping and to identify the strain of a representative number of detected viruses in a given period. Exclusion of COVID-19, at least by a point-of-care test, would be a rational practice when considering empirical antiviral treatment for probable Influenza virus infections, as co-circulation of both viruses does occur. Annual influenza vaccination can be offered to protect those who are most at risk of facing serious illness or death if they get influenza; this includes individuals aged 65 years or older, pregnant women, and individuals with chronic respiratory disease, chronic heart and/or vascular disease, chronic kidney disease, chronic liver disease, chronic neurological disease, diabetes and adrenal insufficiency, immunosuppression, asplenia or dysfunction of the spleen, and morbid obesity and pregnant women.[3] The guidelines recommend post-exposure antiviral prophylaxis to be given to individuals in risk groups as a possible option, but this is only very rarely considered in healthcare settings, due to various practical reasons.[1]

SARS-CoV-2 infection is also known to cause complications among those defined as risk group patients. Therefore, COVID-19 should be considered in the differential diagnosis along with Influenza. Specific antiviral or monoclonal antibody therapy is available to manage risk group patients with COVID-19. Identification of patients from risk groups who are vulnerable to complications, early testing facilities to diagnose COVID-19, and early provision of antiviral drugs or monoclonal antibody therapy are strategies required to successfully manage COVID-19 in risk groups which have a higher risk of complications.

Identified groups of patients who might be eligible for specific COVID-19 treatment include (but not all) individuals with chromosomal disorders affecting the immune system such as Down's syndrome, certain types of cancer or on treatment for certain types of cancer, sickle cell disease and some haematological conditions, chronic kidney disease (CKD)-stage 4 or 5, severe liver disease, organ transplantation, certain autoimmune or inflammatory conditions (such as rheumatoid arthritis or inflammatory bowel disease) and HIV or AIDS (as these patients have a weakened immune system, either inherited or acquired), and individuals with rare neurological conditions such as multiple sclerosis, motor neurone disease, Huntington's disease or myasthenia gravis. Some individuals within these defined risk groups may be eligible to receive new treatment modalities such as neutralising monoclonal antibody or antivirals if they test positive for COVID-19 via a lateral flow test or PCR, but are not admitted to hospital.[4,5] This therapy should only be considered after obtaining expert medical advice and reviewing relevant precautions and contraindications to therapy, as given in local or national guidelines. Validated lateral flow SARS CoV-2 tests can be used for patients in these risk groups to make an early diagnosis of COVID-19 within the first 5 days of onset of symptoms when such treatment is considered but SARS COV-2 PCR testing facilities are limited or time-consuming.

COVID-19 patients who present within 10 days of the onset of symptoms and are admitted to hospital requiring low flow supplemental oxygen, can also be treated with specific antiviral drug therapy. In addition, immune-suppressed patients with COVID-19 can be considered for antiviral therapy regardless of the duration of illness or oxygen requirement. Antiviral therapy should only be considered under strict medical supervision when clinically indicated in patients who do not

have contraindications for the therapy. Antiviral treatment strategies for COVID-19 can change further in the future, depending on new knowledge and discoveries. Therefore, up-to-date local or national guidelines must always be referred to when selecting appropriate antiviral and monoclonal antibody therapy for COVID-19.

In addition to antiviral management strategies, the up-to-date completion of age or/and risk group-specified COVID-19 vaccination is the main strategy to prevent COVID-19-related morbidity and mortality. All immune-suppressed patients should have received 3 primary doses of COVID-19 vaccines in contrast to the two doses prescribed in the primary schedule for immunocompetent people. In addition, all risk group individuals and other eligible staff should have received the recommended reinforcing/booster COVID-19 immunisation. According to epidemiological data on COVID-19, the reinforcing/booster COVID-19 vaccination doses may need to be considered for risk group individuals in the future as well. In addition to the original COVID-19 vaccines, bivalent m-RNA COVID-19 vaccines which contain both the original SARS CoV-2 and the (later) Omicron variant are also available for reinforcing immunisation programmes.

RSV, parainfluenza, adenovirus, and a few other viruses can also cause significant respiratory tract infections among very young children and immune-compromised people. The antiviral agent, ribavirin is used to treat RSV infections in specific risk group patients who are vulnerable to severe complications. Aerosolized ribavirin-based therapy is considered (with special arrangements) in major transplant centres for heterologous stem cell transplant recipients with RSV respiratory tract infection.[6] Although not a common practice, ribavirin may be used to manage life-threatening respiratory tract infections caused by RSV, Parainfluenza and Adenovirus in other immune-suppressed children on a case-by-case basis, under expert medical care.[7]

Adenovirus respiratory tract infections can cause severe disease among immune-compromised patients. It is therefore necessary to investigate for disseminated adenovirus infection, by testing blood samples of transplant recipients, when adenovirus is detected in their respiratory tract. IV cidofovir is used in some instances to treat adenovirus infections in transplant recipients, under local transplant management protocols.

There are several other opportunistic viruses, atypical bacteria, fungi, and parasites which can cause severe respiratory tract infections among immune-suppressed patients, causing significant morbidity and mortality. Therefore, it is important to consider a broad spectrum of differential diagnoses when managing respiratory tract infections among immune-suppressed patients, in contrast to immune-competent individuals.

Conclusion

Influenza Like Illness (ILI), Severe Acute Respiratory Tract Illness (SARI) and COVID-19 surveillance programmes are nationally established in some countries. However, in countries with limited resources, despite the availability of national surveillance programmes, there is still a lack of diagnostic facilities in some peripheral centres. Point-of-care testing facilities can be established in such peripheral settings (where molecular diagnostic facilities are not available), using properly validated test methods and quality assurance programmes. National and regional reference virology laboratory facilities can be upgraded to acquire facilities for virus cell culture, and virus

molecular typing and subtyping for epidemiological characterisation purposes. In addition, stem cell and solid organ transplant centres and cancer institutes need specialised clinical virology testing facilities which use multiplex molecular test methods with rapid turnaround time, to ensure early diagnoses of a wide range of respiratory viruses and other pathogens. In a country with limited resources, a strategic plan with technical details is essential in order to establish such a virology service network in a cost-effective manner.

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