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REVIEW

Challenges presented by MERS corona virus, and SARS corona virus to global health

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Abstract Numerous viral infections have arisen and affected global healthcare facilities. Millions of people are at severe risk of acquiring several evolving viral infections through several factors. In the present article we have described about risk factors, chance of infection, and prevention methods of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV), human coronaviruses (CoVs) frequently cause a normal cold which is mild and self-restricting. Zoonotic transmission of CoVs such as the newly discovered MERS-CoV and SARS-CoV, may be associated with severe lower respiratory tract infection. The present review provides the recent clinical and pathological information on MERS and SARS. The task is to transform these discoveries about MERS and SARS pathogenesis and to develop intervention methods that will eventually allow the effective control of these recently arising severe viral infections. Global health sector has learnt many lessons through the recent outbreak of MERS and SARS, but the need for identifying new antiviral treatment was not learned. In the present article we have reviewed the literature on the several facets like transmission, precautions and effectiveness of treatments used in patients with MERS-CoV and SARS infections.

Contents

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1. Background

In recent times, several life threatening viruses have emerged. They have been responsible for causing significant human mortality, in addition to raising serious public health concerns worldwide. Due to modern life, extensive travel of humans and goods, their outbreak anywhere in the world could potentially be a risk everywhere. Two novel viruses were implicated to be responsible for severe acute illness in recent times, i.e. Middle East Respiratory Syndrome-Corona-Virus (MERS-CoV) and severe acute respiratory syndrome-corona-virus (SARS-CoV) (To et al., 2013; Meyer et al., 2015). These two viruses are causing acute and often fatal illness. Due to their high fatality rate (30–90%), they have had dual effect: fear among public from contracting one or more of them as well as high burden on the healthcare system, including the treating physician and other health care workers. The reservoir of the viruses is usually animal, including: bats, camels, or chimpanzees. Apart from animal to human transmission, human to human transmission has been reported, usually from an infected patient to a member of the health care team and to other patients in the hospital. Although no specific treatment has been recommended for their management so far; supportive treatment has shown to improve the outcome. Antiviral vaccines are under process. These novel viruses represent significant challenges to public health in general and to public health services and infection control in specific. Intensive education awareness and multi directional care does improve disease outcome. Therefore an accurate knowledge of their reservoir, their transmission, presenting symptoms approach to their investigation and best possible management together with preventive steps, is necessary. Close surveillance and vigilance remains a top priority to physicians and health authorities alike. In the present article we have reviewed the literature on several aspects like transmission, safety and efficacy of therapies used in patients with MERS-CoV and SARS infections.

2. MERS corona virus

As of January, 2016 WHO has reported 1638 human cases, including 587 deaths due to Middle East Respiratory Syndrome (MERS co-V) (WHO, 2014; Gostin and Lucey, 2015). According to WHO, MERS a deadly disease caused by corona virus, "is a threat to entire world" (Zaki et al., 2012; Bialek et al., 2014; Azhar et al., 2014; Pereyaslov et al., 2013). MERS-CoV is considered a deadly virus with a single strand RNA (de Groot et al., 2013; Chu et al., 2014).

The MERS-CoV has been identified in various countries in the gulf region, Korea and European region with an obviously high death rate. It is taxonomically similar to the SARS-CoV and has also been linked with serious respiratory disease along with nosocomial transmission in hospital areas. The first human case was reported in 2012 from Saudi Arabia. Later it was isolated from Egypt from a patient's lung. Apart from Saudi Arabia, nearly 22 countries including UAE, Kuwait, Qatar, Indonesia, Thailand, UK, Korea, China and USA were reported to have MERS cases (Azhar et al., 2014; Pereyaslov et al., 2013). In USA the first case of MERS-CoV was identified on 2nd May, 2014, in a traveler who came from the Kingdom of Saudi Arabia. The second instance of MERS-CoV was recorded on 11th May, 2014, which was confirmed in a traveler who is also from the Kingdom of Saudi Arabia. The Republic of Korea's first, or "index", case was confirmed on 20 May 2015 and notified to WHO the same day, till today 185 cases are reported in Korea including 36 deaths.

A team of WHO and King Saud University (KSU) experts, in joint collaboration, isolated MERS virus from nasal swabs of camels and demonstrated that the whole genome sequence of human and camel obtained virus is indistinguishable (Briese et al., 2014). Although person-to-person transmission is low, it does occur from patients to health care workers and close contacts. So far, there is no specific vaccine or treatment for the disease. Maintaining hygiene, avoiding contact with camel or infected patients is mandatory to prevent further spread of MERS.

2.1. Reservoir of virus

Published research suggests that the natural reservoirs of infection are "camels". Many people with MERS (especially primary cases) have had close contact history with camels and drinking camel milk. During August 2013 the Lancet Infectious Diseases reported that 100% of Oman camels and 14% of Spanish camels had specific antibodies against MERS coV. In a study carried out in KSA, it was found that 90% of dromedary camels (one-humped camels) were having MERS-Co-V indicating that dromedary camels are the natural reservoirs, and considered animal sources of MERS-co-V (Reusken et al., 2014).

2.2. Transmission of MERS-CoV

Camels are considered the source of infection to the humans. Subsequently, human to human transmission of MERS-CoV occurs from patients to health care workers through droplet infection, or through touching contaminated surfaces (Chu et al., 2014; Zumla et al., 2015).

2.3. Incubation period of MERS-Co V

The incubation period of MERS-Co V ranges from 2 to 14 days. (Zaki, 2012).

2.4. Epidemiology of MERS-CoV

Throughout the summer season of 2012, in Jeddah, a Saudi Arabian city, an anonymous coronavirus (CoV) was identified from the saliva of a patient with acute pneumonia and renal failure. On 15th September 2012, a similar type of virus, named human coronavirus, was isolated from a patient with severe respiratory infection who traveled from the Middle East to London, United Kingdom. Cases have also been reported in other Eastern Mediterranean countries as: Kuwait, Yemen, Oman, Iran, Lebanon, Tunisia, Algeria, Southeast Asian countries as: Bangladesh, Malaysia, as well as European countries as: France, Italy, Germany, Netherlands, United Kingdom, Greece, Italy, in addition to the United States (Zaki et al., 2012; Bermingham et al., 2012; Gautret et al., 2014; World Health Organization, 2014; Colin et al., 2015).

Recently Oman has confirmed its second MERS-CoV case of 2014—and its fourth overall—apparently a contact of the most recent MERS patient, who has died, according to media reports. The most recent patient infected with MERS-CoV is hospitalized in stable condition, according to the Muscat Daily. After confirming eight MERS-CoV cases in the first 9 days of 2015, Saudi Arabia has now reported 833 confirmed cases, including 358 deaths, for a case-fatality rate of 43%.

2.5. Management of MERS

Till date, no proper treatment or prophylaxis exists for MERS-CoV. Improved diagnosis and therapy remains the basis of patient management.

2.5.1. Infection control

Successful disease control is key to ensure protection for health care employees and patients. Convalescent plasma, lopinavir and interferon (IFN) are prescribed for better management of MERS-CoV infected persons. Interferon and lopinavir are likely to be the most accessible initial treatment. The effect of steroids on viral infection control in MERS is not well known, even though systemic corticosteroid usage delayed clearance of the related coronavirus, SARS CoV. MERS CoV has been linked with delayed replication of other respiratory infections. Subsequently, sequential sampling, diagnosis with PCR must be done in every patient who receives steroids for whichever symptom. Like exacerbations of asthma/COPD, doubted or identified renal problems or refractory septic shock are contraindications for such management scheme. Ribavirin and interferon combined therapy has some beneficial effects (Al-Tawfiq et al., 2014). Cyclosporin A (CsA), cycloheximide, mycophenolate, IFN-β, omacetaxine mepesuccinate, anisomycin, and emetine dihydrochloride hydrate were identified to show the best protective effect from MERS-CoV (Corman et al., 2013).

2.5.2. Signs and symptoms of MERS-CoV

General signs and symptoms comprise: rigor, feeling cold along with shivering, migraine, cough, sore throat, difficulty in breathing, muscular rheumatism, chest pain, kidney failure, pneumonia, giddiness, nausea and vomiting, dysentery, and stomach pain. It has been reported that abnormal symptoms comprising slight respiratory infection without pyrexia and diarrhea will occur before the development of pneumonia. Proper clinical decision should be followed for the diagnosis of patients suffering with MERS-CoV infection. It must be noted that immune-compromised people are thought to be at high risk to get infected by MERS-CoV.

2.5.3. Diagnosis of MERS-Co V

The PCR diagnosis method is used to identify and diagnose several infectious diseases, can be used to confirm MERS-CoV positive cases by collecting sputum or any other sample from the patient. A blood test can decide whether a person has earlier been infected, by diagnosing with antibodies for anti-MERS-CoV (Lee et al., 2003).

The situation of MERS-CoV in KSA remains serious, with the evolution of a new wave of cases during early 2015, with still a high fatality rate ranging from 30% to 40%. It is quite evident that secondary cases represent a bigger proportion of patients, most of them are health professionals involve in provision of healthcare of primary cases of MERS-CoV. Hence, infection control remains the main prevention and control method for this deadly disease. Drinking unsterilized camels' milk must be avoided till convincing proof is obtained, so that chances of infection can be reduced.

3. SARS corona virus

Severe acute respiratory syndrome (SARS) was considered among newly emerged infectious diseases, with a significant morbidity and mortality, when it was first identified in 2002 in China. WHO has defined SARS as a global threat caused by SARS corona virus. Due to a high case fatality rate, accurate knowledge of the SARS-CoV remains a priority. Consequently, as many as 8273 cases were confirmed from 37 countries around the world with 775 deaths, a case-fatality of about 10% (Centers for Disease Control and Prevention,

2014). Although no new SARS-CoV cases are occurring at the moment, yet re-emergence of SARS-CoV remains uncertain and it is speculated that the SARS-CoV is existing in its natural source.

3.1. Transmission of the SARS-CoV

SARS is believed to be transmitted through respiratory aerosols, which were released while an SARS patient coughs or sneezes. Viral infection will spread from the droplets of cough or sneeze of an infected patient are propelled in surroundings via air and will infect the nearby people who are nearby through several ways like mouth, nose or eyes. The virus also can spread by touching infected surfaces, and then touching the mouth, nose, or eye (Centers for Disease Control and Prevention, 2014).

3.2. Signs and symptoms

Incubation period of the SARS-CoV ranges from 2 to 10 days. Signs and symptoms include: high fever, migraine, discomfort in respiration and body pains, slight respiratory problem, diarrhea (10–20%), and cough (after 2–7 days) (Leung and Chiu, 2004).

3.3. Complications

Many patients infected with SARS virus develop pneumonia. Suffocation while breathing will increase, and patient requires mechanical respirator for respiration. SARS will become lethal in a few cases, frequently due to respiratory failure. Other possible problems include cardiac and liver failure. Persons older than 60 years of age—particularly those who have complications such as diabetes or hepatitis—are at greater risk of severe complications (Koren et al., 2003; Müller et al., 2012).

3.4. Diagnosis of SARS-Co V

3.4.1. PCR testing

Because SARS is a new disease in humans, anti-SARS-CoV antibodies are not found in populations that have not been exposed to the virus.

Antibody testing using ELISA and immunofluorescent antibody (IFA) tests are being developed by research laboratories. After sequencing the SARS coronavirus whole genome it has enabled the development of quick and accurate diagnostic tools and methods. Whereas additional antiviral therapy, RNA silencing methods, anti-monoclonal antibody, anti-viral peptides, and vaccines are under development.

3.5. Management

In the initial stages of the disease protease inhibitors such as lopinavir/ritonavir along with ribavirin may help in antiviral therapy, however the role of interferon and general steroids in treatment of immune-mediated lung damages needs additional investigation. Other antiviral therapy, RNA silencing, anti-monoclonal antibody, anti-viral peptides, and vaccines are under development (Geller et al., 2012).

3.5.1. Prevention

Scholars are working on various types of vaccines for the treatment of SARS, but still these vaccines need to be approved to test in humans (Centers for Disease Control and Prevention, 2015).

3.5.2. Following are the safety guidelines recommended by WHO

- *Washing hands:* Cleaning hands regularly with disinfectant or alcohol based hand sterilizing solution and warm water may help in preventing disease transmission.
- Disposable gloves should be used in case of contact with the infected person's body fluids or feces.
- Surgical mask should be used to cover both the nose and mouth, when in the same room as a person with SARS. Wearing eyeglasses also may offer some protection.
- Soap and hot water should be used to wash the utensils, towels, bedding and clothing of someone with SARS.
- Disinfection of exteriors which have been contaminated with respiratory droplets or other body secretions of an infected person.
- Follow all infection control measures for at least ten days even after the patient is totally recovered and did not show any symptoms of the disease.

4. Conclusion

Novel viruses of the millennium cause severe illness and severe case fatality. Modern techniques of identification of viruses by PCR and genetic coding techniques may be unable to provide an early and accurate isolation of the virus. Molecular surveillance has improved the management and outcome of the patients. Even though there is improvement in our knowledge about Corona-virus, numerous queries were still unanswered, together with the absolute origin, possible ways of transmission and exact treatment. More efforts are still needed to accelerate the improvement of an effective therapy and vaccination. However specific medicines for treatment of such viral infections and specific vaccines for the prevention of acute and often fatal illness caused by these novel viruses are not available till date, although tremendous efforts and research are ongoing. Extreme awareness, vigilance and surveillance are highly desired to prevent these life threatening virus illnesses.

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