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REVIEW

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ICU management of severe acute respiratory syndrome

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Abstract *Background:* Severe acute respiratory syndrome (SARS) is a contagious viral illness first recognized in late 2002. It has now been documented in 26 countries worldwide, with significant outbreaks in China, Hong Kong, Singapore, and Toronto. Research into identifying the etiological agent, evaluating modes of disease transmission, and treatment options is currently ongoing. *Discussion:* The disease can produce a severe bilateral pneumonia, with progressive hypoxemia. Up to 20% of patients require mechanical ventilatory support, with a fatal outcome occurring in about 5% of cases. *Conclusions:* We review the current knowledge about this disease, with particular emphasis on ICU management and infection control precautions to prevent disease transmission.

Keywords Severe acute respiratory syndrome · Acute respiratory distress syndrome · Mechanical ventilation · Infection control

Introduction

Severe acute respiratory syndrome (SARS) is a viral illness characterized by a syndrome of fever and respiratory symptoms that can progress to respiratory failure and death. Initial reports of a highly contagious atypical pneumonia originated from Guangdong Province, People's Republic of China, in November 2002. The condition remained isolated to China until February 2003, when an infected physician traveled to Hong Kong. Since then, until 20 April 2003, the disease has spread to affect over 3,500 individuals in 26 countries (WHO 19 April 2003, updates available at www.who.int/csr/sars/en). The largest outbreaks have been described in Hong Kong, Toronto, Canada, and Singapore, related to a contact with this infected physician in a Hong Kong hotel. While the Western world has been aware of this condition for only several weeks, considerable progress has been made in the identification of the responsible viral organism. There is less known about the mode of transmission and treatment of this disease, but likely mechanisms include droplet spread, surface contact, and possibly airborne transmission. This review describes the current state of knowledge of SARS, with particular reference to the management of the critically ill patient and the safety and protection of the ICU staff. The recommendations are based on the sparse published data available, collaborations between physicians in many affected

centers, recommendations from the World Health Organization and Centers for Disease Control, and local experience.

Etiological agent

A novel coronavirus has been isolated from patients meeting the case definition for SARS, using electron microscopy and polymerase chain reaction (PCR) of virus isolated in cell culture [1, 2]. Preliminary serological studies suggest that this virus has not previously infected the population of the United States [1]. The viral genome has been sequenced, and early PCR-based tests are in an evaluation phase.

Clinical features

Case definitions of SARS are currently based on the presence of epidemiological risk factors (close contact with SARS cases or travel to SARS "affected" areas) along with a combination of fever and respiratory symptoms, with or without hypoxia and/or chest radiographic changes [3]. However, as SARS spreads into the general population, our ability to distinguish it from other community-acquired pneumonias based on such epidemiological linkages will become increasingly tenuous. At this time SARS must be considered in the differential diagnosis of any community-acquired or nosocomial pneumonia. A "typical" history (see below), suggestive laboratory values (see below), and failure to respond to conventional antibiotics should raise suspicion. Diagnostic tests will be crucial in the future both to ensure that patients are isolated rapidly, and that treatment is initiated.

The incubation period has been reported as 2–10 days, and early manifestations include influenzalike symptoms such as fever, myalgias, and headache. It is presently not clear at what stage of the disease viral shedding occurs, or whether someone who is infected but asymptomatic can infect others. As our knowledge of SARS and the etiological coronavirus evolves, we will be able to answer these important questions. The viral load may play a role in both the transmission and severity of subsequent disease. The notion of "super spreaders" has been suggested to describe the occasional patient who is associated with spread to large numbers of contacts.

Our current understanding of the illness is that fever occurs in virtually all patients and is often the presenting symptom. Fever may occasionally be absent in the elderly. Some patients have mild respiratory symptoms at the onset, and gastrointestinal manifestations are relatively uncommon. Diarrhea has been reported with increased frequency in recent outbreaks. The respiratory phase starts after 3 – 7 days with dry cough and shortness of breath. In some cases these symptoms are followed by hypoxia and radiological evidence of progressive pulmonary infiltrates. The radiological picture is patchy, of focal infiltrates or consolidation often with a peripheral distribution, which may progress to diffuse infiltration. Pulmonary infiltrates may worsen during the first 10 days, and acute respiratory distress requiring mechanical ventilation has occurred in about 10–20% of patients. The case fatality rate is approximately 3–12% depending on whether the denominator includes both suspect and probable cases (3%) or probable cases alone (12%) [4, 5, 6]. While the mortality rate is higher in older patients particularly those with preexisting comorbidity (e.g., diabetes and immunosuppression), we have also seen young, previously healthy persons succumb to the disease. This may be due to higher viral loads or to their host response.

The disease runs for 7–14 days, and a biphasic course has been described in some patients, with an initial illness, improvement, and subsequent deterioration. This worsening can present as recurrent fever 4–7 days after initial defervescence, new chest infiltrates on radiography, or recurrent respiratory failure. In some patients an initial mild to moderate respiratory illness may initially improve, later to be followed by a progressive deterioration requiring ventilatory support.

Laboratory findings in patients with SARS include thrombocytopenia and leukopenia (in particular lymphopenia). Elevated creatine kinase, lactate dehydrogenase, and transaminases have been noted. There is evidence that the peak lactate dehydrogenase and an initial elevated white cell count may carry a poor prognosis [6]. Epidemiological studies are currently underway to help determine prognostic factors.

Management

Diagnostic testing

Initial diagnostic testing should include a search for other respiratory pathogens, including blood cultures, sputum Gram's stain and culture, and serological tests. Bronchoscopy is valuable to exclude other diagnoses but is not recommended in patients with a typical clinical picture and clear epidemiological link, due to the high risk that bronchoscopy poses to ICU staff. In patients who are immunosuppressed and when concerns regarding other diagnoses are high, the risk of bronchoscopy may be acceptable. Clinicians should save any available clinical specimens (respiratory, blood, and serum) for additional testing until a specific diagnosis is made. Specific tests for the virus, including antibody tests (enzyme-linked immunosorbent assay and immunofluorescence), and PCR tests are in development and evaluation stages.

Table 1 High-risk procedures for transmission of SARS in the ICU

Procedure	Concern	Possible solution
Nasopharyngeal swabs	Coughing	Use nasal swabs
Bag-valve-mask ventilation	Difficult to seal at face	Limit as much as possible
Intubation	Coughing, agitation	Sedation and neuromuscular blockade
Suctioning	Coughing, aerosolization	In-line suctioning
Noninvasive ventilation	Unfiltered aerosolized exhalation	Avoid
High frequency oscillation	Unfiltered exhalation, uncontrolled secretions	Avoid

Treatment

If the diagnosis is uncertain, empirical therapy for community-acquired pneumonia should be considered using antibiotics with activity against both typical and atypical respiratory pathogens. In all series of SARS described to date therapy has included broad spectrum antibiotics, including a fluoroquinolone or macrolide [4, 5, 6]. The treatment regimen for SARS that we follow, as of 11 April 2003, is as follows:

- Antibiotic therapy
  - Respiratory fluoroquinolone or macrolide
- Ribavirin
  - 400 mg intravenously every 8 h for 3 days, followed by
  - 1200 mg orally every 12 h for 7days
- Corticosteroids
  - Methylprednisolone 40 mg intravenously every 12 h for 3 days followed by prednisone 50 mg orally per day for 7 days.

The antiviral drug ribavirin has been used in the majority of patients treated in Hong Kong and in Toronto, without evidence of efficacy or even a strong anecdotal suggestion that patients benefit. The adverse effects of ribavirin are significant, particularly hemolytic anemia and electrolyte disturbances such as hypokalemia and hypomagnesemia. The drug is also teratogenic, and this should be considered when evaluating treatment options.

Anecdotal evidence suggests a benefit of corticosteroids, particularly in the patients with progressive pulmonary infiltrates and hypoxemia. In some but certainly not all patients a dramatic improvement has been noted following steroid therapy. Various regimens have been used in different centers, with doses ranging from methyprednisolone 40 mg twice daily (similar to *Pneumocystis* pneumonia therapy) [8] to 2 mg/kg per day (similar to late-phase therapy for acute respiratory distress syndrome) [7] to pulse doses of 500 mg intravenously per day).

Patients with a late deterioration have usually been restarted on ribavirin and increased doses of steroids. The evidence supporting such practices currently does not exist, and benefit is uncertain. Physicians must remain vigilant and search for another cause of fever and secondary sources of infection.

Oxygenation and ventilation

Management is affected by the increased risk of droplet transmission of virus by certain procedures. Oxygen therapy using aerosol humidifiers may increase the risk of droplet spread. Other high-risk procedures include obtaining nasopharyngeal swabs, bag-mask ventilation, intubation, suctioning, chest physiotherapy in nonintubated patients, nebulized drug therapy, noninvasive ventilation, and extubation (see Table 1). If a ventilated patient desaturates and requires manual bag ventilation, it is important to turn the ventilator to "standby" prior to disconnecting, to avoid droplet spray. In fact, in an intubated patient with SARS we recommend avoiding disconnecting the ventilator unless there is an obvious mechanical ventilator failure, even in the event of a cardiac arrest.

The ventilatory management of patients with SARS does not differ from that for patients with acute respiratory distress syndrome. The use of high-frequency oscillation may be associated with increased risk of droplet spread and exposure to respiratory secretions, and our practice is to avoid this intervention. Jet ventilation for those failing conventional ventilation may be used safely. Little experience exists with the use of interventions such as nitric oxide and prone positioning. Anecdotally, the experience in Toronto and Singapore has been that nitric oxide offers little benefit.

Infectious disease consultation is essential, for up-to-date advice on management and to advise on infection control precautions.

Infection control precautions

This organism appears to be transmitted by droplet spread, although surface contamination and possibly airborne spread may play a role. Recent data suggest that the virus may remain viable for considerable periods on a dry surface (up to 24 h). Staff education and continued vigilance are essential. Infection control measures for

Table 2 Infection control precautions in the ICU

Staff education
High-risk procedures, alternatives, and precautions
Ways of minimizing exposure and effective use of time when in the room
Instructions to staff on how to "undress" and "redress" without contamination
Importance of vigilance and adherence to all infection control precautions
Importance of monitoring own health
Information on SARS as it evolves
Dress precautions
Airborne precautions using a N95 or FFP2 respirator
Contact precautions
Eye protection with a non-reusable goggles or face-shield
Pens, paper, other personal items should not be allowed into or removed from the room
Powered air purification respirator hoods should be used during high-risk procedures
Environment/equipment
Negative pressure isolation rooms with antechambers, and doors closed at all times
Individual isolation rooms stocked with basic supplies and emergency drugs
Alcohol-based hand and equipment disinfectants
Gloves, gowns, masks and disposal units should be readily available
Use of video camera equipment or windows to monitor patients
Careful and frequent cleaning of surfaces with disposable clothes and alcohol-based detergents
No equipment should be shared
Transport
Avoid patient transport where possible
Reflect on need for investigations and whether the benefits justify the transportation risks
Intubated patients should have a filter (Conserve PALL 50) inserted between the bag valve and the swivel connector
Infection control should be alerted
Ventilation
Avoid
Nebulizers
Noninvasive ventilation
High frequency oscillation
Normal saline instillation prior to suctioning
Use
Filters on bag-valve-mask
Two filters per ventilator
Scavenger system for exhalation port

healthcare workers exposed to patients should include (see Table 2).

Negative pressure isolation rooms preferably with antechamber

The antechambers should be equipped with:

- Sinks/disposal units for gowns, gloves, masks, antibacterial soap, and alcohol hand wash
- Fresh boxes of gloves
- An instruction sheet to staff on how to "undress" and "redress" without contamination

To avoid repeatedly breaking the negative pressure barrier individual rooms should be stocked with basic supplies. Modified cardiac arrest carts containing emergency drugs such as epinephrine, atropine, and bicarbonate should be available in the room in the event of urgent need. Staff should remain outside the negative pressure rooms as much as possible. This means timing blood analysis and administration of any therapies to minimize entries and use of video camera equipment or windows to monitor SARS patients without direct staff exposure. An antechamber (preferably with a sink) helps to maintain strict infection control precautions and avoids the potential contamination of a single door room. Pens, paper, and other personal items should not be allowed into or removed from the room.

Dress precautions

- Airborne precautions using a N95 respirator [9] or equivalent (FFP2 respirator): it is important that manufacturer specifications be adhered to, for example, some N95 masks maintain protection for 8 h, some

only for 4 h. Touching the mask or lifting it to wipe the face or nose should be avoided. It is crucial to maintain a close seal to the skin and to ensure proper fit.
- Contact precautions, including the use of double gowns (at least one of which is waterproof) and double gloves, hats, and shoe covers. Gowns, gloves, hats, boots, masks, and goggles should be changed after seeing each SARS patient.
- Eye protection with nonreusable goggles or face shield.
- Staff should change into hospital scrubs upon arrival and change into own clothing at the end of the day to avoid fomite spread. Scrubs should not leave the hospital and should be sterilized after each use.
- Pens and paper should not be brought in and then out of negative pressure isolation rooms. Pagers and watches should be left outside or be carefully covered to avoid contamination.
- Powered air purification respirator hoods should be used by all members of the ICU team in the room during *all* high-risk procedures such as intubation and bronchoscopy.
- ALL precautions must be in place before staff members enter the room, regardless of the patient's condition.

ICU environment

- Surfaces must be carefully and frequently cleaned with alcohol-based disinfectants including nursing stations, computer keyboards, etc.
- No equipment should be shared.
- Air turbulence when changing linens should be minimized.
- No eating may be allowed at nursing stations. Protective gear must be removed and not hung around neck when eating/drinking.
- Staff must monitor their own health, and most centers have set up screening mechanisms for staff on arrival at work.

In the ICU the risk of droplet spread is increased by various procedures (Table 1). Efforts to avoid viral spread include the avoidance of nebulizers for drug administration and limitation or avoidance of the use of noninvasive ventilation. Nebulized humidification for oxygen therapy may carry similar risks, and our practice is to provide nonhumidified oxygen using nasal prongs or a venturi mask. A non-rebreather mask with expiratory port allowing gas filtration is available and may be of value. During bag-mask-valve ventilation a filter should be used on the expiratory port. High-risk procedures include endotracheal intubation and bronchoscopy. Intubation should be performed by the most skilled person available using the method with which they are most comfortable. Awake intubation may be associated with patient agitation and coughing, which can severely compromise infection control precautions. A powered air purification respirator (e.g., 3M Airmate) can be used for these procedures.

Ventilators should have two filters (e.g., Conserve 50 PALL filters) placed so as to eliminate the exhalation of viral particles into the environment and protect as much as possible the inside of the ventilator from contamination. One filter should be interposed between the distal end of the expiratory tubing and the ventilator itself and the second placed on the exhalation outlet of the ventilator. Ideally the exhalation port should then be connected to a central scavenging system which would eliminate release of viral particles into the ICU. Many ventilators have an expiratory filter as an integral component of the exhalation circuit. The use of disposable circuits and humidifiers may also help reduce the risk of contamination to patients and staff.

Transportation

Transporting a SARS patient for testing is an infection control challenge. SARS patients should never be transported while being supported by bag-valve-mask ventilation, and should preferably be intubated. The risks and benefit of any procedure should be considered prior to transporting a patient. If bag ventilation is used, a filter should be placed between the bag and the endotracheal tube. Infection control should be also consulted for their advice on proper precautions.

Limiting visitors and personnel

An important component of infection control is the limitation of personnel and visitors having contact with the patient. It is crucial that staff members do not work if they are ill even if the diagnosis is not clear. Staff members with unprotected contact with a SARS patient are subject to a compulsory 10-day quarantine period at home. Visitors are currently restricted in Toronto hospitals. All visitors are screened for symptoms of SARS and adhere to the same precautions as hospital staff in gowning, gloving, wearing N95 masks and goggles. Visits with SARS patients are prohibited even on compassionate grounds.

Conclusion

SARS has resulted in significant challenges for critical care medicine and likely will change the ICU environment for some time to come. In affected areas the poli-

cies are changing on a daily basis as more information about the virus and the disease is obtained. The ability of this disease to incapacitate staff has resulted in staff safety becoming a priority to maintain adequate critical care services. The concept of "universal precautions" now includes strict respiratory and contact precautions. The guidelines and recommendations will change as our knowledge grows. Information and communication technology have played an important role in allowing collaboration and rapid transfer of information. It is only through such sharing that we can hope to improve the mortality and morbidity of our patients and stay healthy and well ourselves.

Updated information on SARS can be obtained from the following websites:

- Centers for Disease Control: www.cdc.gov
- World Health Organization: www.who.int/csr/sars/
- *New England Journal of Medicine*: nejm.org/earlyrelease/sars.asp

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