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Review Article

Airway Management of Patients with Ebola Virus Disease

Louise Ellard[1], and David T. Wong[2]

ABSTRACT

Aim of review: The 2014-2015 outbreak of Ebola Virus Disease (EVD) in West Africa is the largest in history. This outbreak resulted in the deaths of more than 11,000 people. Although the vast majority of cases occurred in the West African countries of Sierra Leone, Guinea and Liberia, a number of patients were also cared for in Europe and North America. This review gives an overview of the clinical features and management of patients with EVD with emphasis on respiratory symptoms and airway management. Although Ebola is not commonly associated with respiratory conditions, a number of patients required intubation during the recent epidemic.

Methods: Recent literature and guidelines were reviewed and the management of EVD patients with respiratory symptoms was discussed with particular emphasis on those managed outside of West Africa.

Recent findings: A total of 27 patients were cared for in the United States and Europe during the 2014-2015 epidemic. Of these, 9 patients progressed to either non-invasive or invasive mechanical ventilation. Respiratory symptoms are more commonly seen in patients encountered in Northern America and Europe when compared to West Africa. This is possibly related to higher volumes of fluid administration in these patients. Although Ebola is not an airborne virus, airway maneuvers such as bag-mask ventilation and intubation can result in generation of aerosolized saliva or other fluids containing the virus. This is a high risk time for transmission to health care workers and extra precautions are required. The addition of airborne precautions, either a powered air purification respirator system (PAPR) or N95 mask, to standard personal protective equipment is suggested when providing airway management to patients with Ebola. There should be consideration of rapid sequence induction and avoidance of bag-mask ventilation to reduce the risk of aerosolization of virus. Patients with a potentially difficult airway require special consideration.

Summary: The recent outbreak of Ebola virus disease tested the preparedness of many hospitals, including those in Europe and North America. When caring for patients with Ebola, staff protection and avoidance of transmission of virus to healthcare workers is paramount.

From [1]Department of Anesthesiology, Austin Health, Victoria, Australia; [2]Department of Anesthesiology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada.

Correspondence to Dr. David T. Wong at David.wong@uhn.ca.

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The first cases of Ebola Virus Disease (EVD) occurred in 2 simultaneous outbreaks in 1976, one of which was in the Democratic Republic of Congo near the Ebola river after which the disease is named (1). There have been 24 outbreaks since that time, the most recent in West Africa during 2014-2015. Ebola and Marburg viruses are both members of the filoviridae virus family that can cause viral hemorrhagic fever (2). This group of viruses cause severe illness associated with high case fatality rates and to date, there are no specific treatments available.

The first cases in the 2014-2015 epidemic, which was declared a 'public health emergency of international concern' (3) were notified to the world health organization (WHO) on March 21, 2014 (1, 4). The West African countries of Guinea, Liberia and Sierra Leone have been the hardest hit with almost all cases occurring across these three countries. As of June 2016 there were 28,652 confirmed, probable and suspected cases of EVD with 11,325 deaths (5-7). The WHO declared the end of the most recent outbreak of Ebola in West Africa by the end of June 2016 (5). The case fatality rates in West Africa ranged from 29-67%, many times higher than those seen in the 2003 SARS epidemic which were approximately 7-17% (8). Other African countries affected include Mali, Nigeria and Senegal. Patients with Ebola have been cared for outside of Africa, in Europe and USA (5).

Clinical Features

Initial clinical features of EVD are non-specific and include fever, weakness, myalgia, headache, anorexia and hiccups. Subsequently patients may develop conjunctivitis, nausea, vomiting and diarrhea (9). Despite the fact that Ebola was formerly known as viral hemorrhagic fever, less than half of the confirmed cases of EVD have bleeding and when this occurs it does so late in the clinical course (9). Clinical evidence of bleeding includes oozing from puncture sites and gums, hematemesis, melena, epistaxis, conjunctival hemorrhage, hematuria, and hemoptysis (2, 9). Hepatocellular necrosis with reduced production of coagulation factors and consumptive coagulopathy are the likely causes of bleeding (2).

Late in the illness patients may become confused and develop seizures. Rash, respiratory distress and chest pain may be seen. Intravascular volume depletion and edema are common-likely related to disruption of the vascular endothelium and capillary leak (2). As a result, hypoperfusion (evidenced by metabolic lactic acidosis) renal impairment and hypokalemia (secondary to diarrhea) are commonly seen (4). Patients with fatal disease generally have more severe clinical signs early and die from multiorgan failure and septic shock (10).

Diagnosis and Differential Diagnosis

Most returned travellers with fever will not have EVD and other far more common infections including malaria, typhoid fever and other viral or bacterial infections should be considered (3). However, it is important to have a high index of suspicion when patients present with acute fever plus contact with a clinical case during an Ebola epidemic.

Real-time polymerase chain reaction (PCR) detects virus in the blood or tissues during the acute phase (2) and can return results within hours. An alternative is antigen detection using enzyme-linked immunosorbent assay (ELISA). Later in the course of illness or after recovery, virus isolation or IgM and IgG antibody testing is used (3, 9).

Transmission

The index case in an Ebola outbreak is transmitted to humans from the natural Ebola virus hosts, which are thought to be fruit bats. Thereafter, direct human-human transmission occurs (1) via contact with body fluids through mucosal surfaces or skin breaks (1, 2). Virus has been isolated from blood, sweat, saliva, vomitus, urine, feces and semen (2). Humans are infectious from onset of first symptoms for as long as their blood contains virus (1). There is growing evidence that Ebola virus may persist in some survivors for more than 18 months (11).

Although Ebola is not an airborne virus, aerosolized saliva or other fluids containing the virus can be generated during airway maneuvers such as intubation, extubation and mask ventilation (12). This is a high risk time for transmission to health care workers and extra precautions are re-

Table 1. Guidelines for Donning PPE.
1. Engage trained observer who reads aloud each step of the procedure and confirms visually that all PPE has been donned successfully.
2. Remove personal clothing and items and change into surgical scrubs and dedicated washable footwear.
3. Inspect PPE before donning.
4. Put on boot covers.
5. Put on inner gloves.
6. Put on gown or coverall and ensure cuffs of inner gloves are tucked under the sleeve of the gown or coverall.
7. Put on N95 respirator.
8. Put on surgical hood ensuring that hood completely covers the ears and neck.
9. Put on disposable outer apron (if used) to provide an additional layer for the front of the body.
10. Put on outer gloves with extended cuffs, ensuring the cuffs are pulled over the sleeves of the gown or coverall.
11. Put on face shield over the N95 respirator and surgical hood.

quired. Personal protective equipment (PPE) required when caring for a patient with EVD must provide droplet and contact precautions and includes full body suit coverage with face mask and goggles or a face shield. In addition, a powered air purification respirator system (PAPR) or appropriately sized N95 mask is substituted for the face mask and goggles when airborne precautions are required (2, 13). A PAPR with a self-contained filter and blower unit integrated inside the helmet is preferred (13) however when compared to N95 masks, the PAPR is more expensive and less accessible.

Protection of Healthcare Workers

Unfortunately during the 2014-2015 outbreak, a substantial number of healthcare workers were infected with EVD. Developed countries were no exception, with transmission of EVD from patient to healthcare worker seen in North America (2, 14). According to WHO, healthcare workers are between 21-32 times more likely to be infected with Ebola than the general population and two thirds of those infected have died (15).

Hospitals that will care for Ebola patients during an outbreak should have detailed protocols and staff training. In countries outside of Africa where the number of cases is likely to be very small, one major hospital in each region should be designated as the Ebola center for potential patients. For example, 55 hospitals in the USA were designated as Ebola Treatment Centers (16). Guidelines have been published for use in US hospitals (12, 13) and Europe (17). Guidelines are also published for use in Africa where limited resources are a major consideration (9).

Isolation of patients with confirmed or suspected EVD is paramount. The number of healthcare workers who come into contact with such patients should be restricted which involves fewer practitioners working longer shifts (13). However, because PPE is hot and cumbersome there is a limit to the time that doctors and nursing staff can work within an isolation ward (18) and some centers limit the time spent in PPE to 45 minutes (19).

A separate anteroom attached to the patient's room is dedicated to donning and doffing PPE. The healthcare worker must have specific training in donning and doffing PPE and each step should be supervised by a trained observer (13). This 'buddy system' (19) has been shown to minimize errors made during this process. Sufficient time should be allowed for donning and doffing of PPE without disturbances (13).

Guidelines for Donning PPE (13)

Centers for Disease Control and Prevention (CDC) have published guidelines specific for US hospitals, based on either use of the PAPR or N95 respirator (13). These are summarized in table 1.

Guidelines for Removing (Doffing) PPE (13)

Table 2 summaries the removal of PPE is a particularly high risk time, with most cases of healthcare worker transmission occurring during breaches of PPE removal (2).

Treatment

There are no FDA approved vaccines or treatments available for prevention or treatment of EVD although Phase I and II trials for Ebola vaccines are underway (10). A combination of 3 monoclonal antibodies known as Zmab (Mapp Biopharmaceutical, San Diego, CA, USA) was used as experimental treatment during the re-

cent outbreak (15, 20).

Supportive care is the mainstay of treatment and includes fluid resuscitation and correction of electrolyte abnormalities (2, 4), maintenance of blood pressure with vasopressors, oxygen supplementation, pain control, nutritional supports and treatment of secondary bacterial infections (3, 21).

The role of the anesthesiologist in the supportive management of an Ebola patient is likely to be centered around the airway management of these patients, if required. Centres should be encouraged to consult the anesthesiologist early, so that appropriate preparations can be made, as discussed in more detail below.

Airway Considerations

Ebola is not commonly associated with respiratory symptoms, a point of difference from other recent viral epidemics such as SARS (4). However, respiratory insufficiency can occur due to pulmonary edema, respiratory muscle fatigue, hemoptysis, ARDS, transfusion related acute lung injury or concomitant pneumonia. Acute hypoxemic respiratory failure is uncommon in patients with EVD in West Africa in comparison to patients treated outside of Africa (22). During the recent epidemic, of those patients cared for in US and European hospitals, 47% had respiratory failure (23). This generally occurred later in the illness with mean onset at day 9 (23). This difference may be partly attributed to administration of greater volumes of intravenous fluid (22).

A patient with Ebola may require intubation for a non-respiratory reason, such as neurological deterioration (confusion, seizures) or to assist management during progressive shock. During the course of the patient's illness it is possible that a surgical procedure may be required, for example evacuation of uterus and curettage following miscarriage (a common clinical feature) in a pregnant patient with EVD.

Because of the potential for aerosolization of fluids containing the virus, non-invasive ventilation is relatively contraindicated in EVD to reduce risk of transmission to health care workers. In addition, vomiting is common which increases the risk of aspiration (2). Therefore, the clinician needs to be prepared to intubate a patient with EVD. In most West African centers, intubation and ventilation are not practical options due to lack of both piped oxygen and mechanical ventilators (4). There is a single intensive care unit in Sierra Leone (24) that could theoretically manage an intubated patient. Intubation and invasive respiratory management is more likely to be employed in patients repatriated to Europe or the United States. During the 2014-2015 epidemic some 27 patients received care in US and European hospitals (10, 16, 19, 23). Of these 27 patients, 9 (33%) received non-invasive or invasive mechanical ventilation (23).

Table 2. To summarize the removal of PPE, which is a particularly high risk time.

1. Engage trained observer who reads aloud each step of the procedure and confirms visually that the PPE is removed properly.
2. Inspect the PPE to assess for visible contamination, cuts, or tears before starting to remove.
3. Disinfect outer gloves.
4. Remove apron (if used).
5. Disinfect and remove outer gloves.
6. Inspect and disinfect inner gloves.
7. Remove face shield.
8. Disinfect inner gloves.
9. Remove surgical hood.
10. Disinfect inner gloves.
11. Remove gown or coverall.
12. Disinfect inner gloves.
13. Remove boot covers.
14. Disinfect and change inner gloves.
15. Remove and discard N95 respirator.
16. Disinfect inner gloves.
17. Disinfect washable shoes.
18. Disinfect and remove inner gloves.
19. Perform hand hygiene.
20. Healthcare worker can leave PPE removal area wearing dedicated washable footwear and surgical scrubs or disposable garments, proceeding directly to showering area where these are removed.

Intubating Patients with Ebola

Timing of intubation in a patient with EVD should take into account the need to don personal protective equipment in a controlled and careful manner. The healthcare worker is at increased risk of becoming contaminated if they rush to don the PPE (2, 25). For this reason, intubation of a patient with EVD needs to be an electively timed procedure.

During the SARS epidemic, spread to health care workers was unfortunately common. In Toronto, Canada, half of the SARS cases involved health care workers (25). Despite the distinct differences in the way EVD is spread, many lessons should be taken from the SARS experience. If intubation of a patient with EVD is required this should occur in an airborne infection isolation room (12). This room should be isolated to other patients and staff, with restricted entry and exit into the room both during and immediately after the procedure (12). The number of staff involved should be minimized (12). Dedicated equipment including disposable airway equipment should be used wherever possible (12).

The most experienced practitioner available should manage the airway to reduce the time and number of attempts required (25). In most instances, a rapid sequence induction is a sensible choice to prevent aspiration in Ebola patients, given the frequency of gastrointestinal symptoms, as well as reducing potential aerosolization of fluids during bag- mask ventilation. Therefore an airway management plan for a patient with Ebola virus who is not expected to be a difficult intubation could be:

Preparation- ensure reliable intravenous access, pre- oxygenate the patient and communicate plans A-C to the entire team prior to commencing.

Induction of Anesthesia with a combination of benzodiazepine (eg: midazolam 0.2- 0.4 microg/kg) opioid (eg: fentanyl 1-2 microg/kg) +/- propofol depending on the hemodynamic status of the patient. Vasoactive drugs should be prepared in case they are required. A rapid acting muscle relaxant such as succinylcholine 1.5 mg/kg is an ideal choice.

Plan A- Rapid sequence induction using conventional direct laryngoscopy

Plan B- Maintain cricoid pressure and use a bougie in addition to direct laryngoscopy

Plan C- Maintain cricoid pressure and use a videolaryngscope.

If at any time oxygen saturations fall, reversion to oxygenation via bag-mask ventilation or a laryngeal mask airway may be necessary.

Managing an Ebola Patient with a Difficult Airway

If intubation is anticipated to be difficult, the anesthesiologist should consider whether it is necessary to secure the airway awake. To the authors' knowledge, there are no case reports of awake intubation in patients with Ebola. Although we would recommend avoiding awake intubation if at all possible, if it is deemed necessary then special attention should be made to minimize coughing and bleeding. Coughing could result in aerosolization of virus-containing fluids and can be minimized by excellent topicalization, use of an anti-sialogogue (i.e. glycopyrrolate 0.2 mg) and judicious sedation (26). Bleeding is likely to be more common in patients with Ebola and can be minimized by avoiding the nasal route, using a topical vasoconstrictor (26) and employing the most experienced practitioner available.

A difficult airway could be secured asleep with alternatives to standard direct laryngoscopy such as a videolaryngoscope. An ideal choice would be a disposable videolaryngoscope such as an Airtraq® (Teleflex medical, North Carolina, USA) or a disposable bronchoscope such as the Ambu® aScope™ (Ambu Inc, Baltorpbakken, Denmark) Intubation via a supraglottic airway using a bronchoscope and/or Aintree intubation catheter (Cook Critical care, Bloomington, IN, USA) could be considered (27). Benefits of an asleep technique include reduced chance of coughing and need for less cumbersome equipment-all of which must be thoroughly decontaminated after use.

It is likely that any airway management is more challenging when dressed in PPE with a PAPR. The ability to communicate with other members of the team is impaired, as is the use of a stethoscope to confirm endotracheal tube placement (25). The use of a stethoscope with Bluetooth connection was used in a hospital in the Netherlands during the recent outbreak to permit auscultation without physical contact with the patient (19).

Summary

The 2014 outbreak of Ebola virus disease was the largest in its history with over 28,000 cases reported. The vast majority of cases were in West Africa, although hospitals throughout the US and Europe were also required to treat small

numbers of patients.

EVD is not an airborne virus, however aerosol generating procedures including intubation, bag-mask ventilation and extubation need to be managed extremely carefully. If intubation is required, it must be arranged with sufficient advance warning to allow the treating physicians time to safely don PPE. Aerosol precautions including a PAPR or N95 mask should be added to PPE that complies with contact and droplet precautions. Intubation without mask ventilation utilizing a rapid-sequence technique can minimize aerosolization of fluids.

These principles can be applied when airway management is required for any patients with acute infectious diseases. Prevention of transmission to healthcare workers is of paramount importance.

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