A “bottom” up approach to treating Ebola patients

International institutions organized a “top down” response to the Ebola outbreak in West Africa. Millions were spent to provide volunteer healthcare workers, build Ebola treatment units and organize the delivery of supplies and equipment. These efforts did little to improve survival for individual Ebola patients. In most treatment units, case fatality rates exceeded 50 percent.

The international community ignored a promising “bottom-up” approach for treating Ebola patients that is based on universally available, inexpensive generic drugs. By improving survival rates, this treatment would have made it easier for “top-down” interventions to work, even in settings where existing health care systems had little else to offer.

Treating the host response to Ebola

Most patients with severe Ebola virus disease experience massive internal and external fluid losses. Their blood vessels become “leaky”, and this causes their blood pressure to drop and internal organs to fail. Eventually they die.

Earlier this year, clinical trials of experimental Ebola vaccines, antiviral agents and antibody preparations began in West Africa. Companies, foundations, non-governmental organizations and international institutions committed hundreds of millions of dollars to these trials. Even if successful, these interventions probably would have had little impact on Ebola’s high case fatality rate. Early results from a clinical trial in Guinea suggest that one antiviral agent (favipiravir) reduced overall mortality by less than 20 percent.

A new and different approach to Ebola treatment is needed, one that targets the host response to infection, not the virus itself. It is based on two drugs: statins, which were originally developed to lower levels of “bad” cholesterol, and angiotensin receptor blockers (ARBs), which were developed to treat high blood pressure.

In patients hospitalized with bacterial sepsis, community-acquired pneumonia and seasonal influenza, treatment with either a statin or an ARB significantly reduces mortality within the next 30 days. These conditions are also characterized by “leaky” blood vessels. Statins and ARBs correct these abnormalities. They are safe and well tolerated, and using both of them together is better than using either one by itself.

Statin and ARB treatment of Ebola virus disease

In November, thanks to a private donation, local physicians in Sierra Leone were able to treat approximately 100 Ebola patients with a combination of atorvastatin (a statin) and irbesartan (an ARB). All but three inadequately patients survived. One physician described the results as "remarkable."

Treatment involved two tablets each day for up to 10 days, along with the usual care provided in the Ebola treatment units. The drugs presumably stopped the loss of fluid from the bloodstream, and this prevented a deadly drop in blood pressure. As a result, patients lived long enough to develop their own immune responses and get rid of the virus on their own. None of the patients needed an expensive antiviral agent to do this.

Unfortunately, there was no financial or logistical support for an organized clinical trial, and patients were simply treated one after the other. Local physicians documented their treatment results only in letters and memoranda.

A need for change

The World Health Organization and the agencies and institutions involved in the Ebola response have an obligation to obtain the best scientific advice if they are to carry out their missions. For the Ebola response, this should have meant seeking advice not only from Ebola scientists, but also from those who understand the biology of the host response. This was not done.

Treating the host response with statins and ARBs might have saved many of the more than 11,000 Ebola patients who died. These drugs are produced as inexpensive generics by companies located in developing countries. Physicians in West Africa who treat patients with heart disease and high blood pressure are familiar with their use and safety. For an individual Ebola patient, a 10-day course of statin/ARB treatment would have cost a few dollars.

Clinical trials of treatments targeting the host response must be part of efforts to confront the current and future outbreaks of Ebola. Now is the time to plan and initiate these trials.

David S. Fedson, MD

Publication

Immunomodulatory adjunctive treatment options for Ebola virus disease patients: another view.
Fedson DS
Intensive Care Med. 2015 Jul