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Editorial: The Ebola Crisis Issue: Can Experimental Drugs or Vaccines be Ethically Used?

The current epidemic of Ebola virus in Africa is causing great concern among health professionals and populations globally. This deadly Ebola hemorrhagic virus causes death through internal bleeding and shock. The incubation period for the virus is 2–21 days, and the survival rate for the 2014 outbreak is 47%¹, higher than previous outbreaks where the death rate was up to 90%.² This human-to-human virus was first introduced to humans through the handling of infected wild animals. The first Ebola epidemic simultaneously began in Sudan and The Republic of Congo in 1976 with just two cases. In 2003, the World Health Organization (WHO) reported 11 cases of this emerging deadly disease.²

After more than four decades since the first outbreak, the Ebola vaccine still has not been fully developed. A study by the U.S. National Institute of Allergy and Infectious Diseases three years ago showed that an Ebola vaccine can protect monkeys from the virus. Presently, the vaccine is in the process of safety testing for humans.³ The development of a vaccine in Canada also is in similar progress. No licensed vaccine for Ebola virus is available since experimental vaccines are still in the clinical trial stage, and not available for widespread clinical use. Moreover, only limited dosages of experimental drugs have been produced for experimental research.³

The latest epidemic has grown to 4963 cases, with three countries involved, Guinea, Liberia and Sierra Leone, and 2453 people have died.⁴ In August 2014, after the Ebola infection caused over 1,000 deaths in 4 countries, Dr. Margaret Chan, WHO Director-General declared that the experimental drug can be used with the uncontrolled outbreak of Ebola epidemic. The ZMapp, a cocktail of three monoclonal antibodies from living cells, are designed to bind and to neutralize the virus; this new Ebola drug has been given to a few infected health care workers.³ Ethicists, scientists and others are debating the ethics of using a drug that has not been clinically proven, doubtless a matter that has occupied the thinking of WHO staff and others. Canada vaccine manufacturers have donated a number of dosages of non-proven Ebola vaccine to WHO.⁵

The experimental drugs and vaccines use

The use of experimental drugs and vaccines is not new in medical research. Non-licensed experimental drugs and other treatments have been administered to patients under research protocols. The crucial issue is whether these experimental vaccine or drugs can be used on humans. If we apply the Declaration of Helsinki's principles of "non-maleficence", or do no harm, to such situations it is necessary that a drug has passed safety tests in animals and then humans. Four main basic moral principles that apply in consideration of giving people untested drugs or vaccine and form the cornerstone of human research ethics^{6,7} are:

1. *Autonomy*: respect for people and their ability to make their own decisions. This principle helps to protect those with diminished autonomy.
2. *Beneficence*: this refers to doing good in health care, to offering potential benefit and knowledge from a study to the recipients of health care, as well as the study participants.
3. *Non-maleficence*: means no harm should be done to people who are the recipients of treatment and care. For example, all new drugs need to pass safety tests on animals and then humans.
4. *Justice*: refers to the balance between the burden and benefit, who shall to gain benefit and who shall bear its burden.

These general principles bind medical researchers to the Code of Medical Ethics which stipulates that: "The health of my patient will be my first consideration". Thus, research involving human subjects may only be conducted if the importance of the objective outweighs the risk and burdens to the research subjects.^{6,7}

Beneficence and non-maleficence issue

A panel of WHO international experts concluded at the consultative meeting convened by WHO on August 12, 2014 that the use of unproven treatment with unknown efficacy and adverse effects in the Ebola crisis situation is ethical.^{8,9} This decision was no doubt influenced by the view that in such a desperate situation as the current Ebola epidemic where the death rate is high, that saving lives was paramount. The balance of burden and benefit was

deemed to weigh on the side giving benefit. A clinical trial study is currently being implemented as the new drug is used. According to WHO: "There is a moral duty to also evaluate these intervention in the best possible clinical trials under the circumstances in order to definitively prove their safety and efficacy or provide evidence to stop their utilization".⁸ Even the efficiency of the new drug/vaccine is not guaranteed, the study result may add to the more understanding of how to prevent and treat this deadly disease.

In this situation, the autonomy of the subjects to whom this experimental treatment will be offered must be taken into serious account. Under ethical medical research guidelines they need to give individual informed consent for taking an unproven, unlicensed therapy. Their informed consent to take the drug/vaccine will allow research investigators to work closely with them, and it is hoped it will potentially save their lives.

I believe that one of the main ethical dilemmas in this Ebola crises regarding experimental therapy is who will or will not get the "last chance drug". There are only a limited number of dosages of drug/vaccine available as they were produced in a limited amount for research experiments. It is necessary to increase the production of the therapy, but until this happens, medical professionals and researchers might wrestle with justice issues about whom to offer this therapy. At present, the Zmapp drug has been given to only seven people, this was authorized on a case-by-case, 'compassionate use' basis. The Zmapp drug was produced by Mapp Biopharmaceutical of San Diego, California.¹⁰

Conclusion

The case of Ebola outbreak provides a critical case example that tests the community of health professionals for their ability to withstand the pressure of decision making regarding human needs, life and death, and good science. Ethical codes for medical research provide the underlying principles of moral conduct to be applied to human research. But this is not practically limited to paperwork, research protocols and procedures that all researchers need to apply into their studies. All involved in providing medical treatment in this Ebola crisis need to consider how humans can benefit from actions or potential actions, and how these actions can fulfill all four basic moral principles for research. The study of ethics teaches us that there is no perfect answer, just the best answer that can be decided through weighing up the moral principles, risks and benefits of a situation in collaboration with significant others.

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