

Media centre

Experimental therapies: growing interest in the use of whole blood or plasma from recovered Ebola patients (convalescent therapies)

Ebola situation assessment - 26 September 2014

Background

Ebola virus disease currently has no vaccines or medicines approved by national regulatory authorities for use in humans save for the purpose of compassionate care.

To date, the virus has infected 6242 people and killed 2909 of them. These figures, which are far greater than those from all previous Ebola outbreaks combined, are known by WHO to vastly underestimate the true scale of the epidemic.

The Ebola epidemic ravaging parts of West Africa is the most severe acute public health emergency seen in modern times. Never before in recorded history has a biosafety level four pathogen infected so many people so quickly, over such a broad geographical area, for so long.

On 11 August, a group of experts convened by WHO reached consensus that the use of experimental medicines and vaccines under the exceptional circumstances of the Ebola epidemic is ethically acceptable.

Following that advice, WHO convened (from 4–5 September) a consultation on potential Ebola therapies and vaccines.

The meeting was attended by more than 200 experts from around the world, including West Africa, though bans and restrictions on international flights to and from that region diminished the numbers significantly.

The meeting aimed to identify the most promising candidate vaccines and experimental therapies and map out the next most urgent steps to take.

The experts agreed to prioritize convalescent blood and plasma therapies for further investigation. That decision further stimulated already intense interest, with the result that new knowledge is expected to grow fairly quickly.

This assessment looks at what is known about the efficacy of convalescent therapies and the potential role they might play in improving clinical care and reducing the unacceptably high number of deaths.

The current evidence base: limited data – from 1976 up to now

Convalescent therapy was first used for a young woman infected with Ebola in the Democratic Republic of Congo (then Zaire) in 1976 – the year the virus first emerged. The woman was treated with plasma from a person who survived infection with the closely-related Marburg virus. She had less clinical bleeding than other Ebola patients, but died within days.

During the 1995 Ebola outbreak in Kikwit, Democratic Republic of Congo, whole blood collected from recovered patients was administered to eight patients. Seven of the eight recovered.

However, as the study did not include a control group, no firm conclusions could be reached concerning whether the treatment alone was responsible for the favourable clinical outcome or even contributed to this outcome in some way.

In the current outbreak, convalescent therapies have been used in a few patients. The numbers are too small to support any conclusions about efficacy.

In one well-known case, an American doctor, who became infected while working in Monrovia, Liberia, received whole blood from a recovered patient while still in Monrovia.

He likewise fully recovered, though it is not possible to determine whether that recovery can be attributed to convalescent therapy, the administration of the experimental medicine, ZMapp, or the excellent supportive care he received in the United States.

In another well-documented case, a foreign medical doctor, who was infected in Sierra Leone, has been improving following outstanding supportive care. He did not receive treatment with any experimental therapy.

In yet another case, an American doctor, who became infected while working in Liberia, was subsequently treated in the US. As part of that treatment, he received a transfusion of convalescent plasma from blood donated by the first case mentioned above. The infusion was well-tolerated.

Yesterday, he was declared by his attending physicians and the US Centers for Disease Control and Prevention (CDC) to be “virus-free”. He is weak but fully recovered.

Again, as he also received the experimental medicine TKM-EBV, together with outstanding supportive care, it is impossible to know which component of care contributed most – or at all – to his recovery.

The hospital where he was treated will share clinical lessons learned with doctors working in West Africa.

As the epidemic worsens, interest in convalescent therapies grows

WHO has been encouraged by the growth of interest in convalescent therapies as an already bad epidemic gets worse.

In the three hardest-hit countries, Guinea, Liberia, and Sierra Leone, health systems have begun to buckle under the pressure of closed or overflowing hospitals, the difficulties of staffing newly opened treatment centres, and the exceptionally large number of Ebola deaths among health care workers.

The number of cases continues to grow exponentially. The number of treatment beds is grossly and visibly inadequate. Good supportive clinical care is becoming increasingly difficult to implement.

The need to expand the current very limited arsenal of clinical tools is self-evident.

WHO has been approached by several donors, foundations, public health agencies, and development partners seeking guidance and advice.

Major questions need to be answered about the safety and efficacy of convalescent therapies, and the feasibility of implementation in countries with shattered health systems and an acute shortage of medical staff.

WHO is also being asked to assess whether rapid scaling up of convalescent therapy is feasible to an extent that could begin to reduce the estimated 70.8% case fatality rate seen consistently across the three outbreak sites.

Some partners and donors are asking for rough estimates of what needs to be in place to support rapid implementation on the largest possible scale. They have questions about the number of staff needed and their training requirements, safety risks and how to manage them, laboratory capacities and how to enhance them, specific needs for equipment and supplies, and what all of this might cost.

As initial supplies of these therapies will inevitably be limited, questions about which groups should have priority access also need to be addressed.

WHO is currently holding discussions with health experts in the Democratic Republic of Congo, Guinea, Liberia, Nigeria, and Sierra Leone. These discussions aim to identify practical needs for implementation and potential bottlenecks that could stand in the way.

One great appeal of this drive to assess and introduce convalescent therapies is the opportunity to strengthen basic public health infrastructures by helping these countries develop good quality blood services.

The list of common and severe health problems that could benefit from safe and well-functioning blood services is long – ranging from malaria, dengue, Lassa fever, and yellow fever to complications of childbirth and injuries following accidents and traffic crashes.

The current situation is so dire that, in several areas that include capital cities, many of these common diseases and health conditions are barely being managed at all.

Technical guidance for experts

Early next week, WHO is issuing new interim guidance on *Use of convalescent whole blood or plasma collected from patients recovered from Ebola virus disease for transfusion during outbreaks*.

The document is addressed to national health authorities and blood transfusion services.

A link to the new document will be added here once it is released.

WHO media contacts:

Fadéla Chaib

Telephone: + 41 22 791 3228

Mobile: + 41 79 475 5556

E-mail: chaibf@who.int

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