Trial of blood-based Ebola therapy disappoints

Death rates weren't reduced by transfusing survivors' plasma into Ebola patients.

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An Ebola survivor donates blood plasma.

The first clinical trial to transfuse blood plasma from Ebola survivors into virus-infected patients has found that the treatment didn't reduce the risk of death — but experts say it's too early to rule out the idea as an Ebola therapy.

"The results are disappointing," says Ian Lipkin, a virologist and outbreak specialist at Columbia University in New York, who was not involved in the study.

From February 2015, an international consortium of researchers collected plasma from the blood of Ebola survivors and gave it to 84 patients at the Donka Ebola treatment centre operated by Médecins Sans Frontières in Conakry, Guinea's capital. The researchers hoped that antibodies in the survivors' plasma might have a protective effect.

Administering 'convalescent' plasma is a long-established therapy that was widely used in the early

twentieth century to treat infectious diseases such as mumps, diphtheria and measles. It fell out of favour following the development of antibiotic and antiviral treatments, although it is still used to treat some diseases (such as Argentine haemorrhagic fever).

Although an Ebola vaccine proved highly successful in trials last year, a therapy is still needed because there are no effective drugs against the virus, says David Heymann, an infectious-disease researcher at the London School of Hygiene and Tropical Medicine. As the number of Ebola survivors increases during an outbreak, using their plasma could be a fast and easily scaled-up way to tackle the infection. “It was a study that needed to be done,” he says.

Lessons learned

But the results of the trial, published on 7 January in the *New England Journal of Medicine*[1], show that the death rate of 31% in the plasma-treated group was little different from the 37.8% death rate in a control group of 418 people with Ebola who were cared for at the centre in the 5 months before the trial began. After adjusting the raw data to take into account the ages and viral loads of the patients, researchers estimated that the difference between the two groups was just 2.6%, and not statistically significant.

Still, the trial showed that the therapy is safe, that donors were willing to give plasma and that it was possible to organize the medical infrastructure needed to collect the plasma, even during an epidemic, says Stephen Hoffman, an infectious disease expert and chief executive of the malaria-vaccine company Sanaria, in Rockville, Maryland. "This is an excellent demonstration of what clinical investigators can do in the most difficult circumstances," he says.

It would be premature to rule out convalescent plasma as a therapy for Ebola, says Hoffman. Infants and pregnant women given plasma in the trial had strikingly high survival rates, he points out. In particular, only one of 5 infants died in the treated group, compared to 15 of 23 in the control group — but the trial tested too few infants to make this a statistically significant result.

And both he and Lipkin suggest that the donated plasma might not have contained sufficient levels of antibodies to protect patients. It wasn’t possible to check this at the time because West Africa has no laboratories with the necessary top grade of biosafety (BSL4) that is needed to conduct such tests — and shipping samples of the plasma overseas would have delayed the trial.

But the scientists have now sent stored plasma samples to a BSL4 lab in Lyon, France, where over the next 6 months they will retrospectively measure whether there was a correlation between antibody levels and patient survival.

"There is still hope that we will get indications of efficacy," says Johan van Griensven, a researcher at the Institute of Tropical Medicine in Antwerp, Belgium, which led the trial consortium. "The likely scenario is still that convalescent plasma works but that you need to give high amounts of antibodies," he says.

Next steps

If this is the case, it might prove more effective to recruit donors with higher levels of antibodies in their blood plasma, administer the plasma in a more concentrated form or give patients more plasma in higher volumes. (In the Guinea trial, patients were given about half a litre of plasma in two doses.)

The Ebola epidemic is almost at an end — if there are no more reported cases, the World Health Organisation will declare West Africa Ebola-free on 14 January — so scientists will have to wait for another outbreak to test out these ideas. Researchers had hoped also to test plasma from Ebola survivors in separate trials in Liberia and Sierra Leone, but they only managed to recruit nine patients, so the trials never got off the ground.

An “obvious next step”, says Heymann, would be to extract and concentrate antibodies from the many plasma samples already collected from survivors, so as to be ready to trial them immediately in future outbreaks.

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References

1. van Griensven, J. *et al. N. Engl. J. Med.* **374**, 33–42 (2016).

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