New treatment for rabies advances after successful phase 1 trial in India

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With the potential to save tens of thousands of lives each year, a new cost-effective rabies therapy developed by MassBiologics at the University of Massachusetts and the Serum Institute of India took an important step forward with positive results from a Phase 1 study. The recently completed study showed that a new monoclonal antibody (RAB-1) resulted in protective antibody levels in the serum of treated subjects equal to the current standard of treatment, which is often not available in the areas of the world hit hardest by rabies.

Details of the study were reported on September 14 at the American Society for Microbiology's 50th annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) meeting in Boston, Massachusetts in a poster presentation titled, "A Human Monoclonal Antibody to Rabies Virus Provides Protective Neutralizing Activity: Results of a Phase 1 Study," by researchers from MassBiologics; the Serum Institute of India in Pune, India; and King Edward Memorial Hospital (KEM) in Mumbai, India.

"We are very encouraged by the results from this trial," said Donna Ambrosino, MD, executive director of MassBiologics and a professor of pediatrics at the Medical School.

Subhash Kapre, PhD, of the Serum Institute of India, agreed saying, "The next step for clinical studies is already in the planning, and we are hopeful that this new therapy will have a major impact on rabies across the globe in the not too distant future."

The World Health Organization estimates that more than 10 million people are exposed to rabid animals each year, resulting in more than 55,000 deaths. Approximately 95 percent of human deaths from rabies occur in Asia and Africa. Untreated, the rabies virus causes an acute encephalitis that is fatal once symptoms appear; however the infection is preventable by prompt treatment following exposure, a procedure known as post-exposure prophylaxis (PEP) that involves administration of a rabies vaccine and rabies immune globulin (RIG) soon after exposure.

While the vaccine is often available, the preferred human rabies immune globulin (HRIG), which is derived from human blood, is expensive material and typically not available in developing countries. As an alternative to HRIG, equine immune globulin derived from horse serum is used in many parts of the world, but it is also scarce, expensive and can carry significant side effects. Too frequently, however, there is neither HRIG nor equine product available to treat all those in the developing world who are bitten by rabid animals.

To address the supply problems and side-effect issues, MassBiologics and the Serum of Institute of India launched an effort to develop a monoclonal antibody (MAB) that could be used in place of HRIG. Pre-clinical testing of RAB-1 showed that it neutralized all isolates available from a panel of rabies viruses. MassBiologics then partnered with the Serum Institute of India, which is one of the world's largest manufacturers of vaccines, including a major supplier of the rabies vaccine, to develop the capacity to produce monoclonal antibodies in India, and advance RAB-1 into clinical trials.

In the Phase 1 trial run at the KEM hospital, 74 healthy volunteers were randomized into several groups that either received escalating doses of RAB-1 or of HRIG combined with vaccine. The RAB-1 was well tolerated by all subjects, with no serious adverse side-effects caused by the MAB. Blood samples were then analyzed and showed the volunteers

who received RAB-1 and vaccine at a dose of 0.150 mg/kg had levels of rabies antibodies equal to or higher than the levels from those volunteers who had received the standard does of HRIG and vaccine. The half life of RAB-1 was 18-19 days.

Blood samples were also analyzed by the Kansas State Veterinary Diagnostic Laboratory to determine if antibodies present in the volunteers' bloodstream could neutralize rabies virus in a cell-based assay using two different strains of virus. That data showed that volunteers who received RAB-1 at 0.150 mg/kg with vaccine had similar or better protective serum levels when compared to those who received HRIG with vaccine.

Following the successful conclusion of this Phase 1 trial, the Serum Institute of India and MassBiologics are moving ahead in a clinical trial in India to evaluate the efficacy of RAB-1 combined with vaccine compared to the standard of care for patients who have been exposed to potentially rabid animals. "Monoclonal antibodies can be produced in large quantities and at much lower costs than blood products, which could make this new therapy broadly available in Asia and India," Dr. Kapre said. "We remain optimistic that this program will eventually prevent thousands of deaths from rabies each year."

Provided by University of Massachusetts Medical School