ICU
MANAGEMENT & PRACTICE

Monitoring of Immune Function in Critically Ill Children With Influenza Reveals Severe Immune Suppression in Non-Survivors

Investigators from 15 children's medical centers, including Nationwide Children's Hospital, observed and evaluated critically ill children with influenza to evaluate the relationships between levels of systemic inflammation, immune function and likelihood to die from the illness. The study appears in the January issue of Critical Care Medicine.

The innate immune system is the cellular arm of the immune system that serves as a first-responder to new threats, and is thought to drive the inflammatory response in many forms of critical illness. Recent evidence indicates that suppression of innate immune system function can occur in critically ill patients.

This immune suppression can be quantified in the laboratory through measurement of the capacity of the patient's blood to produce a specific cytokine, tumor necrosis factor (TNF)-α , when stimulated with lipopolysaccharide (LPS), a substance which should induce a robust TNF α response. Patients with innate immune suppression produce reduced amounts of TNFα when their blood is stimulated. In its most severe form, this condition is known as immunoparalysis. Severe reductions in TNFα production capacity have been associated with the development of secondary bacterial infections and death in critically ill adults and children.

Immune function is not routinely measured in patients with influenza, though some therapies used in this population, such as corticosteroids, can be potently immunosuppressive.

"Both pro- and anti-inflammatory therapies have been proposed as additional treatment options for influenza infection," explains lead study author Mark Hall, MD, Critical Care specialist and principal investigator in the Center for Clinical and Translational Research at Nationwide Children's Hospital. "However, a lack of immune monitoring data in the pediatric population has made therapeutic decision-making difficult in children."

In this first-of-its-kind, multicenter observational study, blood samples from critically ill children with influenza were tested using highly standardized techniques to determine the capacity of the participants' innate immune system to produce TNFα when stimulated with LPS. Healthy control subjects also had their blood tested for the same properties.

Results indicated that despite high levels of circulating pro-inflammatory cytokines, critically ill children with influenza demonstrated lower TNFα production capacity compared with healthy control subjects. Further, children who died from influenza had markedly lower TNFα production capacity compared with survivors. Patients who were co-infected with influenza and the bacteria Staphylococcus aureus showed the greatest degree of immune suppression.

While the reduced capacity to produce TNFα among the critically ill children compared to healthy subjects was expected, the degree of reduction in capacity was severe enough to be highly predictive of death from the illness.

"The study demonstrates a strong relationship between mortality and reduced innate immune responsiveness in critically ill patients," said Dr. Hall, also a faculty member at The Ohio State University College of Medicine. "It also demonstrates the feasibility of large-scale immune monitoring of the kind necessary to develop and test therapies for these critically ill children. The identification of potential treatment thresholds is important because strong evidence suggests that innate immune suppression associated with critical illness may be reversible."

Advocating for additional studies, investigators suggest that patient-specific immune monitoring could aid in determining the most effective treatment for these critically ill patients. Therapies that stimulate the immune system may have a significant role in the treatment of high-risk children with severe immune suppression associated with influenza infection.

Source: Nationwide Children's Hospital
http://www.nationwidechildrens.org

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