ICU MANAGEMENT & PRACTICE

Therapeutic Hyperthermia and Survival in Critically Ill Afebrile Sepsis Patients

A major feature of infection is fever. However, less than half of critically ill patients with sepsis have a fever at the time of diagnosis. Afebrile patients with sepsis have nearly twice the mortality and are more likely to develop secondary infections than patients with fever. Fever is thus an adaptive response to the infection and is critical for survival. Studies have shown elevated temperature could have beneficial effects on adaptive and innate immunity.

Sepsis is associated with pro- and anti-inflammatory mechanisms that could lead to prolonged periods of immunosuppression. Some biomarkers may induce this suppression. These include reduced expression of human leukocyte antigen (HLA)-DR, decreased lipopolysaccharide-induced tumour necrosis factor-alpha (TNF-α) production, decreased anti-CD3/anti-CD28-stimulated interferon-gamma (IFN-γ) production, and persistent lymphopaenia.

Therapeutic hyperthermia has been used for immunomodulation to treat cancer. It is believed that this strategy can improve the function of natural killer cells, dendritic cells, and T cells. Perioperative warming has also been shown to decrease postoperative infections. It is thus logical to conclude that therapeutic hyperthermia may be an effective treatment for sepsis. However, this has not been extensively evaluated.

A study was conducted to test the hypothesis that forced-air warming of afebrile critically ill patients with sepsis improves immune function compared to standard temperature management. The hypothesis of the study was that warmed patients would exhibit higher levels of (HLA)-DR expression and CD3/CD28-stimulated IFN-y production and a reduced prevalence of persistent lymphopaenia.

Fifty-six patients were enrolled in the study. Study participants were mechanically ventilated septic adults diagnosed with sepsis within 48 hours of enrolment, with an anticipated need for mechanical ventilation of greater than 48 hours and a maximum temperature less than 38.3°C 24 hours before enrolment. The primary outcome of the study was (HLA)-DR expression. Secondary outcomes included CD3/CD28-induced IFN-γ production, mortality, and 28-day hospital-free days. Study patients were allocated to external warming using a forced-air warming blanket for 48 hours. The goal temperature was 1.5°C above the lowest temperature documents in the previous 24 hours.

Findings showed that patients allocated to external warming had lower 28-day mortality and more 28-day hospital-free days than patients in the control group. The forced-warming group did not have a difference in the HLA-DR expression or IFN-y production. No differences were observed between 28-day ventilator-free days or 48-hour delta-SOFA score. Secondary infections were common but not different between the two groups. Patients in the therapeutic warming group had similar vasopressor doses and vital signs during the intervention period compared to the control group.

Overall, these findings show that therapeutic hyperthermia in afebrile critically ill patients with sepsis was feasible, but there was no major difference in monocyte HLA-DR expression, induced IFN-γ production, or lymphopaenia. There was also no major difference in adverse events between the two groups. However, the therapeutic warming group demonstrated decreased mortality and increased hospital-free days. These are important findings, but there is a need for larger trials to confirm these findings and to better understand the changes in sepsis physiology with temperature modulation.

Source: Critical Care Medicine
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