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Therapeutic Hyperthermia and Survival in Afebrile Sepsis Patients

Fever is an important feature of infection. However, fewer than half of patients with sepsis present with fever at the time of diagnosis. Afebrile sepsis patients have nearly twice the mortality and are at a higher risk of developing secondary infections than patients with fever.

Fever is an adaptive response to infection that may be critical for survival. Studies show that elevated temperature can benefit adaptive and innate immunity, including increased antibody production, T-cell activation, macrophage function, and heat shock protein response.

Sepsis can lead to prolonged periods of immunosuppression. Some biomarkers that have been associated with sepsis-induced immunosuppression 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 lymphopenia. Patients with depressed levels of these markers suffer from higher mortality and increased secondary infections than patients with intact immunity.

Therapeutic hyperthermia refers to artificially raising body temperature through external warming. It has been used for immunomodulation to treat several types of cancer. Therapeutic hyperthermia is believed to improve the function of natural killer cells, dendritic cells, and T cells and can decrease postoperative infections.

A study was conducted to test whether forced-air warming of critically ill afebrile sepsis patients improves immune function compared to standard temperature management.

Fifty-four patients were enrolled in the study. All patients were mechanically ventilated septic adults with a diagnosis of sepsis within 48 hours of enrollment, with an anticipated need for mechanical ventilation greater than 48 hours and a maximum temperature of less than 38.3°C within the 24 hours before enrollment. The primary outcome of the study was monocyte human leukocyte antigen (HLA)-DR expression, with secondary outcomes of CD3/CD28-induced interferon-gamma (IFN-γ) production, mortality, and 28-day hospital-free days.

The interventions used were external warming with a forced-air warming blanket for 48 hours and a goal temperature 1.5°C above the lowest temperature documented in the previous 24 hours.

As per the results of the study, no differences were observed between the groups in HLA-DR expression or IFN-γ production. However, patients who received external warming had lower 28-day mortality and more 28-day hospital-free days.

These findings show that patients randomised to external forced-air warming did not have a difference in HLA-DR expression or IFN-γ production. However, the 28-day mortality in this group was lower. More research is needed to better understand the impact of temperature modulation in these patients.

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