Letter

Direct effects of modest hyperglycaemia on susceptibility to infection in the critically ill patient

Matt P Wise, Anton G Saayman and Paul J Frost

Adult Critical Care, University of Hospital of Wales, Heath Park, Cardiff CF14 4XW, UK

Corresponding author: Matt P Wise, mattwise@doctors.org.uk

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See related research by Otto *et al*., http://ccforum.com/content/12/4/R107

In their recent study, Otto and colleagues suggested that the adverse effects of hyperglycaemia on immune function may be mediated by hyperosmotic stress [1]. In granulocytes both oxidative burst and phagocytosis were suppressed by hyperosmolar stress with mannitol, but no significant effect was observed on cytokine release from peripheral blood mononuclear cells [1]. The concentration of glucose (and mannitol) used in these experiments (500 mg/dl or 27.8 mmol/l), however, is rarely encountered in critically ill patients – and then only transiently. One may question how relevant this mechanism is, when it appears that modest levels of hyperglycaemia (11.1 mmol/l) have deleterious effects in this population [2].

Modest hyperglycaemia has been demonstrated to directly perturbate immune function by more than one mechanism. Macropinocytosis by macrophages involves nonspecific sampling of pathogens in extracellular fluid, which are then directed towards antigen processing with subsequent presentation of microbial peptides to T cells, linking innate and adaptive immunity. Macropinocytosis is reduced in a dose-dependent manner by glucose but not by mannitol. Increasing glucose from 5.5 to 11.1 mmol/l inhibited macropinocytosis by 55% [3]. Surfactant proteins A and D and mannose-binding lectin are important host defence molecules (collectins), which bind pathogens, augment opsonisation, phagocytosis and killing by macrophages and neutrophils, and activate complement. Deficiency in mannose-binding lectin is associated with septic shock and death in critically ill patients [4]. Glucose competitively inhibits pathogen binding by collectins [5] and represents an eloquent mechanism of how modest hyperglycaemia may increase susceptibility to infection.

We would suggest that the benefits of strict glycaemic control on immune function in critical care might be explained by the direct effects of glucose rather than by reductions in hyperosmolar stress.

Competing interests

The authors declare that they have no competing interests.

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