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Review

Intensive insulin therapy, insulin sensitisers and insulin secretagogues for burns: A systematic review of effectiveness and safety

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ABSTRACT

This systematic review investigated the effectiveness and safety of intensive insulin therapy (IIT), insulin secretagogues and sensitisers in burn patients. PubMed, Embase, clinicaltrials.gov and Cochrane central were searched from 1990 to 2016. Title/abstract screening, full-text review, critical appraisal and data extraction were carried out by two independent reviewers. Inclusion criteria were hospitalised burn patients, IIT, insulin sensitisers or secretagogues and the outcomes mortality, length of stay, resting energy expenditure, blood glucose, catabolism, or complications. We identified 594 potential studies of which 13 were included. Five studies investigated IIT in paediatric patients, 3 investigated IIT in adults and 5 investigated sensitisers or secretagogues. Glycaemic targets differed with age group — paediatric studies compared IIT to loose glycaemic control while adult studies compared IIT to more moderate control. Meta-analyses were limited by differences in outcome reporting, however mortality was increased in children by loose glycaemic control (OR=3.78, 95%CI 1.19–12.02) but not significantly affected in adults by moderate compared to tight control. Meta-analyses could not be performed for sensitisers or secretagogues. These findings support recommendations that moderate insulin administration (130–150mg/dL) is the prudent approach in burn patients. The evidence is relatively sparse and further research is warranted.

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1. Introduction

Severe thermal injuries cause patients to enter a persistent hypermetabolic state characterised by increased metabolic rate, organ dysfunction, catabolism and susceptibility to infection [1]. Hypermetabolism in burn patients is additionally accompanied by insulin resistance leading to hyperglycemia which is associated with a heightened risk of mortality in burn [2] and other trauma patients [3].

The results of several studies suggest that critically ill patient morbidity and mortality could be improved through the implementation of therapeutic strategies which aimed to achieve tight glycaemic control in patients [4]. This was generally attempted through the use of intensive insulin therapy (IIT). Insulin secretagogues, used to stimulate the production of autologous insulin, or insulin sensitisers, used to decrease insulin resistance, can also be applied as adjuncts or alternatives. However, a very large study – the NICE SUGAR study [5] – which was carried out in 2009 and involved 6104 intensive care unit (ICU) patients from multiple sites and nations showed that therapies which aimed to achieve tight glycaemic control did not decrease mortality (instead

increasing it by 2.6%). One caveat, however, noted by the study authors themselves, was that the findings did not rule out that IIT could benefit some ICU patients and, indeed, their data showed a trend which suggested that the subgroup of trauma patients might have lower mortality when treated with IIT.

In particular, burn patients were not specifically examined in the NICE SUGAR study. Due to the induction of the hypermetabolic state by burns there is an increased potential that strategies to achieve tight glycaemic control may have a different outcome in burn patients compared to the general ICU population. However, hypoglycaemia – which is more common in patients receiving IIT [5] – has also been shown to correlate with worse outcomes in burn patients [6,7], creating the risk of harm.

Studies carried out in burns care generally have small sample sizes. However, if conducted correctly [8], systematic reviews can help to mitigate the problems created by small sample sizes (lack of statistical power, greater likelihood of spurious findings) by synthesising the findings of multiple studies to produce an overall effect estimate which can be used with greater confidence to inform evidence-based healthcare [9,10]. As such, this systematic review has been undertaken to identify and synthesise the findings of all studies on the

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