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Research paper

A retrospective audit of insulin infusion management involving a locally developed dynamic insulin infusion guideline in a tertiary ICU

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ABSTRACT

Background: The ideal target blood glucose range for intensive care patients on insulin infusions is controversial. Avoidance of hyperglycaemia and hypoglycaemia are well supported goals.
Methods: An audit of insulin infusion management was conducted following the institution of an insulin infusion guideline in a tertiary adult intensive care unit (ICU). The primary aim was to evaluate this guideline for safety and efficacy. Secondary aims were to compare outcomes such as ICU and hospital mortality, rate of severe hypoglycaemia, length of time within target zones, length of stay in ICU and hospital, ventilator hours and use of renal replacement therapy. Data analysis involved descriptive statistical techniques to allow comparison with other reported outcomes.
Results: Thirty-eight (38) patients were included, representing 137 days of insulin infusions and 2537 blood glucose readings. The mean insulin infusion treatment time was 86.4 h (sd ±86.4), median 48 h (IQR 14.4–141.6). The mean insulin dose per day was 97.6 units (sd ±115.7), with a median of 68.7 (IQR 38.9–108.3). Blood glucose level (BGL) readings were within the desired target (6–9 mmols/L) and/or the buffer zones (4–6 and 9–12 mmols/L), 92.3% of the time. There were no episodes of severe hypoglycaemia (BGL ≤ 2.2 mmols/L).

The median length of ICU stay was 5.9 days. Eighty-four (84) % of the cohort received mechanical ventilation and 26% received renal replacement therapy. The mean ventilation and renal replacement duration were days 6.9 and 9.4 days, respectively. The ICU and hospital mortality was 13.2% and 18.4%, respectively.
Conclusion: The use of this locally developed insulin infusion guideline for hyperglycaemia within this ICU appears safe and effective. When compared to related published randomised controlled trials, the outcomes of this small scale single centre retrospective audit appear congruent. It achieved a severe hypoglycaemic rate of zero, with BGLs within target and buffer zones greater than 90%. It may be worthwhile for intensive care units to consider evaluating their own locally developed insulin infusion guidelines to ensure safety and efficacy.

1. Introduction

The ideal target blood glucose range for adult intensive care patients on insulin infusions is controversial. Avoidance of hyperglycaemia and hypoglycaemia are well supported goals. In the

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light of ongoing uncertainty regarding insulin infusion management in ICUs, individual units may wish to ensure their own locally developed and implemented protocols are compatible with current relevant guidelines[1–3] and that they achieve results within suggested safety parameters. Comparing related morbidity and mortality outcomes to published literature may also provide useful points of comparison.

A quality assurance audit of ICU patients receiving an insulin infusion for hyperglycaemia at this institution was conducted. The primary aim of this study was to establish whether the locally developed insulin infusion guideline is safe and effective, according to suggested parameters in guidelines for insulin infusion management for hyperglycaemia in ICUs.[1,3] Secondary goals were to compare other endpoints such as ICU and hospital mortality, rate of severe hypoglycaemia, length of time within target zones, length of stay in ICU and hospital, ventilation hours and use of renal replacement therapy with other published data.

2. Background

A 2001 seminal "proof of concept" randomised controlled trial[4] (RCT) demonstrated a significant reduction in mortality and morbidity for adult surgical ICU patients who received intensive insulin therapy (IIT) to maintain blood glucose level (BGL) 4.4–6.1 mmols/L (80–110 mg/dL). The IIT arm was compared to the control group of conventional insulin therapy (CIT) which commenced an infusion for BGL > 11.9 mmols/L (215 mg/dL) with a target range of 10–11.1 mmols/L (180–200 mg/dL). A similar trial was conducted in a medical ICU by the same Leuven group and the published results in 2006[5] indicated that morbidity was reduced, but not mortality, for this patient cohort. The largest benefit was found for patients who were treated for three or more days but these patients could not be identified prior to commencing treatment.

Following these studies other similar trials were conducted which failed to replicate the benefit conferred by IIT. A single centre RCT from a Colombian mixed medical and surgical ICU reported in 2008[6] no reduction in morbidity or mortality, as well as an increased risk of hypoglycaemia. In the same year, reported results of a German multi centre randomised study[7] indicated it was ceased early because IIT was associated with an increased rate of severe hypoglycaemia and a trend towards longer ICU length of stay. The available data for analysis indicated no difference in mortality, nor in secondary endpoints such as rate of renal failure, ventilator free days or use of vasopressors. It was also reported that hypoglycaemia was identified as an independent risk factor for death from any cause, along with commentary indicating that this might only be a marker of poor outcome independent of insulin therapy. Additionally in 2008, a RCT in a medical and surgical ICU from Saudi Arabia[8] reported no difference in mortality nor in secondary endpoints, but increased hypoglycaemic events with IIT.

In 2009, the results of two multi centre RCTs exploring IIT were published. The landmark Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial[9] was conducted in Australia, New Zealand and Canada and compared IIT targeting BGL 4.5–6 mmol/L (81–108 mg/dL) to conventional treatment with a target of 10 mmol/L (180 mg/dL) or less. The control arm target was different from that used in the Leuven studies[4,5] and represented a range as identified through practice surveys in participating countries.[10] NICE-SUGAR reported increased mortality for IIT as well as increased episodes of severe hypoglycaemia. There were no significant differences for other endpoints. In a post hoc analysis the NICE-SUGAR investigators reported intensive glucose control leads to moderate and severe hypoglycaemia which is associated with an increased risk of death although this may not be a causal relationship.[11]

The Glucontrol study that involved twenty-one mostly European medical and surgical ICUs was ceased early due to a high rate of unintended protocol violations which resulted in an underpowered study.[12] Similar to NICE-SUGAR a lower control target range of 7.8–10 mmols/L (140–180 mg/dL) was used compared to the Leuven studies. The available data from 1101 admissions indicated that there was no benefit of IIT and there was an increased rate of hypoglycaemia compared to the control arm.

A meta-analysis[13] that included twenty-six trials (NICE-SUGAR amongst them), involving 13,567 patients concluded overall that IIT provided no mortality benefit for critically ill patients but did increase the risk of hypoglycaemia. However, it was suggested that there may be some benefit of IIT for surgical ICU patients in the light of pooled results that indicated mortality was improved for this group. In addition, it was reported that heterogeneity between studies largely stemmed from two surgical ICU RCTs, and since mortality was increased in surgical patients in NICE-SUGAR, it was further suggested that the possible benefit of IIT in surgical ICUs would need confirmation. Issues raised by this meta-analysis in addressing differences in results between the RCTs included questions about: the possible differences regarding elective surgical patients; implementation of study interventions and the accuracy of different modes of BGL checking; variability in conventional care such as the different targets in the control arms of the Leuven studies and NICE-SUGAR; blood glucose fluctuations may be significant yet reported average results may not be indicative of this; and the impact of different nutrition regimes, including disparate approaches for administering intravenous glucose.

A published RCT in 2011[14] from a mixed ICU exploring permissive underfeeding and IIT utilising the target ranges of the Leuven studies concluded that there was no significant differences in mortality or other outcomes for patients in the IIT or CIT groups, apart from hypoglycaemia which was increased in the IIT group. It was found that permissive underfeeding might be associated with decreased mortality compared to the group receiving targeted feeding of 90–100% of calculated requirements. These results lend credence to the suggestion that the impact of nutrition, and thereby presumably exogenous glucose sources, in association with insulin infusion management may be significant and may help account for some of the differences found in related RCT outcomes. (See Table 1 for a summary comparison of selected RCTs.)

The "Guidelines for the use of an insulin infusion for the management of hyperglycaemia in critically ill patients"[1] was published in 2012 by members of the Society of Critical Care Medicine who made up the Guideline Task Force. Most of this group's recommendations were "suggestions" due to the quality of evidence being graded as "very low". Some of the suggestions of this guideline include: commence insulin infusion for BGL ≥ 150 mg/dL (8.3 mmols/L) and maintain BGL level < 180 mg/dL (10 mmols/L) using a protocol that achieves a low rate of hypoglycaemia (BGL ≤ 70 mg/dL (3.9 mmols/L));

> ...ICUs develop a protocolized approach to manage GC [glycemic control]. Components include a validated insulin administration protocol, appropriate staffing resources, use of accurate monitoring technologies, and a robust data platform to monitor protocol performance and clinical outcome measures.
>
> A standard insulin infusion protocol should include a requirement for continuous glucose intake, standardised IV insulin infusion preparation, a dosing format requiring minimal bedside decision-making, frequent BG monitoring, provisions for dextrose replacement if feedings are interrupted, and protocolized dextrose dosing for prompt treatment of hypoglycaemia (p 3268);