Management of Parenteral Nutrition Associated Hyperglycaemia: A Comparison of Subcutaneous and Intravenous Insulin Regimen

Abstract

PN is associated with significant hyperglycaemia, which may be detrimental to clinical outcome. There are few data on the management of insulin therapy in non-critically ill patients. In our unit, we studied the efficacy of intravenous and subcutaneous insulin regimens in PN-associated hyperglycaemia. Many of the patients on a protocol-based intravenous insulin delivery as compared to subcutaneous insulin prescribed individually outside of the critical care setting were within glycaemic target for more time and spent less time in hyperglycaemia. A total of 122 who developed PN-associated hyperglycaemia were identified. Those on the intravenous insulin regimen were within glycaemic target for more time than the subcutaneous insulin regimen (62% vs 43%, p<0.008). We therefore conclude that outside of the critical care setting, intravenous insulin delivers better glycaemic control and should therefore be considered optimum therapy for patients with PN-associated hyperglycaemia.

Introduction

Parenteral nutrition (PN) is used in a wide variety of clinical scenarios, and it is widely accepted that adequate nutritional support is an important part of successful recovery from critical illness. However, PN has been associated with significant hyperglycaemia in intensive care units. In our unit, we studied the efficacy of intravenous and subcutaneous insulin regimens in PN-associated hyperglycaemia. This effect is particularly evident in patients with acute pancreatitis, where the addition of PN almost doubles the rate of hyperglycaemia. Hyperglycaemia is associated with poor outcomes in the context of critical illness and PN use with higher infection rates, higher mortality and renal injury. PN-associated hyperglycaemia also correlates with increased rates of cardiovascular complications and systemic sepsis. Hyperglycaemia therefore, results in greater lengths of stay in intensive care units (ICUs), and greater lengths of stay in hospital generally.

Outside of the critical care setting, prospective data in humans confirm that there is an increased risk of mortality associated with PN in non-critically ill patients who develop hyperglycaemia at a serum glucose level of 10mmol/l or higher, when compared to those with a serum glucose level less than 7.8mmol/l. However, there are few data on the effects of insulin treatment in reducing this risk. In particular there is a dearth of data to inform healthcare providers on which modality of insulin therapy can offer the best outcomes. Studies using rat models of sepsis have shown survival in PN-associated hyperglycaemia is improved when intravenous insulin is used compared to subcutaneous insulin. There have been human studies in specific cohorts, such as patients post-gastrectomy for gastric cancer, which have reported improved outcomes with intensive glycaemic control.

However, this has not been well replicated in the non-critically ill patient. Current guidelines recommend maintaining blood glucose concentrations between 7.8 and 10mmol/l when on PN. Therapy can be most effectively delivered when a specific protocol is utilised to guide health providers. Current guidelines recommend maintaining blood glucose concentrations between 7.8 and 10mmol/l when on PN, however, this has not been well replicated in the non-critically ill patient.

Materials and Methods

We conducted a retrospective review of all patients who received PN therapy from January 2009 to January 2010. Patients who were treated with subcutaneous insulin on individually prescribed supplemental scales. In this regimen, the doses of insulin prescribed subcutaneously were not standardised and varied from patient to patient. We compared those who had received the subcutaneous insulin regimens with those who had received intravenous insulin regimens. Patients were identified from a detailed hospital-based clinical register of those receiving PN therapy outside of the critical care setting. From these records, medical and surgical patients who were commenced on insulin therapy for hyperglycaemia during the two-year period up to January 2010 were identified. The ICU and critical care patients were excluded, as the focus of our study was the efficacy of the two insulin modalities in non-critically ill patients. This study was completed in accordance with Beaumont Hospital ethical guidelines. Those on the intravenous protocol had dose titrations under nurse supervision in accordance with the protocol (Table 1). Those on subcutaneous insulin had a mixture of rapid acting insulin analogues and basal insulin, which was prescribed by the primary medical or surgical team, often in consultation with the diabetes care team.

An anonymised study database was constructed. Clinical parameters including gender, age, body mass index (BMI), admission diagnosis, indication for PN, and steroid use were recorded. The length of time PN was used, patient length of stay and length of stay on PN were also recorded in the study database. Patients who had a diagnosis of diabetes before admission to the hospital had additional measurements including HbA1c levels. Duration of diabetes and the individual pre-admission glycaemic therapy were also recorded. Blood glucose levels were tested using point of care testing four times a day while on PN. All patients had glycaemic profiles recorded with reference to the rate of change. Blood glucose readings were recorded between 4.0 and 10.0mmol/l inclusively, and mean daily capillary blood glucose levels. Descriptive statistics were used and we compared those patients who received the intravenous insulin protocol with subcutaneous insulin using Student’s t-test and Mann-Whitney U tests for parametric and non-parametric data respectively. Regression analysis was used in the cohort as a whole to evaluate for associations between use of each insulin treatment paradigm and glycaemic and clinical outcomes. Statistical significance was assessed at p<0.05. All statistics were completed on the R software (Version 2.11.1).

Results

We identified 555 patients who received PN in the study period. Of these, 523 received PN outside of the critical care setting. PN remained for a median of 14 days (IQR 4-42). The majority of patients had a BMI of greater than 25. Of those treated with subcutaneous insulin, 32 of 53 patients who had complete records of this analysis group of 53 patients, 32 (60%) were treated with intravenous insulin as per protocol.

On comparing the intravenous insulin group to the subcutaneous insulin group, there were no statistically significant differences in age or BMI (Table 2). However, there were differences in glycaemic outcomes (Table 3). The group treated with intravenous insulin had a significantly lower daily mean capillary blood glucose level (9.6 ± 2.1mmol/l vs 11.2 ± 2.6mmol/l, p=0.009), and spent a greater proportion of time in glycaemic target (62% vs 43%, p=0.008). There was no...
significant difference in hypoglycaemia rates (1% Vs 2%, p = 0.14). On regression analysis, intravenous insulin was associated with a greater time spent in glycaemic target (p = 0.02) and a lower mean blood glucose level (p = 0.03). There was no association with other glycaemic variables. The use of intravenous insulin was not associated with hypoglycaemia.

Length of hospital stay (61 - 49 days Vs 43 - 35 days, p = 0.08) and survival to discharge (77% Vs 67%, p = 0.2) were comparable between groups. Of the total cohort, 73% survived to discharge. Male gender was positively associated with survival to discharge (p = 0.003). Men comprised 73% of survivors, and only 20% of those who died in hospital. Length of stay was significantly associated with duration of PN (p = 0.001). Intravenous insulin use was not associated with length of stay. Pre-admission diabetes requiring insulin therapy was significantly associated with a longer length of stay on logistic regression analysis (p = 0.04). Pre-existing diabetes was not associated with mortality.

Discussion
This study demonstrates that use of a standardised intravenous insulin infusion protocol in the treatment of PN-associated hyperglycaemia results in improved glycaemic outcomes outside of the critical care setting. The mean capillary blood glucose levels were lower, and users of intravenous insulin therapy spent more time in glycaemic target as compared to those prescribed subcutaneous insulin on an individual basis without an increased rate of hypoglycaemia. These data are in agreement with previous studies that report improved outcomes with prescribed protocols as compared to the ad hoc insulin prescription strategy. Our data shows that an intravenous insulin protocol is superior to subcutaneous insulin delivered on an individual basis, and outside of a prescribed protocol, in PN-associated hyperglycaemia outside of the critical care setting. Our data is retrospective and has limitations, including the lack of randomization. This may have introduced selection bias. The absence of a control group or a parallel design also weakens the conclusions. Intravenous insulin offers the flexibility to address this problem given the rapid onset of action and clearance. Our findings support the use of intravenous insulin protocols in the management of PN-associated hyperglycaemia. This can deliver significant improvements in glycaemic control in the non-critical inpatient setting.

Complete prescription records were not always available in the subcutaneous insulin group, resulting in over half of the initial group being excluded from the data. Unfortunately, the ad hoc insulin prescribing in that group, and the absence of formal prescription protocols to facilitate complete prescription recording and insulin delivery, mean that reliable data were not available for comparison. This is a weakness of our study. However, this illustrates another strength of the prescribed intravenous insulin protocol, as it offers a clear record of the insulin prescribed and given, and is likely to reduce drug prescribing and administering error. Our data in the subcutaneous group are comparable to several clinical scenarios still employing ad hoc subcutaneous insulin protocols. In the present study, insulin delivery was not specifically designed as an intravenous insulin protocol as patients are often experiencing acute physiological stresses which can lead to rapid fluctuations in glycaemia. Our intravenous insulin protocol offers the flexibility to address this problem given the rapid onset of action and clearance. Our findings support the use of intravenous insulin protocols in the management of PN-associated hyperglycaemia. This can deliver significant improvements in glycaemic control in the non-critical inpatient setting.

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References

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