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RESEARCH EVALUATING AN INTENSIVE INSULIN TRANSITION PROTOCOL IN AN INTENSIVE CARE SETTING

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ABSTRACT

In this study, a standardized transition order set was evaluated to determine whether it provides effective and safe transition from a continuous insulin infusion regimen to a subcutaneous insulin regimen in patients in no cardiovascular surgery intensive care units. Methods: This study was a retrospective one. The study was not conducted on patients suffering from hyperosmolar hyperglycemic syndrome or diabetic ketoacidosis. The transition order set was implemented in 50 patients before and 50 patients after the order was implemented. In the days following the transition, blood glucose levels were monitored for up to three days Results: We analyzed the data from 57 patients: 42 before transition protocol and 15 after. The transitioned patients are all on basal insulin, compared with the prior to protocol group. It was found in 45% of cases that when patients followed the transition order, hypoglycemia did not increase as long as the blood sugars remained within the desired ranges. Those in the group before and after the protocol, there were 6.68 and 9.00 hyperglycemic events per person, respectively (p=0.05).). In the off-protocol group, sliding scale coverage reduced by 40% and correctional insulin coverage dramatically decreased (p=0.01). Conclusion: In transition regimens that included basal insulin, hyperglycemic events decreased, while hypoglycemic events did not increase. There were fewer hyperglycemic events in patients transitioning "per protocol"; their mean blood sugars were lower at 2 and 3 days; and their insulin requirements were lower. An ICU transition protocol that follows a standardized glycemic control protocol showed benefits.

INTRODUCTION

As a result of hospitalization, hyperglycemia is a common occurrence. It is especially concerning in intensive care units (ICUs). An increase in stress hormones can lead to hyperglycemia when medications such as glucocorticoids are administered, or when parenteral feeding is administered to a patient with a critical illness. Infections, electrolyte abnormalities, and mortality are associated with poor glycemic control [1-8] Normoglycemia is an important aspect of ICU management [10-15].

Keeping blood glucose levels less than or equal to 180 mg/dL is recommended for controlling blood sugar without increasing the risk of hypoglycaemia. [8] The optimum method of administering insulin in the ICU is via an insulin infusion.

In the study site, ICU patients whose blood glucose levels exceed 180 mg/dL two times in a row are recommended continuous insulin infusions. A nurse draws blood glucose levels every hour or so to calculate insulin infusion rate adjustments using Glucommander TM devices, which were incorporated into the study site in 2009. An insulin infusion rate adjustment is provided by the GlucommanderTM based on blood glucose levels entered into the device.

It is not possible to treat hyperglycemia with continuous insulin infusions outside the intensive care unit using the GlucommanderTM machines; however, the machines provide safe and effective control of blood

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glucose levels. Medical-surgical units require patients to transition off insulin infusions before they can be transferred. According to the current literature, scheduled subcutaneous insulin is preferable to reactive, sliding scale insulin that provides pro-active blood glucose control [7]. However, the evidence on the best way to transition patients safely to a subcutaneous regimen is still limited. The rounding physician decided when to withdraw patients from Glucommander TM at the study site. Insulin infusions were re-instituted at times due to inconsistent transition regimens that failed and were often ineffective.

In this transition order set, physicians are guided in choosing insulin regimens as well as standardizing how patients are transitioned to insulin therapy. Patients were transitioned from one regimen to another according to their nutritional intake. The patient transitioned to long-acting insulin and correctional insulin injections twice daily if they required parenteral nutrition or continuous tube feeding. In patients who tolerated an oral diet, long-acting insulin, prandial insulin, and correctional insulin were injected once daily. By calculating insulin sensitivity factor using the Glucommander TM, we selected the amount of insulin to be administered. Blood glucose control following discontinuation of insulin infusion requires further investigation for safety and efficacy.

This study aimed to determine the effectiveness of the new protocol in controlling blood glucose up to 3 days after discontinuation of continuous insulin infusions (goal blood glucose <180 mg/dL). Hypoglycemia and hyperglycemia were examined as secondary objectives. An individual with hypoglycemia is one whose blood glucose level is below 70 mg/dL, as defined by hospital protocol. As high blood sugar levels are defined as 180 mg/dL or higher, hyperglycemia is present. In addition to the number of patients transitioned correctly per protocol, additional secondary objectives included the amount of correctional insulin coverage necessary for transitioned patients.

METHODS

In a local community hospital with 600 beds, a retrospective study was conducted. ICUs for noncardiovascular surgery were present in two of the facilities. Both medical and surgical ICU patients were included in the review, which consisted of approximately 38 beds.

Our analysis included GlucommanderTM patients who have been using the device for more than 24 hours, insulin sensitivity factor stable patients, and patients transitioning from continuous insulin infusions to glucommanderTM after 24 hours. A patient with diabetic ketoacidosis, a patient with hyperglycemic hyperosmolar syndrome, or a patient who didn't transition following a transition order were excluded.

A Human Subject Protection Board approval was obtained. Online databases provided secure identification of patients. As part of the prior protocol, 50 patients were required to be on continuous insulin infusions during hospitalization. In accordance with current practices, a time frame was selected.

Following the formal implementation of the transition order-set, 50 additional patients requiring continuous insulin infusions were included. A formal transition order-set incorporated the patient. According to the formal transition order-set, those who transitioned in compliance with the protocol were called "per protocol," and those who transitioned differently, known as "off protocol," were called "off protocol." In addition to baseline demographic data, comorbidities, transition regimens, concurrent steroids, nutrition, and blood glucose levels after transitioning were also collected. In order to collect data, a standard data collection form was used. SPSS for Windows Release 18.0 was used to analyze data using descriptive and inferential statistics. There were different statistical methods used, including frequencies, percentages, means, standard deviations, Kruskal-Wallis tests, and Mann-Whitney U tests. The statistical significance level was set at 0.05.

RESULTS

An analysis of 100 patients' charts was conducted retrospectively, of which 57 patients met the inclusion criteria. 15 charts were reviewed after applying the formal transition order set. Pre and post transition orders were reviewed on 42 charts. The after-protocol groups were characterized by deaths before transition or patients who were not able to follow the transition protocol.Males (42.75%) and females (57.25%) were equally represented in the entire sample (n=57). A mean age of 55.85 years (SD=11.25) was observed in patients between the ages of 23 and 80. Only two patients had Type 1 diabetes, and 18 patients did not have a preexisting diagnosis of diabetes. Most patients had Type II diabetes, and only two had Type 1 diabetes. It was 4.05 (SD=1.27) for the average hemoglobin A1C (HgbA1C). In Table 1 there are 25 patients on simultaneous steroid medication (43.85%) and 32 patients not on steroids (56.14%). In general, hypertension accounted for 50.3% of the total comorbidities, coronary artery disease accounted for 16.1%, hyperlipidemia accounted for 15.5%, and cerebral vascular accidents accounted for 5.1% (Table 1).

We conducted a Kruskal-Wallis nonparametric analysis of variance (ANOVA) to compare the treatment groups prior to, according to, and off protocol. Based on chi-square analyses, each of the three groups had significantly different mean blood glucose levels on day two. Following Holm's sequential Bonferroni method, follow-up tests were conducted to evaluate pair-wise differences between the groups. In the "off protocol" and "per protocol" groups, significant differences were found between the groups prior to protocol and off protocol. As compared to the "per protocol" group, the level of blood

glucose in the prior-to-protocol group was higher (M=178.65) and the level in the "off-protocol" group was higher (M=214.69) than in the "per protocol" group (M=169.31). Additionally, the average blood glucose level remained lower for the group following protocol (147.85) than that of the group following prior protocol (169.24) and group off protocol (211.14).

According to the test results, the total amount of correctional insulin for the 3 days was lower for the group following protocol (M=11 units) than for the group following the prior protocol (M=14 units) or the group following the off protocol (M=18.4 units). In the pre-protocol, "per protocol," and "off protocol" groups, respectively, there was no significant increase in the rate of hypoglycemic events. Table 2 shows that the "per protocol" group had no severe hypoglycemic events in comparison with the other groups.

The Mann-Whitney U test was used to evaluate how well the formal transition order set is being used by comparing the "per protocol" and "off protocol" groups. Both groups showed significantly different mean blood glucose levels during the 2- and 3-day post-transition periods, as well as the amount of insulin corrected within the 3-day period. Within the timeframe of the study, the group that followed protocol had a significantly lower number of hyperglycemic events than the group not following protocol. Within 24 to 48 hours after transition, the "per protocol" group's mean glucose level was significantly lower than the "off protocol" groups.

A significant difference was observed between the "per protocol" group and the "off protocol" group between 48 and 72 hours after a transition. There is a significant difference between the "per protocol" and "off protocol" groups with respect to the amount of corrective insulin required within 3 days of sliding scale coverage (M=11 units, SD=8.96), z=62.50, p=0.04). Compared to the "off protocol" group, only 3% of those on protocol had hypoglycemia, while 5% had it.

Table 1: Groups of patients, based on their baseline demographics

	Total Samples (n=57)	Before Protocol (N=42)	"Per Protocol" (n=8)	"Off Protocol" (n=7)
Mean Age in Yrs.	55.85 yrs.	58.12	57.25	52.23
Gender (Male: Female)	25:32	16:26	5:3	4:3
Weight in kg	86.6	86.2	88.8	91.0 (68.3-125.0)
Avg. BMI	25.64	26.45	27.45	26.18
History of Diabetes	37	28	6	6
Non-insulin Treated	16	10	3	3
Insulin Treated	23	17	3	3
Avg. HgbA1c	7.9	7.8	7.1	8.9
Total Days on Continuous Insulin Infusion (range)	2.7	2.9	2.5	2.4
Concurrent Use of Steroids	25	18	4	3
Insulin Sensitivity Factor on Transition (range)	0.061	0.079	0.039	0.049
BBG Discontinuation of Insulin Infusion in mg/dL (range)	119.10	112.8	117.1	118.25
Initial Units of Basal Insulin Given (range)	12.2	7.6	22.4	19.8

Table 2: A stratified analysis of blood sugar control after a switch from continuous insulin infusion to subcutaneous insulin, stratified by group, for 72 hours

	Before Protocol	"Per Protocol"	"Off Protocol"
No. of patients	42	8	7
No. of BBGs	577	99	97
% Transitioned with basal insulin	20 per cent	50 per cent	50 per cent
% of hypoglycemic BBGs (<70 mg/dL)	2per cent	3 per cent	5 per cent
% of hyperglycemic BBGs (>180 mg/dL)	49 per cent	52 per cent	29 per cent
% of in target range BBGs (70-180 mg/dL)	51 per cent	46 per cent	68 per cent
Mean BBG 48 hours (mg/dL)	179.25	205.15	208.45
Mean BBG 24 hours (mg/dL)	178.65	169.31	214.69

Mean BBG 72 hours (mg/dL)	169.24	147.85	211.14
Avg. amount of supplemental insulin given per person	14 units	11 units	18.4 Units

DISCUSSION

The current standard of care for hyperglycemia management recommends combining basal and postprandial insulin. For blood glucose control overnight and in between meals, insulin glargine was administered subcutaneously as a long acting insulin. During prandial administration, insulin lispro is infused into the subcutaneous tissue before meals. Normal pancreatic insulin secretion is best simulated by this method.

The use of basal-prandial insulin regimens has proven beneficial for critically ill patients with hyperglycemia. This patient population has had varying blood sugar goals over the past decade. NICE-SUGAR Investigators increased the blood sugar threshold to 110 to 180 mg/dL for hypoglycemia minimization and optimal outcomes [8]. Target blood glucose levels were consistent with current recommendations while on continuous insulin infusion and during transition. Both hypoglycemia and hyperglycemia should be addressed by adjusting the regimen if blood glucose levels fall outside of target range at any time.

On average, regimens were not changed for "per protocol" or "off protocol" until 33 or 45 hours following their implementation. As blood glucose levels change, the protocol regimen is adjusted. A drug regimen increase or a drug regimen decrease should be utilized according to the clinical status of the patient to address the constant uncontrolled blood glucose levels or to accommodate a return to normal insulin response as the condition improves. The clinical practice of normalizing blood sugar levels and preventing hypoglycemia requires further observation.

According to this study, improving glycemic control through standardized intensive insulin transition protocols was highly effective. The protocol provides a proactive approach to controlling blood sugar by transitioning patients to basal insulin. When patients transitioned correctly, the number of hypoglycemic events did not increase significantly, despite the inherent risk of hypoglycemia associated with basal insulin. Patients transitioning "per protocol" needed less insulin correction and experienced fewer hyperglycemic events than those in the control group prior to the protocol.

A significant difference was found between patients transitioned "per protocol" and patients transitioned "off protocol." In the first 24 hours, all groups had poor blood glucose control, but by 48 hours, the "per protocol" group had significantly better blood glucose control. A further improvement was observed in blood glucose control after 72 hours. There were also fewer hyperglycemic events in the group that followed protocol.

Due to the high risk and acuity of continuous insulin infusions, they are not practical in non-ICU settings. A formal transition order-set was developed to standardize the procedure of discontinuing continuous insulin infusions, similar to that recommended by The Northwestern Experience by DeSantis [6]. Patients with diabetes or patients with elevated blood sugar levels who do not have a history of diabetes are able to select an effective transition regimen without having to guess what to pick.

Patients could transition to an oral diet regardless of their critical illness or nutrition status, in contrast to DeSantis's protocol, in which patients were switched from continuous insulin infusion to oral diet once they tolerated an oral diet. In the DeSantis study, 80% of the average daily insulin infused continuously was initially administered subcutaneously. To eliminate potential mathematical and documentation errors, the insulin sensitivity factor was used to select the transition regimen in the current study. The insulin transition regimen was determined by one value, making the process simpler and safer for physicians.

According to recommendations of the American Association of Clinical Endocrinologists and NICE-SUGAR Trial, the study's goal was to achieve a glucose level below 180 mg/dL [8,14]. According to comparative studies, hypoglycemia or severe hypoglycemia was defined as 40 or 50 mg/dL, so the current study's cutoff is lower than what comparative studies use. As defined by the study hospital (blood glucose limit of 70 mg/dL), two percent of blood sugar levels in the "per protocol" group were hypoglycemic; however, when using the standards in the comparative literature, no blood sugars were below 50 mg/dL.

However, the protocol was not utilized as much as it should have been by intensivists. Previously, these patients did not require insulin therapy due to concern about hypoglycemia. Moreover, more basal insulin was administered than was recommended in the protocol to patients transitioning from one to another. Studies have found that using the recommended amount of basal insulin does not significantly increase hypoglycemia risks. The correctional insulin dose was increased for hyperglycemia in patients transitioning from higher basal insulin doses to lower basal insulin doses. Consequently, hypoglycemia was more common among patients transitioning off protocol.

Because of the retrospective design and the lack of usage of the transition order set, the sample size for this study was limited. The sample size should be increased in future studies. It is necessary to investigate the relationship between blood sugar control and diabetes history or hemoglobin A1C at baseline in addition to existing studies.

CONCLUSIONS

In patients transitioning off of continuous insulin

infusions with minimal adverse effects, implementation of a formal transition order set significantly improved glycemic control. Patient outcomes have improved with normoglycemia by reducing infection rates and mortality. Moreover, controlling hyperglycemia acutely can help minimize long-term organ damage from poor glucose control, a known consequence. An intensive insulin transition protocol in the ICU was found to be effective in this study.

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