Initial experience with an intensive care hyperglycemia protocol in a Saudi Arabian intensive care unit

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ABSTRACT

Objectives: To study the efficacy of nurse-driven intensive glucose management protocol in an intensive care setting.

Methods: This cohort study took place at King Abdul-Aziz National Guard Hospital, Al-Hasa, Saudi Arabia from April 2005 through June 2005. We modified a validated nurse-driven glycemic protocol when glucose level was >11.1 mmol/L. Protocol was applied to 103 consecutive patients. Three months after implementing the protocol, we analyzed the glucose control and relevant patient variables. To check the efficacy, glucose values were compared with patients admitted consecutively 2 months prior to the implementation of the protocol. Duration and mean insulin infusion rates were also recorded. A brief nursing survey was also conducted.

Results: The median blood glucose upon ICU admission was 8.7 mmol/L (interquartile range 6.9-12.05). Our cohort included 45 patients with history of diabetes while the remaining 58 were non-diabetics. Mean blood glucose decreased from 10 $\pm$ 4.4 mmol/L on admission to 8.2 $\pm$ 1.8 mmol/L for the duration of ICU stay. Protocol was effective in both diabetics and non-diabetics. Insulin infusion was employed in 33 patients. Median insulin infusion rate required throughout the ICU length of stay was 4.3 units/hour. Duration and rate of insulin infusion were not statistically significant between diabetics and non-diabetics. The glucose control was significantly better when compared with the prior practices of glucose control.

Conclusion: Our study demonstrates that nurse-driven hyperglycemia protocol were manageable to used in critically ill patients. Moreover, the protocol is equally effective in both diabetic and non-diabetic patients.

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Control of glucose is frequently impaired in critically ill patients regardless of presence or absence of diabetes mellitus.[1] Hyperglycemia in critical care setting has been shown to increase mortality and length of intensive care unit (ICU) stay.[2-4] In recent years, the use of standardized protocols has been popularized after a significant mortality benefit was shown in a randomized trial targeting a certain glucose value (4.4-6.1 mmol/L) in a surgical setting.[4] Subsequently, similar mortality benefit was shown in predominantly medical ICU with less stringent blood glucose (<7.8 mmol/L) target values.[5] The benefit of

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controlling blood glucose also extends to decreased ICU length of stay, infection rates, and new onset renal dysfunction.[3,5] Several mechanisms have been proposed for these benefits and ongoing studies are being designed to further explore theses mechanisms. Diabetes mellitus is prevalent in Saudi Arabia. In a large community based study, the prevalence was found to be 23.7%.[6] It has been shown that the presence of diabetes in itself worsens outcome in critically ill patients.[7] Traditionally used subcutaneous insulin sliding scales frequently required adjustments, labor intensive and ineffective. Therefore, the use of nurse-driven standardized insulin protocol is the optimal way to manage hyperglycemia. In this study, we intended to determined the efficacy of a nurse-driven hyperglycemia protocol in ICU and our initial experience is presented here.

Methods. King Abdul-Aziz National Guard Hospital, Al-Hasa (KAH), Saudi Arabia is a 300-bed community based hospital that serves national guards and their dependents. The ICU is an 8-bed close unit that caters medical, cardiac and surgical patients. The ICU is headed by Board Certified Intensivists along with staff physicians (background training in ICU). In March 2005, in collaboration with our endocrinology division, we developed a nurse-driven insulin protocol based on Krinsley's study.[5] The protocol is shown in ***Appendix 1**. We aimed to target blood glucose values <7.8 mmol/L. After a short period of in-service, the protocol was implemented from April 2005. Our initial experience from April through June 2005 is presented here. During the study period, the insulin protocol was used in 103 consecutive patients admitted to ICU. Patients' data including age, gender, history of diabetes, admission diagnosis, type of admission and APACHE II scores during the first 24 hours were obtained from the ICU data collection forms. We recorded the glucose values, dose and mode of insulin using a blood glucose flow sheet. The admission glucose was obtained from serum chemistry panel and subsequent blood glucose values were obtained by standard glucometer (Lifescan, Johnson & Johnson, CA, USA) as mentioned in the protocol. Insulin infusion was started when 2 consecutive blood glucose levels were >11.1 mmol/L. We compared blood glucose levels of protocol group requiring intravenous insulin infusion with a cohort of 85 patients consecutively admitted to our ICU 2 months prior to the implementation of the protocol. From this cohort, patients with any blood glucose >11.2 mmol/L were used for comparison because this was the blood glucose cut point recommended for subsequent insulin infusion. We identified 30 hyperglycemic control patients who were given some kind of insulin therapy. Severe Hypoglycemia was defined as blood glucose levels <2.2mmol/L. All clinical data were mentioned in mean ± standard deviations and percentage. Categorical variables were compared by chi square test and nominal data by student t-test. A p value of <0.05 was considered significant.

The study was approved by the institutional review board of National Guard health affairs for Eastern region of Saudi Arabia.

Results. Baseline characteristics of patients are shown in **Table 1**. **Table 2** shows the distribution of admission diagnosis. Only 7 surgical patients were admitted during this period and medical ailments. The median blood glucose upon ICU admission was 8.7 mmol/L (interquartile range 6.9-12.05). Our cohort included 45 patients with history of diabetes while the remaining 59 were non-diabetics. According to the protocol, 70 patients were managed by subcutaneous insulin and only 33 patients required insulin infusion for their control of hyperglycemia. **Table 3** summarizes the important variables in diabetic and non-diabetic groups. **Table 4 and 5** describe patients who required sub-cutaneous insulin and insulin infusion. Of 33 patients received insulin infusions, the median duration was 54 hours. The mean blood glucose at insulin infusion initiation was 10 ± 4.4 mmol/L (median 8.75 mmol/L), and the mean time required to achieve first target blood glucose level (<7.8 mmol/L) was 6.7 ± 9.8 hours. Once the first target glucose level was achieved, 47.5% of subsequent glucose values were within the range of 3.4-7.8 mmol/L, 30.3% glucose values decrease to 7.9-10 mmol/L while 11.3% were in the range of 10.1-11.2 mmol/L. In 3 patients, glucose values was <11.2 mmol/L during their ICU stay. Only 4.5% of total glucose values were between 2.3-3.3mmol/dL. None of the blood glucose values were <2.2 mmol/L (severe hypoglycemia). There were no events of symptomatic hypoglycemia in our cohort patients. The main reason for extremely rare incidence of hypoglycemia was a relatively less stringent target glucose level, which in itself served as a shield against hypoglycemia. There were 2 episodes of hypoglycemia requiring intravenous dextrose in control patients although the blood sugar levels were in the range of 2.4 and 3.3 mmol/L. Overall, the median insulin infusion rate required throughout the ICU length of stay was 4.3 units/hour. However, there were no significant

*The full text including Appendix 1 is available in PDF format on SMJ website (www.smj.org.sa)

Table 1 - Demographics of hyperglycemia protocol group patients (n=103).

Variable	No. of patients (%)
Age	59.9 ±17.7
Male	56 (54)
Type of admission	
Medical/Surgical	49 (47.1)
Cardiology	55 (52.9)
Diabetes mellitus	46 (44.2)
Admission glucose mean±SD (mmol/L)	10 ± 4.4
Glucose during ICU stay mean±SD (mmol/L)	8.2 ± 1.8
APACHE II median (inter quartile range)	13 (9-17)

ICU - intensive care unit,
APACHE II - Acute Physiology and Chronic Health Evaluation II

Table 2 - Distribution of diagnosis in hyperglycemia protocol group patients.

Diagnosis	n (%)
Primary Cardiac disease	54 (52.4)
Respiratory diseases	13 (12.6)
Renal diseases	7 (6.8)
Surgical/RTA	7 (6.8)
Sepsis	5 (4.8)
Malignancy	3 (2.9)
Neurological disease	3 (2.9)
Others*	11 (10.9)

*Hematology and Oncology, Gastrointestinal, Endocrine, Obstetrics and Gynecology, post code, overdose, RTA - road traffic accidents

Table 3 - Characteristics of diabetics versus non-diabetics in hyperglycemia protocol group patients.

Variables	Diabetics (n=45)	Non-Diabetics (n=58)
Age	65.6 ± 11.6	55.2 ± 20.3
Male (%)	23 (51.1)	32 (55.2)
APACHE II	13 (10-15)	13 (7.5-20)
Diagnosis (%)		
Medical/Surgical	13 (28.9)	30 (51.7)
Cardiology	32 (71.1)	29 (48.3)
Mean glucose during stay (mmol/L)	8.7 ± 1.6	7.6 ± 1.6
Admission glucose (mmol/L)	11.4 ± 5	8.7 ± 3.1
Time to achieve target (hours)	8 ± 10	5.4 ± 9.6

APACHE II - Acute Physiology and Chronic Health Evaluation II

differences between median insulin infusion rates for diabetic (4.2+1.6 units/hour) and non-diabetic (4.5+1.6 units/hour, p=0.25). Insulin requirements were not significantly affected by age, gender, and type of admission but affected significantly (p=0.034) by the severity of illness (APACHE II score). To assess the general effectiveness of the hyperglycemia protocol compared with our previous practice standards, glucose levels in protocol group requiring intravenous insulin infusion (IIF) were compared with historic control group. There were similar proportions of diabetic patients in the control group and IIF group (80% versus 79%, p=0.90). Admission blood glucose levels were comparable between the control and IIF patients (10.1 ± 4.4 versus 10.7 ± 3.9 mmol/L, p=0.12). Despite a greater severity of illness in control group (APACHE II score 14.8 ± 8.5 versus 13.6 ± 4.9, p<0.02), our IIF patients had better glycemic control than their counterparts (p<0.008). **Figure 1** compares blood glucose (in percentage) between the 2 patient groups and revealed the statistically significant differences at different blood glucose levels. In order to obtained nursings' staff input, we evaluated the following: ease of use, efficacy, and workload imposed by insulin protocol. Eighteen nurses filled in the survey on 5-point Likert scale. All the nurses agreed that the protocol was easy to use and 77.7% agreed that the protocol was effective in achieving its goal. Approximately, 38.8% nurses strongly agreed and another 66.6% agreed that protocol has increased their workload.

Discussion. Hyperglycemia has been associated with increased mortality and morbidity in critically ill medical, surgical and cardiac patients.[2,7] Van den Berghe et al[3] published the first randomized control trial (RCT) in predominantly surgical patients, which showed mortality and morbidity benefit of euglycemia

Table 4 - Characteristics of diabetrics versus non-diabetics in hyperglycemia protocol group patients managed without insulin infusion.

Variables	Diabetics (n=24)	Non-Diabetics (n=46)
Age	65.1 ± 13.4	53.2 ± 21.4
Male n (%)	12 (50)	28 (60.9)
APACHE II	13 (13-15)	13 (7-19.5)
Admission glucose (mmol/L)	8.9 ± 3.6	8 ± 2.2
Mean glucose during stay (mmo/L)	8.3 ± 1.7	7.5 ± 1.6
Time to achieve target (hours)	5.15 ± 7.9	2.75 ± 6.3

APACHE II - Acute Physiology and Chronic Health Evaluation II

Table 5 - Characteristics of diabetics versus non-diabetics in the Hyperglycemia protocol group patients required insulin infusion.

Variables	Diabetics (n=26)	Non-diabetics (n=7)
Age	66.12 ± 10.1	62 ±11.6
Male n (%)	11 (40.7)	5 (71.4)
APACHE II	11 (9-22)	20 (12.2-29.3)
Admission glucose (mmol/L)	14.5 ± 4.5	12.6 ± 5.3
Duration of infusion (hours)	58.7 ± 52.4	47 ± 30.3
Infusion rate required to achieve first target glucose level (units/hour)	4.2 ± 1.6	4.5 ± 1.6
Infusion rate required for maintenance after first target glucose level Units/hour)	2.6 ± 0.9	2.2 ± 1.2
Blood glucose during infusion (mmol/L)	9.3 ± 1.45	9.3 ± 2.5
Time to achieve first target glucose value (hour)	12.5 ± 12	13.4 ± 11.3

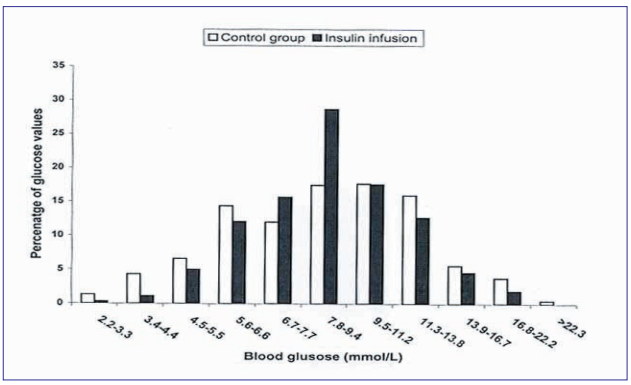

Figure 1 - Percentage of blood glucose values in insulin infusion versus control group.

4.4-6.1 mmol/L.[3] Several studies also demonstrated the increased mortality after myocardial infarction in patients with hyperglycemia.[2,7] There are no RCTs to evaluate similar benefits in medical patients. Krinsley reported a before/after study in a community medical ICU setting, which interestingly showed similar mortality and morbidity benefits, but with a less stringent glucose (<7.8 mmol/L) targets,[5] several mechanisms have been proposed for worse outcomes in hyperglycemic patients. These include impaired immune response, endothelial dysfunction and impaired glucose consumption by various organs.[5] Further studies are underway to explore these mechanisms. Implementation of a targeted blood glucose protocol has several concerns related to safety, efficacy and increased workload on the nursing staff. Several protocols have been described in the literature.[3,4,8-10] Most of the protocols are nurse driven and utilize insulin infusion from the start. Moreover the target insulin levels vary from euglycemia to blood glucose levels <8.33 mmol/L. Our simple and relatively conservative protocol was well accepted by our nursing staff. Moreover our predominant cardiac and medical population also suited for this kind of protocol. Although, the reasonable glucose control and extremely rare incidence of hypoglycemia makes this an acceptable protocol but long-term effects on our population remains to be observed. Our patients had less median APACHE II scores than Krinsley (13 versus 15) but our cohort had much higher number of diabetics as compared to Krinsley (18.1% versus 44.2%), which may explain relatively higher glucose levels after implementation of protocol (7.26 ± 3.06 versus 8.2 ± 1.8) (5). None of our patients had glucose values <2.2 mmol/dL (0.34% in Krinsley's cohort of treated patients). Results of our observational study have some important implications. We demonstrated similar efficacy of protocol in both diabetics and non-diabetics. Moreover, a significant population was controlled by subcutaneous arm of protocol, which proved to be an important factor in convincing our nursing staff regarding workload concerns. There are several limitations of our study. We originally started the project to implement hyperglycemia protocol in our ICU and thus no control group was established. Subsequently, we had to use historic controls for comparing with our prior practice of glucose control which may not be an ideal way. There were no major differences of care between the care of patients for 2 intervals but, control patients had higher APACHE II values. Our goal of such comparison was to document the efficacy of the protocol with our prior practice. We chose a level of 7.8 mmol/L predominantly for the safety purpose and our predominant medical and cardiac patient population who has shown to be benefited from keeping blood glucose levels <10 mmol/L.[2] The long-term effects of glucose control including mortality, infection rates and ICU length of stay remains to be answered in Saudi population where diabetes and coronary artery diseases are rampant.

In conclusion, this initial work demonstrates that a nurse-driven insulin protocol can be safely adopted in a relatively small community hospital. We identified our ICU as a medical/cardiac ICU and chose the value of 7.8 mmol/L as a target glucose. Whether adopting this strategy will change long-term outcomes needs further large well designed trials.

References

1. McCowen KC, Malhortra A, Bistran BR. Stress-induced hyperglycemia. ***Crit Care Clin*** 2001; 17: 107-124.
2. Malmberg K, Ryden L, Efendic S, Herlitz J, Nicol P, Waldenstrom A, et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. ***J Am Coll Cardiol*** 1995; 26: 57-65.
3. Van den Berghe G, Wouters PJ, Bouillon R, Weekers F, Verwaest C, Scehtz M, et al. Intensive insulin therapy in critically ill patients. ***N Engl J Med*** 2001; 345: 1359-1367.
4. Furnary AP, Gao G, Grunkemeier GL, Wu Y, Zerr KJ, Bookin SO, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. ***J Thoracic Cardiovasc Surg*** 2003; 125: 1007-1019.
5. Krinsley JS. Effect of an Intensive Glucose Management Protocol on the Mortality of Critically Ill Adult Patients. ***Mayo Clin Proc*** 2004; 79: 992-1000.
6. Al-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, Al-Harthi SS, Arafah MR, Khalil MZ, et al. Diabetes mellitus in Saudi Arabia. ***Saudi Med J*** 2004; 25: 1603-1610.
7. Malmberg K, Ryde´n L. Myocardial infarction in patients with diabetes mellitus. ***Eur Heart J*** 1988; 9: 256-264.
8. Zimmerman CR, Mlynarek ME, Jordan JA, Rajda CA, Horst HM. An insulin infusion protocol in critically ill cardiothoracic surgery patients. ***Ann Pharmacother*** 2004; 3 8: 1123–1129.
9. Goldberg PA, Siegel MD, Sherwin RS, Halickman JI, Lee M, Bailey VA, et al. Implementation of a safe and effective insulin infusion protocol in a medical intensive care unit. ***Diabetes Care*** 2004; 27: 461–467.
10. Chant C,Wilson G, Friedrich JO. Validation of an Insulin Infusion Nomogram for Intensive Glucose Control in Critically Ill Patients. ***Pharmacotherapy*** 2005; 25: 352-359.