Southern African Journal of Anaesthesia and Analgesia 2014; 20(4):185-189

South Afr J Anaesth Analg
ISSN 1608-4356 EISSN 1727-9835

Research

Blood sugar control in the intensive care unit: time to relook

Rapsang AG, *Assistant Professor Anesthesiology and Critical Care, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER)*
Devajit CS, *Assistant Professor Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER)*
Author e-mail: amy_rap@yahoo.com

Abstract:

The choice of blood sugar control technique in the ICU has long been debated. Intensive insulin therapy to achieve normoglycaemia has been shown to reduce mortality, morbidity and the length of ICU stay; but, at the same time it also requires frequent glucose monitoring, adjustment of insulin dose and increase in the medical personnel workload. Despite its clinical benefits, intensive glucose control (IGT) is, however, not favoured by the intensivist, because of the risk of hypoglycaemia**.** This article provides the reader with an interesting thought: Can intensive blood sugar control be implemented in the ICU, while avoiding hypoglycaemia, and without an increase in hospital cost, and thus change existing blood sugar control protocols in the ICU? Is this possible with the use of continuous glucose monitoring (CGM) devices, which have recently emerged as a tool to maintain proper glucose levels? If further developed, CGM technology could ultimately prove clinically useful in the ICU. However, further research is warranted to confirm its benefits in the implementation of tight glucose control policies in the ICU.

Key words: blood glucose**,** continuous glucose monitoring**,** intensive care, intensive glucose control.

Introduction

The impact of glycaemic control on in-patient mortality has been long debated and the optimal target range for blood glucose in critically ill patients remains unclear. Hyperglycaemia, defined by a blood-glucose level exceeding the normal fasting level of 5.5 mmol/l is common during critical illness.[1] Glucose elevation in critically ill patients is commonly attributed to associated increased levels of cortisol, glucagon and adrenaline, thus resulting in increased gluconeogenesis and decreased peripheral uptake of glucose, hence leading to high circulating levels of glucose.[2] This glucose elevation increases the cellular glucose overload and associated pronounced side effects of glycolysis and oxidative phosphorylation, thereby causing irreversible damage to cellular function and structure, reflected by various organ dysfunctions (liver, renal, cardiac, endothelial and cellular immune system).[3,4] Although this stress hyperglycaemia was long deemed to be a beneficial, adaptive response to provide energy to those organs that predominantly rely on glucose as metabolic substrate, many studies have confirmed that there is a link between hyperglycaemia and increased mortality.[5] In fact, Mesotten D and Van den Berghe G,[5] showed that the statistical association between blood-glucose level and risk of death, in many observational studies follows a J-shaped curve, with normal, fasting blood levels associated with lowest risk of death.

Intensive versus conventional glucose control

The choice of blood sugar control technique (conventional versus intensive control) in the ICU, however, has long been debated. Insulin-based treatment regimens decrease morbidity and mortality in critically ill patients,[6] yet tight control of blood sugar, was not favoured by many intensivists – due to an increased risk of hypoglycaemia. Hypoglycaemia remains the most significant concern regarding implementation of tight glucose control policies because it can induce irreversible brain lesions. Severe hypoglycaemia (<2.2 mmol/l)[7] has been shown to be an independent risk factor for mortality in the ICU[8] and it occurs 5-10 times more in intensive glucose control (IGC) as compared to conventional glucose control (CGC). Moreover, as the majority of ICU patients have decreased levels of consciousness and increased stress, the detection of hypoglycaemia in these patients depends solely on glucose monitoring.

From an economic standpoint, a cost analysis study of IGC in critically ill adult patients revealed that IGC saved an average of $1580 per patient[9] attributed to shorter ICU and hospital length of stay, decreased ventilator-dependent days, and reduced total laboratory costs. In another study on mechanically ventilated patients admitted to a surgical ICU, the excess cost of hospitalisation in patients treated with CGC compared to those treated according to the IGC regimen was €2638 per patient.[10] Hence, given the improved clinical outcomes of IGC and its cost effectiveness, it is probably worth pursuing.

To show a relationship between hyperglycaemia and mortality risk, many randomised controlled trials (RCTs) that target and achieve different blood-glucose levels have been conducted. The 2001 Leuven Surgical Trial[11] was one of the first to demonstrate a clinical benefit amongst predominantly surgical ICU patients treated with IGC. Subsequent RCTs were then conducted in a heterogeneous population in ICU, but these studies failed to support the subsequent benefit of these intensive glucose control practices in this environment, probably because these

investigations lack the methodological rigor of the initial studies and have provided few data that can be effectively extrapolated to the care of the ICU population.[12] Table 1 shows the different studies conducted "for and against" a tight glucose control policy.

The NICE-SUGAR encountered major criticisms:[12]

- The use of different target ranges for blood glucose in the control and interventional groups (7.7-10 mmol/l *vs* 10-11.9 mmol/l in Leuven studies
- Different routes for insulin administration; types of infusion system used
- Difference in sampling sites
- Different glucometers used and difference in nutritional strategies.

Despite these criticisms, this trial contradicted and over-rode the trend towards IGC in the ICU that began with the earlier Leuven trials. Therefore, in view of the detrimental effects shown by NICE-SUGAR trial, IGC cannot be generally recommended for all ICUs. Although the ideal target glucose remains unclear, the standard of care in many medical and surgical ICUs targets 7.7-10 mmol/l. In fact, several guideline-issuing bodies recommend CGC:

- The 2012 Surviving Sepsis Campaign recommends a glycaemic target of ≤ 10 mmol/l in patients with severe sepsis.[19]
- The "International recommendations for glucose control in adult non-diabetic critically ill patients" strongly suggest avoidance of severe hyperglycaemia (> 10 mmol/l) in adult ICU patients and avoidance of IGC in an emergency situation.[6]
- The 2009 American Association of Clinical Endocrinologists and American Diabetes Association guidelines recommend a goal range of 7.7-10 mmol/l.[20]
- The 2011 Institute for Healthcare Improvement guidelines recommend glucose <10 mmol/l for critically ill patients.[21]

Blood glucose measurement

To measure point-of-care blood glucose, two common procedures are used: venous or arterial blood by way of an intravascular catheter and capillary blood/ finger prick. Venous or arterial blood sampling is not only time-consuming but it also carries a risk of infection and involves a relatively large amount of blood drawn. Finger pricking, however, is prone to measurement errors, as shown in a study by Ting C and Nanji AA.[22] In their study, they found that as many as 62% of values obtained in ICUs deviate from the reference laboratory values by >20%. Another study[23] showed that in shock patients, only 36% of patients had finger stick-derived capillary glucose levels within 20% of the measured reference. These discrepancies in glucose levels

Table 1: Summary of intensive/ tight glucose control studies.

Study	Study synopsis	Results	Outcome
Leuven Surgical Trial[11]	In a surgical ICU, IGC (targeting a blood glucose of 4.4-6.1 mmol/l) was compared to CGC (targeting a blood glucose of 10-11.1 mmol/l), particularly amongst patients who were in the ICU for ≥ 5 days.	Decrease in ICU morbidity and lower incidence of systemic infections, acute renal insufficiency, anaemia, polyneuropathy, duration of artificial ventilation, and length of stay in the ICU.	Tight glucose control recommended.
Griesdale et al[13]	A meta-analysis of 26 RCTs involving a total of 13 567 patients, intensive insulin therapy was compared to conventional insulin therapy in the ICU.	Even though intensive insulin therapy significantly increased the risk of hypoglycaemia and conferred no overall mortality benefit among critically ill patients. This this therapy, however, may be beneficial to patients admitted to a surgical ICU.	Tight glucose control may be beneficial to patients admitted to a surgical ICU.
Wiener et al[14]	A meta-analysis of 34 RCTs totalling 8 432 patients, intensive insulin therapy was compared to conventional insulin therapy in the ICU.	Hospital mortality did not differ between IGC versus CGC. Even though IGC was associated with an increased risk of hypoglycaemia, it was also associated with a decreased risk of septicaemia.	Tight glucose control may be considered to decrease risk of septicaemia.
Scalea et al[15]	Examined the impact of IGC policy on outcomes (from a 24 month period before the implementation of IGC protocol to a 24 month post intervention phase) associated with hyperglycaemia in critically injured patients.	IGC group falls in the improving pattern of glucose control; and a decrease from 29% to 21% in the incidence of early infection (develop in first 2 weeks) was observed after introduction of their tight glucose control protocol.	Tight glucose control may be considered.
NICE-SUGAR multicentre trial.[16]	NICE-SUGAR randomised 6 104 medical and surgical ICU patients to IGC (targeting a blood glucose of 4.5-6 mmol/l) versus CGC (targeting a blood glucose of ≤10 mmol/l).	Increased mortality among medical and surgical ICU patients who received IGC.	Tight glucose control not recommended.
VISEP multicentre trial.[17]	Designed to assess the efficacy of fluid resuscitation and of blood-glucose control (IGC versus usual care) in patients with severe sepsis and septic shock. In this study, blood glucose targets were 4.4-6.1 mmol/l and 10–11.1 mmol/l for the intensive and control groups respectively.	The study had to be stopped early after the incidence of hypoglycaemia (12.1%) in the IGC group was considered unacceptably high.	Tight glucose control not recommended.
The Glu-control multicentre trial[18] (larger than the VISEP trial)[17]	Investigated whether IGC to 4.4-6.1 mmol/l versus a conventional target of 7.7–10 mmol/l improves survival in critically ill patients.	The study had to be stopped early because the target glycaemic control was not reached and the incidence of hypoglycaemia was 9.8%.	Tight glucose control not recommended.

IGC: Intensive Glucose Control, CGC: Conventional Glucose Control, NICE-SUGAR: Normo-glycaemia in Intensive Care Evaluation and Surviving Using Glucose Algorithm Regulation, VISEP: Volume substitution and Insulin therapy in severe SEPsis.

Table 2: Effects of different conditions and treatments on the accuracy of CGM devices in the ICU.

Author(s)	Year	Condition of the patient	n	Outcomes
Lorencio et al[30]	2012	Patients on insulin therapy.	41	Accuracy was significantly better in patients with septic shock in comparison with the other patient cohorts.
Holzinger et al[31]	2009	Patients on inotropic support.	50	No interference in accuracy of CGM devices with inotropic therapy.
Price et al[32]	2008	Patients on inotropic support.	17	No interference in accuracy of CGM devices with inotropic support.
De Block et al[33]	2006	Septic shock, renal failure and patients on inotropic support.	50	Compared with patients on no inotropes and in those without renal failure and septic shock, the accuracy is worse in patients on inotropic support and better in renal failure and septic shock.
Pfützner et al[34]	2006	Patients with ketosis.	12	No interference in accuracy of CGM devices in ketosis patients when compared with patients without ketosis.
Piper et al[35]	2006	Patients with ooedema, hypothermia, and on inotropes.	20	No interference in accuracy of CGM devices in such patients when compared with the other patient cohorts.
Goldberg et al[36]	2004	Oedema, hypotension and patients on inotropic support.	21	No interference in accuracy of CGM in such patients when compared with patients without oedema, hypotension and inotropic support.
Monsod et al[37]	2002	Hyperinsulinaemia	11	Interference in accuracy of CGM devices with hyperinsulinaemia.

CGM: Continuous glucose monitoring.

would potentially impact on the dosing of insulin. These may be due to device performance, alterations in skin temperature, or variations in local perfusion of the site of measurement (usually low perfusion states commonly encountered in ICU patients), together with increased regional glucose utilization which may result in a biased capillary glucose measurement)[24,25]

Continuous glucose monitoring (CGM) devices

In order to improve ICU outcome, IGC should ideally not be associated with hypoglycaemia, increased hospital cost or frequent blood sampling, or finger pricking. This may be possible with the use of next generation glucose monitoring devices in the implementation of tight glucose control strategies. These novel devices which provide continuous or near continuous monitoring capabilities, give "real-time" glucose readings, thus allowing immediate therapeutic adjustments. Glucose levels are continuously reported from a small electrode inserted into interstitial fluid under the skin, usually in the abdomen or upper arm. Almost all the subcutaneous CGM devices on the market utilise comparable glucose-oxidase methodology of glucose measurement and derive their results from interstitial fluid glucose, converted by a specific algorithm to reflect blood glucose.[24] CGM equipment is typically worn by the patient for 3 to 5 days, and is especially useful for detecting nocturnal hypoglycaemia or dawn phenomenon and postprandial hyperglycaemia, which can be missed by other methods of blood glucose monitoring, and hence may have an advantage over "point-of-care" testing.

Designed to successfully improve glucose control, CGM provides information about glucose concentration, directional trends and rate of change of blood glucose over a period of several days. These systems have a sensor life which varies between 3-7 days and they also have user-set alarms for rate of change and predictive alarms for low or high blood glucose levels. Having this information, hypo- or hyperglycaemic excursions can be avoided and glycaemic control could be improved. Thus, mortality and morbidity may possibly be reduced by the prevention of newly acquired kidney injury, faster weaning from mechanical ventilation and accelerated discharge from the ICU.

Accuracy of continuous glucose monitoring devices in the ICU

Although it seems to be a cost effective technology, the major disadvantage of CGM, however, is that the accuracy is not equivalent to that of glucose meters, as there is a physiologic lag between blood and interstitial space glucose of approximately 5 to 10 minutes and this lag is accentuated when glucose levels are undergoing rapid change.[26] Even though some studies[27,28] have demonstrated a reasonable correlation between abdominal interstitial fluid and arterial blood glucose measurements in critically ill patients in the ICU, glucose levels in the abdominal subcutaneous interstitial fluid may be affected by local blood flow and temperature (which may be substantially affected by manifestations of critical illness, such as shock, sepsis, or external cooling), the dynamics of systemic blood glucose changes, and the distance between the sensor and the blood vessel supplying the area of interest[29] thus creating a major bias in glucose assessments. In fact, the relationship of interstitial fluid to blood in the critically ill patient , has been investigated only to a limited degree. Most of these studies[30-37] have evaluated the accuracy of CGMs and address specific critical concerns such as hypotension, use of inotropes, hypothermia, oedema, renal and hepatic failure, hyperinsulinaemia, and acidosis. However, these studies were small and generally not powered to assess each of those variables.

Table 2 shows the different studies evaluating the accuracy of CGMs and their conclusions. Most studies showed that the accuracy of CGMs is not affected by the presence of oedema, hypotension, hypothermia, ketosis or inotropic support.[30-32,34-36] However, hyperinsulinaemia itself reduced sensor glucose compared with venous glucose readings by about 20% in humans.[37]

In a study by Holzinger et al,[38] real-time interstitial fluids CGM was compared with point-of-care blood glucose measurements to guide intravenous insulin infusion over 72 hours in 124

patients on mechanical ventilation. They found that real-time CGM reduces hypoglycaemic events but does not improve glycaemic control compared with intensive insulin therapy guided by an algorithm. A randomised study by Mraz et al,[39] showed that CGM provided better glycaemic control without hypoglycaemia in comparison with standard monitoring to manage glycaemia in an intensive insulin treatment protocol. In another study, Tonyushkina et al[40] showed that 97% of readings in CGM patients were clinically acceptable with no episodes of hypoglycaemia over 24 hours, whereas hypoglycaemia occurred in 50% of patients in the control group. However, Rabiee et al[41] found that the CGM generally overestimated the actual serum glucose and missed 50% of the 30 actual hypoglycaemic episodes as determined by their glucometer, leading the authors to conclude that it was not sufficiently safe to be used in an ICU setting. Based on the limited available data related to accuracy of CGM devices, the Endocrine Society (USA) clinical practice guideline on CGM[42] does not recommend the use of CGM in ICU settings where patients are unable to provide feedback about hypoglycaemic symptoms. They concluded that the potential danger in their use in guiding insulin administration in an acute care setting outweighs the possible convenience and trend awareness that the technology provides.

The future of continuous glucose monitoring devices: intravascular sensors

Automated blood glucose measurement systems that reside in the peripheral vein are under development and may be more accurate than the current FDA-approved CGM systems that monitor glucose via interstitial fluid.[43] This will probably minimise the sources of bias of capillary and interstitial fluid glucose typically encountered in critically ill patients; not to mention that it will also minimise risk of contamination and infection involved in repetitive sampling from indwelling vascular catheters and also reduce medical personnel workload. In their porcine model, Skjaervold et al[44] reported preliminary data on a novel indwelling vascular continuous glucose sensor (which detects blood sugar fluctuations over a wide range. From less than 1 mmol/l to more than 15 mmol/l), by employing a unique hydrogel matrix that changes size continuously in relationship to ambient glucose concentrations, thus providing ongoing real-time reporting of results.[44] This technology, research and concept have paved a way towards safer avenues to glucose control in our ICUs. Until the clinical benefit and safety of such state-of-the-art glucose management systems is clearly demonstrated in human studies, CGM will, however, not be ready for use in glucose control protocols in the ICU.

Conclusion

The technology of CGM devices provides a valuable and rapidly progressing area of research to determine whether or not the application of such novel devices will be sufficient for use with intensive insulin therapy in the ICU population. Even though the use of CGM appears promising, it must undergo a larger testing in the ICU setting before it can be used for implementation of tight glucose control policies in the ICU. Further development of long-term implantable sensors for measuring glucose continuously or as a "real-time" glucose vascular sensor, CGM technology could ultimately prove to be a blessing in the ICU, by decreasing medical personnel workload and by providing alarm signals for impending glycaemic excursions. RCTs examining the use of these new technologies to achieve tight glycaemic control while minimising the risk of hypoglycaemia would, however, still be necessary prior to adopting these devices in critical care.

Sources of financial support

None

Conflicts of interest

The authors certify that there are no actual or potential conflicts of interest linked to continuous glucose monitoring devices in relation to this article.

References

1. Mizock BA. Alterations in carbohydrate metabolism during stress: a review of the literature. The Am J Med 1995; 98: 75–84.
2. Capes SE. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with or without diabetes: a systemic overview. Lancet 2000; 355(9206):773-8.
3. Van den Berghe G. How does blood glucose control with insulin saves lives in intensive care. J Clin Invest 2006; 114(9):1187-95.
4. Ellger B, Debaveye Y, Vanharebeek I et al. Survival benefits of intensive insulin therapy in critical illness: impact of maintaining normoglycemia versus glycemia-independent actions of insulin. Diabetes 2006; 55(4):1096-105.
5. Mesotten D, Van den Berghe G. Clinical benefits of tight glycaemic control: focus on the Intensive Care Unit. Best Pract Res Clin Anesthesiol 2009; 23: 421-29.
6. Langley J, Adams G. Insulin-based regimens decrease mortality rates in critically ill patients: a systematic review. Diabetes Metab Res Rev. 2006 Nov 6;23(3):184-92.
7. Ichai C, Preiser JC. International recommendations for glucose control in adult non diabetic critically ill patients. Crit Care 2010, 4: R166.
8. Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. N Engl J Med 2006; 354: 449-61.
9. Krinsley JS, Jones RL. Cost analysis of intensive glycaemic control in critically ill adult patients. Chest. 2006 Mar;129(3):644-50.
10. Van den Berghe G, Wouters PJ, Kesteloot K, et al. Analysis of healthcare resource utilization with intensive insulin therapy in critically ill patients. Crit Care Med. 2006 Mar;34(3):612-16.
11. Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. N Engl J Med 2001, 345:1359-67.
12. Du Bose JJ, Scalea TM. Glucose elevation and outcome in critically injured trauma patients. Adv Surg 2011; 45:185-96.
13. Griesdale DEG, de Souza RJ, Van Dam RM, et al. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. CMAJ 2009; 180(8):821-27.
14. Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults. A meta-analysis. JAMA 2008; 300:933-44.
15. Scalea TM, Bochicchio GV, Bochicchio KM. Tight glycemic control in critically injured trauma patients. Ann Surg 2007; 246:605-10.
16. NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SY, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med 2009; 360:1283-97.
17. Brunkhorst FM, Engel C, Bloos F, et al. Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis? N Engl J Med 2008; 358:125-39.
18. Preiser JC, Devos P, Ruiz-Santana S, et al. A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study. Intensive Care Med 2009; 35:1738-48.
19. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013; 41(2): 580-637.

20. Moghissi ES, Korytkowski MJ, Di Nardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. Endocr Pract. 2009; 15(4):353-69.
21. Institute for Healthcare Improvement Guidelines Implement Effective Glucose Control. Available from http/www.ihi.org/knowledge/pages/changes/implement eac.aspx
22. Ting C, Nanji AA. Evaluation of the quality of bedside monitoring of the blood glucose level in a teaching hospital. CMAJ. 1988 Jan 1;138(1):23-26.
23. Atkin SH, Dasmahapatra A, Jaker MA, et al. Finger stick glucose determination in shock. Ann Intern Med. 1991 Jun 15;114(12):1020-24.
24. Weiss R, Lazar I. The Need for Continuous Blood Glucose Monitoring in the Intensive Care Unit. J Diabetes Sci Technol 2007;1(3):412-14.
25. Haupt A, Berg B, Paschen P, et al. The effects of skin temperature and testing site on blood glucose measurements taken by a modern blood glucose monitoring device. Diabetes Technol Ther. 2005 Aug;7(4):597-601.
26. Garg SK, Voelmle M, Gottlieb PA. Time lag characterization of two continuous glucose monitoring systems. Diabetes Res Clin Pract 2010; 87:348-53.
27. De Block C, Vertommen J, Manuel-y-Keenoy B, et al. Minimally-invasive and non-invasive continuous glucose monitoring systems: Indications, advantages, limitations and clinical aspects. Curr Diabetes Rev 2008; 4: 159-68.
28. Joseph JI, Hipszer B, Mraovic B, et al. Clinical need for continuous glucose monitoring in the hospital. J Diabetes Sci Technol 2009; 3: 1309-18.
29. Heinemann L. Glucose Monitoring Study Group. Continuous glucose monitoring by means of the micro-dialysis technique: underlying fundamental aspects. Diabetes Technol Ther. 2003;5(4):545-61
30. Lorencio C, Leal Y, Bonet A, et al. Real-Time Continuous Glucose Monitoring in an Intensive Care Unit: Better Accuracy in Patients with Septic Shock. Diabetes Technology & Therapeutics 2012;4(7):568-75.
31. Holzinger U, Warszawska J, Kitzberger R, et al. Impact of shock requiring norepinephrine on the accuracy and reliability of subcutaneous continuous glucose monitoring. Intensive Care Med 2009;35:1383–89.
32. Price GC, Stevenson K, Walsh TS. Evaluation of a continuous glucose monitor in an unselected general intensive care population. Crit Care Resusc 2008;10:209–16.
33. De Block C, Manuel-Y-Keenoy B, Van Gaal L, et al. Intensive insulin therapy in the intensive care unit. Diabetes Care 2006;29:1750–56.
34. Pfützner J, Forst T, Butzer R, et al. Performance of the continuous glucose monitoring system (CGMs) during the development of ketosis in patients on insulin pump therapy. Diabet Med 2006;23:1124–29.
35. Piper HG, Alexander JL, Shukla A, et al. Real-time continuous glucose monitoring in paediatric patients during and after cardiac surgery. Paediatrics 2006;118:1176–84.
36. Goldberg PA, Siegel MD, Russell RR, et al. Experience with the Continuous Glucose Monitoring system in a medical intensive care unit. Diabetes Technol Ther 2004;6:339–47.
37. Monsod TP, Flanagan DE, Rife F, et al. Do sensor glucose levels accurately predict plasma glucose concentrations during hypoglycaemia and hyperinsulinemia? Diabetes Care 2002;25:889–93.
38. Holzinger U, Warszawska J, Kitzberger R, et al. Real-time continuous glucose monitoring in critically ill patients: A prospective randomized trial. Diabetes Care. 2010; 33: 467-72.
39. Mraz M, Kopecky P, Blaha J, et al. The use of continuous glucose monitoring combined with computer-based eMPC algorithm for tight glucose control in cardio-surgical ICU: a feasibility study. Proc 69th scientific sessions of the American diabetes association, new Orleans, la, 2009.
40. Tonyushkina K, Nichols JH. Glucose meters: a review of technical challenges to obtaining accurate results. J diabetes sci Technol 2009;3:971–80.
41. Rabiee A, Andreasik RN, Abu-Hamdah R, et al. Numerical and clinical accuracy of a continuous glucose monitoring system during intravenous insulin therapy in the surgical and burn intensive care units. J diabetes sci Technol 2009;3:951–59.
42. Klonoff DC, Buckingham B, Christiansen JS, et al. Continuous Glucose Monitoring: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2011;96 (10): 2968–79.
43. Ganesh A, Hipszer B, Loomba N, et al. Evaluation of the VIA Blood Chemistry Monitor for Glucose in Healthy and Diabetic Volunteers. J Diabetes Sci Technol 2008; 2:182-93.
44. Skjaervold NK, Solligard E, Hjelme DR, et al. Continuous measurement of blood glucose: Validation of a new intravascular sensor. Anaesthesiology 2011; 114:120–25.