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BRIEF COMMUNICATION

Artificial Liver, Pancreas

Accuracy and reliability of continuous blood glucose monitoring during pediatric cardiopulmonary bypass

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Abstract

The purpose of this study was to assess the accuracy and reliability of a continuous blood glucose monitoring system (artificial endocrine pancreas; STG-55, Nikkiso, Tokyo, Japan) during pediatric cardiopulmonary bypass surgery. Twenty-five pediatric patients scheduled to undergo cardiovascular surgery with cardiopulmonary bypass (age 4 months to 11 years; body weight 5.6–59.7 kg) were enrolled. The glucose sensor line of the artificial endocrine pancreas was connected to the venous side of the cardiopulmonary bypass circuit and used for continuous blood glucose monitoring. We obtained 192 samples for blood gas assessment from the cardiopulmonary bypass circuit, and i-STAT (Abbott, East Windsor, NJ, USA) was used for conventional blood glucose assessment. The accuracies of continuous glucose measurements (STG-55) and conventional intermittent glucose measurements (i-STAT) during cardiopulmonary bypass were compared by means of Clarke error grid analysis. The results were divided into five zones, A, B, C, D, and E, and 78.6% of paired measurements were in zone A, while 21.4% were in zone B. We confirmed that the results of this continuous blood glucose monitoring system for cardiopulmonary bypass during pediatric cardiovascular surgery were highly reliable. An artificial endocrine pancreas may facilitate the safe use of intensive insulin therapy during pediatric cardiovascular surgery.

Keywords Continuous blood glucose monitoring · Intensive insulin therapy · Artificial endocrine pancreas · Pediatric cardiovascular surgery · Cardiopulmonary bypass

Introduction

Intensive insulin therapy (IIT) may reduce mortality and morbidity in critically ill patients [1, 2]. While the viability of IIT for children has been reported [3], the variations of blood glucose levels during cardiopulmonary bypass (CPB) for children are extensive, making control of the blood glucose level difficult.

The STG-55 (Nikkiso, Tokyo, Japan) is a next-generation artificial endocrine pancreas with a closed-loop glycemic control system that provides continuous blood glucose monitoring through a glucose sensor electrode and automatically administers subsequent insulin and glucose infusions to maintain appropriate blood glucose levels [4, 5]. The purpose of this study was to assess the accuracy and reliability of a continuous blood glucose monitoring and control system (STG-55) during pediatric CPB.

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Materials and methods

This investigation conformed to the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Ethics Committee on Human Studies of Tokushima University Hospital, and written informed consent was obtained from the patients' parents.

Intraoperative management

Twenty-five pediatric patients scheduled to undergo cardiovascular surgery with CPB (three for atrial septal defects, 12 for ventricular septal defects, four for tetralogy of Fallot, and six for other defects; age 4 months to 11 years; body weight 5.6–59.7 kg) were enrolled in the study. There are no surgical patients with type 1 diabetes and/or preoperative glucose intolerance in this study. Standard monitoring included pulse oximetry, electrocardiogram lead II for heart rate and automated ST-segment trend analysis, and end-tidal capnography. General anesthesia was induced using sevoflurane, and cannulas were inserted into a peripheral vein and radial artery. Neuromuscular blocking was obtained by rocuronium. Following tracheal intubation, the lungs were mechanically ventilated with a combination of oxygen and air, and the tidal volume was adjusted to produce normocapnia (end-tidal carbon dioxide between 30 and 40 mmHg). Anesthesia was maintained with sevoflurane, fentanyl, and midazolam.

Equipment

The artificial endocrine pancreas provides continuous blood glucose monitoring through a dual lumen catheter blood sampling technique, high-quality roller pump (multichannel pump), and glucose sensor electrode with a glucose oxidase membrane. After calibration of the equipment, blood was sampled continuously from the peripheral vein at a rate of 2 ml/h and continuously diluted with a heparinized isotonic solution. This blood was further diluted with an isotonic buffer solution of phosphoric acid, pH 7.4, after which the glucose sensor electrode was exposed to the sampled blood. The multichannel pump and glucose sensor electrode were each accurate to within ± 5%. The STG-55 device is equipped with a disposable and modular tubing circuit with an auto-priming function and a sensor set-up with automatic calibration and quick response time, and has a compact structure. It has been specifically modified to comply with surgical and intensive-care unit (ICU) requirements (Fig. 1).

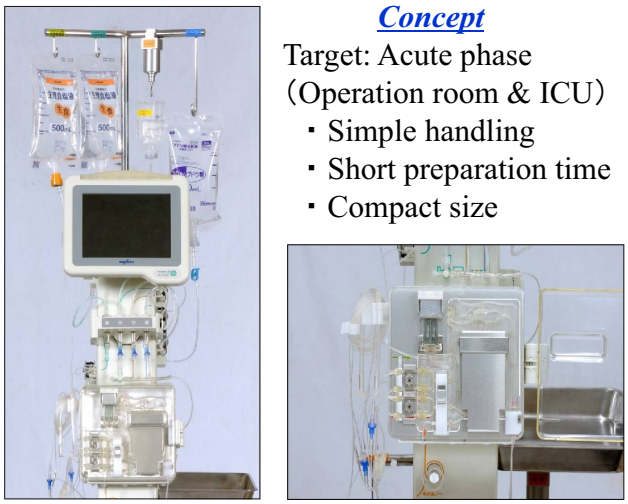

Fig. 1 The newly developed next-generation artificial endocrine pancreas (STG-55, Nikkiso Co., Ltd., Tokyo, Japan)—a bedside-type artificial endocrine pancreas with a closed-loop system. The STG-55 is equipped with a disposable and modular tubing circuit with an auto-priming function, automatic calibration with quick response in the sensor set-up, and a compact structure

For this study, we used this device only for glucose monitoring purposes.

Data collection

We developed a novel blood sampling method, utilizing an artificial endocrine pancreas via the cardiopulmonary bypass circuit [6]. The glucose sensor line of the artificial endocrine pancreas (STG-55) was connected to the venous side of the CPB circuit and used for continuous blood glucose monitoring. The blood glucose determination was carried out approximately once every 30 min, to ensure a stable condition. We obtained 192 samples for blood gas assessment from the CPB circuit. An i-STAT (Abbott, East Windsor, NJ, USA) was used for conventional blood glucose assessment.

Statistical analysis

The accuracies of continuous glucose measurements (STG-55) and conventional intermittent glucose measurements (i-STAT) during CPB were compared by Clarke error grid analysis [7]. The results were divided into five zones: A, B, C, D, and E. Values in zones A and B represent accurate or acceptable glucose results. Values in zone C may prompt unnecessary corrections, leading to poor outcomes. Values in zone D represent a dangerous failure to detect and treat. Values in zone E represent 'erroneous treatment.' In short, the more values that appear in zones

A and B, the more accurate the device is in terms of clinical utility.

Results

Blood sampling via the venous side of the CPB circuit showed that continuous blood glucose monitoring was stable and reliable even during pediatric CPB. Continuous monitoring enhances awareness of typical changes in blood glucose levels during cardiovascular surgery for children. There were no complications related to use of the STG-55. A good correlation between blood glucose measured by i-STAT and that measured by STG-55 were indicated. In the Clarke error grid, 78.6% of paired measurements were in zone A, while 21.4% were in zone B; 100% of paired measurements were in the clinically acceptable zones, A and B (Fig. 2).

Discussion

Our study is the first to assess the accuracy and reliability of continuous blood glucose monitoring (artificial endocrine pancreas: STG-55) during cardiovascular surgery for pediatric patients. Continuous blood glucose monitoring during CPB for pediatric cardiovascular surgery was remarkably reliable. In the Clarke error grid, 100% of paired measurements were in the clinically acceptable zones, A and B. There were no complications related to use of the STG-55. This artificial endocrine pancreas is currently the only continuous blood glucose monitoring device in the world. An artificial endocrine pancreas can facilitate the safe use of IIT during pediatric cardiovascular surgery.

Many studies have shown an association between hyperglycemia and adverse outcomes of critical illnesses, in both adult [8] and pediatric patients [9]. Variability in blood glucose concentrations and hypoglycemia are also associated with adverse outcomes [10]. Hyperglycemia occurs frequently in patients with and without diabetes during cardiovascular surgery, especially during CPB. However, glucose control is difficult to achieve during cardiovascular procedures that require CPB because of the stresses of surgery, including anesthesia, cardioplegia, and inotropic support [11].

There is limited information on glucose control in pediatric cardiac surgery patients. Yates et al. [12] performed a single-center retrospective study comprising 184 patients less than 1 year of age who underwent cardiac surgery requiring CPB. The mortality of their cohort was 11.3%. They found that hyperglycemia in the postoperative period was associated with increased morbidity and mortality in pediatric cardiac patients.

Van den Berghe et al. also reported a pediatric study [3]. IIT reduced the duration of pediatric ICU stay and, more specifically, the need for extended intensive care. However, hypoglycemia occurred in 87 (25%) patients in the intensive insulin group (70 infants and 17 children), and in 5 (1%) in the conventional group (3 infants and 2 children). Children are particularly susceptible to hypoglycemia due to their higher blood glucose metabolism, and can easily become dehydration. Conventionally, the risk of hypoglycemia has been particularly emphasized for children. They mentioned that an accurate continuous blood glucose sensor for use in the pediatric ICU, which was not available when they undertook their study, would help to minimize the risk of hypoglycemia. We believe that continuous blood glucose monitoring is also essential for strict glycemic control during pediatric cardiovascular surgery, although minimal data are available from intraoperative pediatric cardiac patients.

The next-generation artificial endocrine pancreas (STG-55), equipped with a disposable and modular tubing circuit with an auto-priming function, automatic calibration with

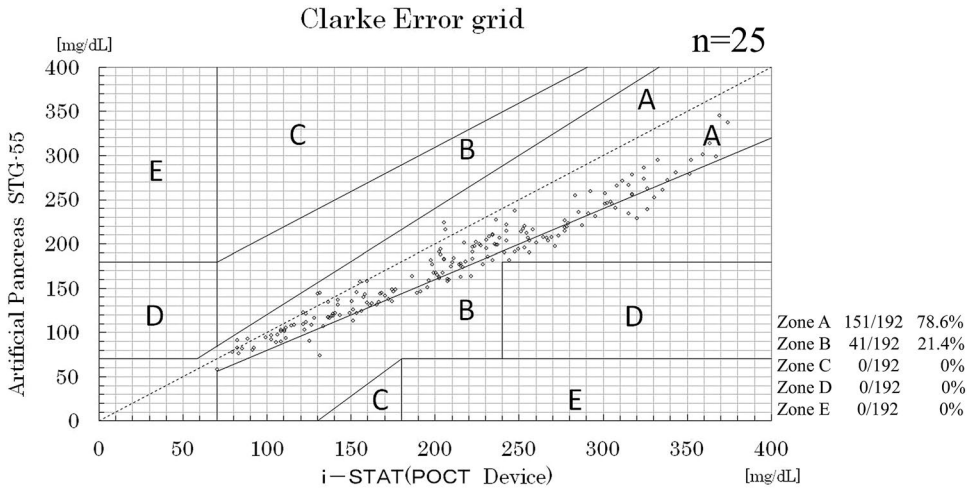

Fig. 2 Clarke error grid analysis for the evaluation of blood glucose measured by STG-55 compared with measurements by i-STAT during pediatric cardiopulmonary bypass

quick response in sensor set-up and a compact structure, was developed with the aim of improved usability. Clinical evaluations using STG-55 indicated stable and safe glycemic control within the target blood glucose range [4, 5]. We are using this device for patients with unstable intraoperative blood glucose control, including diabetic patients and those with insulinoma, or those who had undergone a total pancreatectomy or liver transplantation, hepatectomy, other than cardiovascular surgery. We believe that this novel artificial pancreas (STG-55) will become a standard modality to achieve glycemic control in patients who need strict and safe glycemic control.

The causes of insufficient blood drawing during CPB include hypothermia, peripheral circulatory failure (low perfusion), vasoconstriction, and posture (especially with arms elevated or bent) [11]. This potential problem was solved by sampling blood via the venous side of the CPB circuit [6], rendering the continuous blood glucose monitoring stable and reliable even during cardiovascular surgery with CPB.

Our study had several limitations. First, the sample size was small. Second, we used blood glucose values measured by i-STAT point-of-care analyser not those measured by central laboratory. However, the high precision of the blood glucose determination of i-STAT has been already reported [13]. Third, the STG-55 is a blood glucose control device by intravenous insulin or glucose infusion based on the continuous venous blood glucose measurements and not a device only for continuous blood glucose monitoring. For this study, we used this device only for glucose monitoring purposes, because there is not sufficient evidence to indicate that the advantage of controlling blood glucose level outweighs the risks of accidental hypoglycemia in pediatric patients. Highly precise continuous blood glucose monitoring is essential for strict glycemic control during cardiovascular surgery. Our study confirmed that this method is useful for pediatric patients. Our final goal is the establishment of a new superior perioperative blood glucose control method using an artificial endocrine pancreas during pediatric cardiovascular surgery.

Conclusion

There were no complications related to use of the STG-55 (for blood glucose monitoring) and a good correlation between blood glucose measured by i-STAT and that measured by STG-55 was indicated. In the Clark error grid, 100% of paired measurements were in the clinically acceptable zones, A and B.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R. Intensive insulin therapy in the critically ill patients. N Engl J Med. 2001;345:1359–67.
2. Van den Berghe G, Wilmer A, Milants I, Wouters PJ, Bouckaert B, Bruyninckx F, Bouillon R, Schetz M. Intensive insulin therapy in mixed medical/surgical intensive care units: benefit versus harm. Diabetes. 2006;55:3151–9.
3. Vlasselaers D, Milants I, Desmet L, Wouters PJ, Vanhorebeek I, van den Heuvel I, Mesotten D, Casaer MP, Meyfroidt G, Ingels C, Muller J, Van Cromphaut S, Schetz M, Van den Berghe G. Intensive insulin therapy for patients in paediatric intensive care: a prospective, randomized controlled study. Lancet. 2009;373:547–56.
4. Tsukamoto Y, Kinoshita Y, Kitagawa H, Munekage M, Munekage E, Takezaki Y, Yatabe T, Yamashita K, Yamazaki R, Okabayashi T, Tarumi M, Kobayashi M, Mishina S, Hanazaki K. Evaluation of a novel artificial pancreas: closed loop glycemic control system with continuous blood glucose monitoring. Artif Organ. 2013;37:E67–73.
5. Mita N, Kawahito S, Soga T, Takaishi K, Kitahata H, Matsuhisa M, Shimada M, Kinoshita H, Tsutsumi YM, Tanaka K. Strict blood glucose control by an artificial endocrine pancreas during hepatectomy may prevent postoperative acute kidney injury. J Artif Organ. 2017;20:76–83.
6. Kawahito S, Higuchi S, Mita N, Kitagawa T, Kitahata H. Novel blood sampling method of an artificial endocrine pancreas via the cardiopulmonary bypass circuit. J Artif Organ. 2013;16:508–9.
7. Clarke WL, Cox D, Gonder-Frederick LA, Carter W, Pohl SL. Evaluating clinical accuracy of systems for self-monitoring of blood glucose. Diabetes Care. 1987;10:622–8.
8. Kawahito S, Kitahata H, Oshita S. Problems associated with glucose toxicity: role of hyperglycemia-induced oxidative stress. World J Gastroenterol. 2009;15:4137–42.
9. Faustino EV, Apkon M. Persistent hyperglycemia in critically ill children. J Pediatr. 2005;146:30–4.
10. Wintergerst KA, Buckingham B, Gandrud L, Wong BJ, Kache S, Wilson DM. Association of hypoglycemia, hyperglycemia, and glucose variability with morbidity and death in the pediatric intensive care unit. Pediatrics. 2006;118:173–9.
11. Kawahito S, Kitahata H, Kitagawa T, Oshita S. Intensive insulin therapy during cardiovascular surgery. J Med Invest. 2010;57:191–204.
12. Yates AR, Dyke PC 2nd, Taeed R, Hoffman TM, Hayes J, Feltes TF, Cua CL. Hyperglycemia is a marker for poor outcome in the postoperative pediatric cardiac patient. Pediatr Crit Care Med. 2006;7:351–5.
13. Oyaert M, Van Maerken T, Bridts S, Van Loon S, Laverge H, Stove V. Analytical and pre-analytical performance characteristics of a novel cartridge-type blood gas analyzer for point-of care and laboratory testing. Clin Biochem. 2018;53:116–26.