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An insulin-dose error assessment grid: A new tool to evaluate glucose meter performance

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ABSTRACT

Objective: To develop a tool to assess the clinical accuracy of glucose meter performance using an insulin dosing protocol to assess the frequency and extent of error in insulin dose categories.
Methods: Retrospective comparison of 1815 glucose meter and central laboratory glucose results obtained from 1698 critically ill patients was conducted using the Parkes error grid, Surveillance error grid and an insulin dose error assessment grid with a sliding scale insulin dosing protocol used to manage critically ill patients.
Results: Parkes error grid and Surveillance error grid analyses indicated little risk conferred with the glucose meter results. Insulin dose error assessment grid complemented the aforementioned consensus error grids by determining quantifiable metrics, insulin dose category errors. Insulin dose error analysis indicated that 76.8% (1395/1815) would not have any change in insulin dose, 99.2% (1800/1815) within ± 1 insulin dose category, 99.9% (1814/1815) within ± 2 categories and 100% within ± 3 insulin dose categories.
Conclusions: Analysis with an insulin dose error grid provides information about the frequency and extent of insulin dose category errors with a specific insulin dosing protocol and describes potential clinical impact of glucose meter error.

1. Introduction

The performance and reliability of blood glucose meters is assessed by determining precision, bias relative to a reference method and susceptibility to interference by hematocrit, pharmaceuticals, biomaterials or biochemicals. The statistical and analytic performance characteristics of glucose meters have been translated into clinical qualities such as clinical accuracy or medical risk using error grids or contour plots [1,2]. Clinical accuracy is a term used to describe clinical treatment decisions based on test results which can ultimately affect clinical outcome [1]. The importance of assessing clinical accuracy is not trivial. With respect to glucose, it represents a spectrum of activity from optimizing patient care through changes in insulin dose to minimizing hypoglycemic episodes and avoiding life threatening events. Insulin administration protocols continue to change and have involved sliding insulin scale (subcutaneous or continuous infusion) and basal-bolus infusion that are all affected by blood glucose measurement. Error grids are visual representations of the difference in results between two analytical methods and the potential effect of this difference on clinical decision making. The Parkes error grid and Surveillance error grid are expert opinion based guides that were developed to assess post-market clinical risk with glucose meter use [3,4]. Those error grids are convenient tools to use and are designed to accommodate data from all patient populations into common sets of interpretations. In addition to using those expert consensus-based error grids, it would be useful to assess glucose performance in specific patient populations, such as critically ill patients that are managed with distinct glycemic control protocols. The aim of this study was to develop and describe a tool that is a new error grid for glucose meter assessment that depicts the frequency and extent of insulin-dose category errors attributed to glucose meter analytic performance among critically ill patients.

2. Materials and methods

2.1. Study design

Retrospective comparison of 1815 pairs of glucose meter results Statstrip® (Nova Biomedical, Waltham, MA, USA) and central

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laboratory glucose method results from 1698 critically ill patients were analyzed with the Parkes error grid (PEG), Surveillance error grid (SEG) and an insulin dose error assessment (IDEA) error grid. The central lab methods assessed plasma glucose by a hexokinase method on a cobas modular P800 (Roche Diagnostics, Indianapolis, IN) and a glucose oxidase method on a UniCel Synchron DxC (Beckman Coulter, Brea, CA). Data was collected from medical, surgical and burn intensive care units at five international clinical sites (Netherlands, Belgium and United States) with institutional ethics approval previously described [5]. Blood samples for both the laboratory and meter methods were collected from central lines.

2.2. Parkes error grid analysis

The PEG displaying the 1815 paired glucose results was constructed according to the recommendations outlined by Pfützner et al for Type 1 diabetes [7] and previously reported by DuBois et al, [5].

2.3. Surveillance error grid analysis

The SEG analysis was conducted using the Excel macro program available through the Diabetes Technology Society website (www.diabetestechnology.org/SEGsoftware) [4,8].

2.4. Insulin dose error assessment (IDEA) grid analysis

Glycemic control among critically ill patients is often guided by an institutional protocol that provides a sliding or dynamic scale of insulin dose in response to measurement of blood glucose. For the purpose of this report, the sliding scale insulin dose protocol reported by Karon et al, [6] was used for the construction of the IDEA error grid. Fig. 1 depicts the frequencies of 1815 pairs of glucose values observed by the reference method and glucose meter in each insulin-dose-category.

Fig. 2 was created to depict if differences in reference method glucose and meter glucose were associated with differences in insulin treatment. The IDEA grid plot consists of the reference method glucose on an ordinal axis and the meter glucose on the abscissa with an overlaid shaded grid determined by the insulin-dose-categories in the protocol. When the reference method and glucose meter values coincide within the same interval for determination of the insulin dose (within the protocol), there is no insulin dose error. This is shown by the white shaded diagonal line of equivalence in Fig. 2, '0' insulin dose category errors. When a glucose meter value exceeds the reference method glucose by one (or more) insulin dose categories, the error of the glucose meter is +1 (or more) insulin dose category and the position of the insulin dose error is indicated on the grid with red shading. When a glucose meter value is less than the reference method glucose by one (or more) insulin dose categories, the error of the glucose meter is −1 (or more) insulin dose category and the position of the insulin dose error is indicated on the grid with blue shading. The frequencies of observed pairs of glucose values on the error grid were counted and represented in histograms.

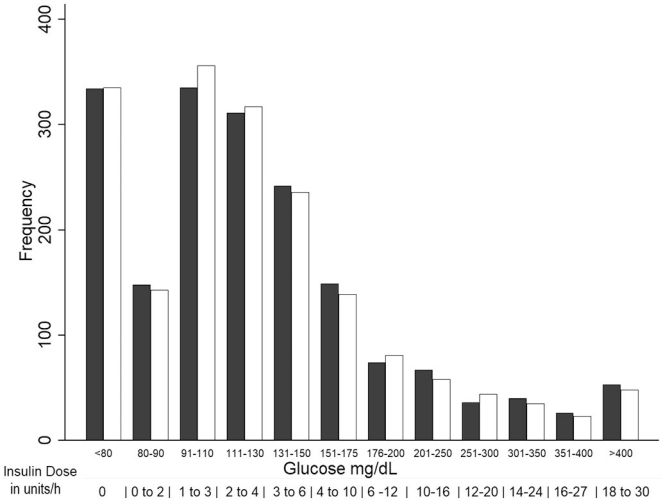

Fig. 1. Frequency histogram of observed glucose values and the insulin dose protocol used for critical care adult patients ($n = 1815$). The black bars represent the frequency of reference method glucose and white bars represent the frequency of glucose meter values in mg/dL. The sliding scale of insulin dose in units/h by glucose concentration is indicated under the ordinal axis. Pairs of patient glucose results from the reference method and meter method may fall into different insulin dose categories.

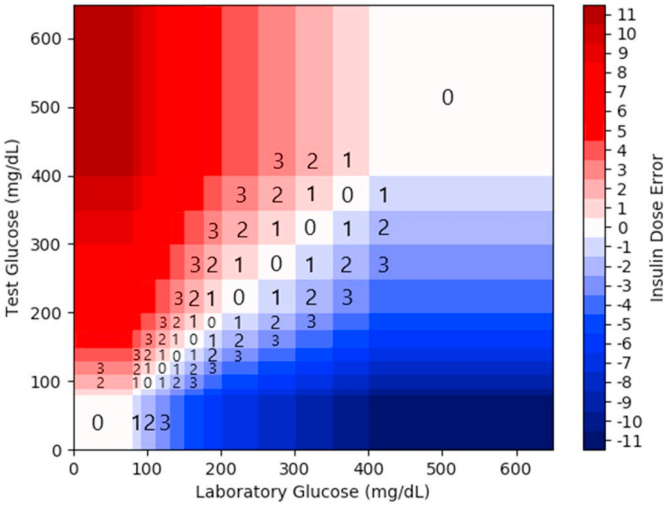

Fig. 2. An insulin dose error assessment grid example. The axes indicate the reference laboratory glucose concentration and the test method glucose concentration. An insulin dose protocol for a patient population under evaluation is used to establish the shaded grid pattern that indicates the number of insulin dose category errors between the two glucose methods.

3. Results

To assess the potential risk with using a glucose meter, different error grid methods were compared with the same dataset of glucose values. A frequency distribution of the patient glucose meter and reference laboratory data along with the insulin dose protocol is shown in Fig. 1.

3.1. Parkes error grid analysis

PEG analysis of the 1815 glucose results from 1698 critical patients was previously published and found 99.3% of the results were in Zone A (clinically accurate, no effect on clinical action) and the remaining 0.7% in Zone B (altered clinical action, little or no effect on clinical outcome) [5]. Table 1 summarizes the distribution of these data according to the zones identified by the Parkes error grid. The reportable range for the Parkes error grid is up to glucose concentrations of 600 mg/dL.

3.2. Clinical laboratory standards institute POCT12-A3

The criteria of POCT12-A3 were applied to the 1815 pairs of glucose results. The glucose results met all criteria (Table 1A electronic data supplement) and the distribution of paired results is shown in Fig. 2A (electronic data supplement).

Table 1
Comparison of the clinical risk denoted by the PEG, the SEG, CLSI POCT12-A3 and the IDEA error grid for the dataset (n = 1815) of critical care patients. The PEG has Zone A (no risk), Zone B (altered clinical action, no or benign treatment), Zone C (altered clinical action, likely to affect clinical outcome), Zone D (altered clinical action, could have significant medical risk), Zone E (altered clinical action, could have dangerous consequences), (11). The SEG has zones of no risk, slight risk, moderate risk, great risk and extreme risk, (12). The CLSI POCT12-A3 criteria were used to indicate the fraction of results that met the criteria. The IDEA error grid has a zone of no change in insulin dose, and errors of +1, +2 and + 3 insulin dose category errors, and − 1, −2 and − 3 errors.

Error grid		Risk classification						
Parkes	Zone D	Zone C	Zone B	Zone A	Zone B	Zone C	Zone D	Zone E
	0	0	10	1802	3	0	0	0
Surveillance	Great	Moderate	Slight	None	Slight	Moderate	Great	Extreme
	0	0	41	1755	1	0	0	0
Insulin dose error	−3	−2	−1	0	1	2	3	
	1	12	257	1395	148	2	0	

3.3. Surveillance error grid analysis

This grid differs from the Parkes grid in that 15 color coded zones, dark green to brown, were developed with associated levels of risk. The reportable range for the Surveillance error grid is 20 to 600 mg/dL which resulted in the analysis of 1798 of the 1815 data points (99.1%). Fig. A1 (electronic data supplement) illustrates the results displayed on the Surveillance error grid. Ninety seven point 6% (1755/1798) were located in the green zone that indicated no clinical risk. The light green zone contained 2.3% (41/1798) that denoted slight low risk and 0.1% (2/1798) were detected in the yellow zone which signified slight high risk. The PEG and SEG were designed as flexible tools to evaluate patient risk in many clinical situations. The PEG and SEG consistently indicated very little risk conferred by using this glucose meter summarized in Table 1 and this was also supported by evaluation with the CLSI POCT12-A3 criteria (Table 1A electronic data supplement).

3.4. Insulin dose error assessment grid analysis

Patient data were overlaid on the IDEA grid illustrated in Fig. 3 to assess the clinical impact of glucose error. The data points that fell into the white or unshaded squares on the grid indicate no change in insulin dose, according to the protocol. Several data points fell out of the white squares and this is summarized in a frequency distribution of insulin dose category errors in Fig. 3A panel A (electronic data supplement).

Fig. 3 indicates that 76.8% (1395/1815) would not have any change in insulin dose. 99.2% (1800/1815) within ± 1 insulin dose category, 99.9% (1814/1815) within ± 2 categories and 100% within ± 3 insulin dose categories. The frequency histogram in Fig. 3A-Panel 1 (data supplement) provides a graphic summary of these observations. Information about the frequency and extent of errors in insulin dose categories is clinically useful, intuitive to interpret and specifically relates to the insulin protocol and patient population under study. Previous studies have offered interpretations that errors of one or two insulin dose categories have low clinical risk but error of three or more insulin dose categories have risk [2,6].

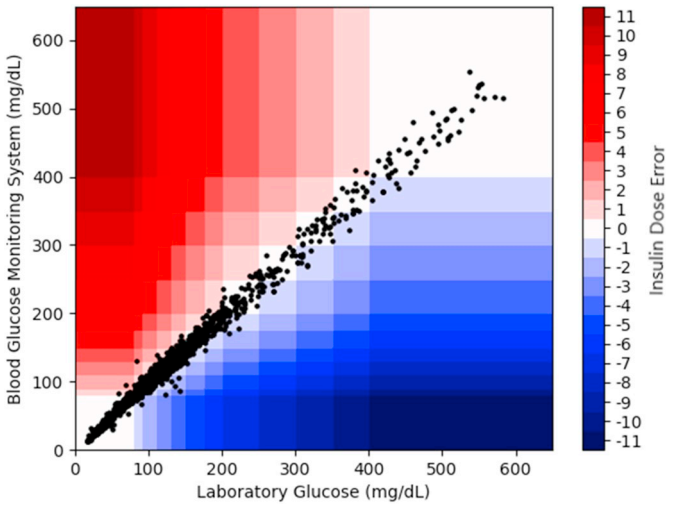

Fig. 3. IDEA error grid analysis: Patient glucose data (n = 1815) plotted on the error grid. The red shaded squares indicate anticipated excess insulin administration measured as positive insulin dose category errors. The blue shaded squares indicate anticipated under administration of insulin measured as negative insulin dose category errors. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

To illustrate the complementary utility of the PEG, SEG and IDEA grids, summary data is listed in Table 1. All three data grids show there was little risk with this dataset. The PEG and SEG grids had a similar distribution (> 99%) of data predominantly in the no risk zone. The utility of the insulin-dose error grid tool was further assessed by adding 5% additional random error or a 5% fixed bias to each value glucose meter results as described by Boyd et al [2] and the frequency and extent of errors in insulin protocol were plotted (Fig. 3A panels B and C).

4. Discussion

The aim of this study was to develop a tool to assess the clinical accuracy of glucose meter performance using an institutional insulin dosing protocol to assess the frequency and extent of error in insulin dose categories. In addition to using the expert consensus supported PEG and SEG error grids, the evaluation of glucose meters with an additional error grid that enables the detection of a quantifiable metric such as insulin dosing category differences could be beneficial for specific patient populations like the critically ill patients with distinct glycemic control protocols.

In 1994, Parkes et al., surveyed 100 diabetic expert physicians and subsequently developed two separate error grids for type 1 diabetic patients and type 2 diabetic patients receiving insulin [3]. Later, the use of the type 1 grid was preferred and the type 2 grid became obsolete. The Parkes error grid identifies five zones, A through E, based on the extent of analytic differences between two glucose methods. Glucose results in zones A and B were associated with the least clinical risk whereas results in zones C, D and E represented increasing clinical consequences. When this grid was published, it was necessary for glucose meters to perform within 20% of the comparative glucose method for results to be situated in zone A. Significant technological advances have occurred in glucose meter design and development since 1994 which have resulted in meaningful improvement in the analytical performance of glucose meters. In 2014, the Surveillance error grid was established in response to a survey of 206 diabetes expert physicians [4]. The SEG differs from the PEG in that 15 color coded zones were developed with associated levels of clinical risk. These zones were applied to all patient subgroups and specimen types which was an improvement from the PEG.

In this study, we developed an error grid to assess risk by describing

glucose measurement error in terms of the size and frequency of insulin dosage error in a model with a sliding scale of continuous insulin infusion. Boyd and Bruns used an insulin dose error approach to theoretically estimate the influence of glucose meter bias and imprecision on the clinical risk [2]. Karon et al applied the Boyd and Bruns approach to investigate how glucose meter error could influence insulin dosing errors with a tight glycemic control protocol for intensive care patients [6]. Specific institutional insulin dosing protocols (*e.g.* sliding or dynamic) have been established to support moderate and tight glycemic protocols. The current version of the IDEA grid readily accommodates sliding scale dosing protocols. Karon et al [6] reported that insulin dose errors of one category were very common with combinations of glucose method bias up to ± 20% and imprecision up to 20%. The clinical risk associated with ≥3 insulin dosing error was considered substantial and signified a significant risk of a harmful hypoglycemic event. In contrast to sliding scales of insulin infusion, use of basal-bolus insulin administration protocols are anticipated to be less sensitive to glucose error, but this has not yet been formally studied by simulation.

The error grid based on insulin dose errors depicted in Fig. 3 is specific for the insulin dose protocol used in this report and complements general interpretations provided by the PEG and SEG. As summarized in Tables 1, 2 of 1815 (0.1%) of the glucose meter results would have resulted in administration of excessive insulin (+2 insulin dose categories). It was also shown that 13 glucose meter results would have resulted in insufficient insulin administration: 12 of 1815 (0.7%) glucose meter results would have resulted in errors of −2 insulin dose categories, and 1 result (0.06%) occurred with −3 category insulin dose category errors. Among critical care patients, withholding insulin administration represents less clinical risk than inappropriately administering too much insulin and causing hypoglycemia. The PEG and SEG interpretations of little clinical risk are consistent with the information provided by an insulin dose error grid and the information of the frequency and extent of insulin dose category errors can supplement the assessment of glucose meter performance achievable with PEG and SEG error grids. An advantage and limitation of the IDEA grid is that the size and frequency of insulin dose category errors is dependent on the insulin dose protocol used, so it is difficult to compare the frequency and size of insulin dose errors generated with different insulin dose protocols.

In conclusion, the IDEA grid is a clinical accuracy tool that describes differences in glucose measurement in terms of insulin dosing error category. Information obtained with the IDEA grid complements glucose meter performance interpretations provided by the PEG, CLSI POCT12-A3 and SEG.

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