Effects of two different levels of computerized decision support on blood glucose regulation in critically ill patients

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\textbf{Abstract}

Introduction: Although the use of computerized decision support systems (CDSS) in glucose control in the ICU has been reported, little is known about the effect of the systems' operating modes on the quality of glucose control. The objective of this study was to evaluate the effect of providing patient-specific and patient non-specific computerized advice on timing of blood glucose level (BGL) measurements. Our hypothesis was that both levels of support would be effective for improving the quality of glucose regulation and safety, with patient specific advice being the most effective strategy.

Patients and methods: A prospective study was performed in a 30-bed mixed medical-surgical intensive care unit (ICU) of a university hospital. In phase 1 the CDSS provided non-specific advice and thereafter, in phase 2, the system provided specific advice on timing of BGL measurements. The primary outcome measure was delay in BGL measurements before and after the two levels of support. Secondary endpoints were sampling frequency, mean BGL, BGL within pre-defined targets, time to capture target, incidences of severe hypoglycemia and hyperglycemia. These indicators were analyzed over the course of time using Statistical Control Charts. The analysis was restricted to patients with at least two blood glucose measurements.

Results: Data of 3934 patient admissions were evaluated, which corresponded to 119,116 BGL measurements. The BGL sampling interval, delays in BG sampling, and percentage of hypoglycemia all decreased after introducing either of the two levels of decision support. The effect was however larger for the patient specific CDSS. Mean BGL, time to capture target, hyperglycemia index, percentage of hyperglycemia events and “in range” measurements remained unchanged and stable after introducing both patient non-specific and patient specific decision support.
1. Introduction

Studies have shown that critically ill patients could benefit from blood glucose regulation during their stay in the intensive care unit (ICU) [1,2]. Recent studies have shown that frequent and timely BGL measurements improved the quality and safety of blood glucose regulation [3,4]. Continuous blood glucose monitoring would have provided timely measurement of blood glucose, but devices to do this are expensive and are not commonly available yet.

Clinical computerized decision support systems (CDSS) can be computer programs that are intended to help healthcare workers in making decisions [5]. A CDSS can be characterized by the level of support. The level of decision support varies from non-patient specific (general support) to patient specific support. For the purpose of this study, non-patient specific CDSS is defined as showing the protocol without interpreting the patient’s data. On the other hand, patient specific CDSS refers to making a conclusion or giving advice after interpreting the patient’s data. The difference between the effects of these levels of support has not been studied yet, at least not in this domain.

ICU staff increasingly use patient data management systems (PDMS) allowing them to access data, but these systems often do not provide active support for making decisions. Based on the literature and our recent systematic reviews [6,7] we hypothesized that both levels of support, patient non-specific as well as patient specific, would increase the adherence to protocol sampling rules in terms of reducing blood glucose sampling delays, and that the patient specific support would give better results. The underlying idea is that improving adherence to the protocol leads to improving quality and safety of glucose regulation. The purpose of this study was to test this hypothesis and measure the effect of the two different levels of support, patient non-specific and patient specific support, embedded in a PDMS, on adherence to sampling rules of a locally developed glucose regulation protocol.

2. Methods

2.1. Study location

Collection of data was prospectively performed in a 30-bed “closed-format” mixed medical-surgical ICU of an academic hospital in the Netherlands. For each patient there was one ICU nurse who stayed near to the patient bed. The ICU uses a patient data management system (PDMS) (Metavision, IMDsoft Sassenheim, the Netherlands) since March 2002. There is a bedside computer available for each bed. The ICU teams used the PDMS to complete all patient charting and documentation such that no information had paper as its primary storage mechanism. The laboratory computer interface conveyed BGL measurement results to the PDMS. Consequently, the PDMS processes and displays all values directly after their measurement with a maximum delay of 1 min, introduced by the interface.

2.2. Local glucose control protocols

Table 1 shows the protocol’s characteristics. According to the protocol when the latest BGL is in the normal range it should be rechecked after 4 h. When the latest BGL is out of the pre-defined range it should be generally rechecked after 1 h. When the latest BGL is in a hypoglycemic range it should be rechecked after 30 min.

2.3. Measurement of BGL

Arterial blood samples were used for BGL measurements. These measurements were obtained by blood gas analyzers (Rapidlab 865®, Bayer, Germany) in the ICU and a glucose analyzer (Modular P800® system, Roche Diagnostics GmbH, Germany) in the hospital’s central laboratory.

2.4. Patients

A local ICU database identified all patients admitted to the ICU. The hospital information system and PDMS were searched for

<table>
<thead>
<tr>
<th>Table 1 – Protocol characteristics.</th>
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<tbody>
<tr>
<td><strong>Type of protocol</strong></td>
</tr>
<tr>
<td><strong>Present in what form</strong></td>
</tr>
<tr>
<td><strong>Who is responsible for glucose control</strong></td>
</tr>
<tr>
<td><strong>Start of insulin</strong></td>
</tr>
<tr>
<td><strong>Dosing of insulin</strong></td>
</tr>
<tr>
<td><strong>Correction of hypoglycemia</strong></td>
</tr>
<tr>
<td><strong>Protocol thresholds and targets</strong></td>
</tr>
<tr>
<td><strong>Start of insulin (mg/dL)</strong></td>
</tr>
<tr>
<td><strong>BGL targets (mg/dL)</strong></td>
</tr>
<tr>
<td><strong>Timing of BGL-measurements</strong></td>
</tr>
<tr>
<td><strong>described in or mandated by the protocol</strong></td>
</tr>
<tr>
<td><strong>Rules on stopping insulin</strong></td>
</tr>
<tr>
<td><strong>Threshold to stop insulin infusion</strong></td>
</tr>
<tr>
<td><strong>Other reason for stopping insulin</strong></td>
</tr>
<tr>
<td><strong>Action in case of hypoglycemia</strong></td>
</tr>
<tr>
<td><strong>BGL &lt;40 mg/dL</strong></td>
</tr>
</tbody>
</table>

The term “sliding scale” here refers to a dynamic protocol for intravenous insulin infusion. The protocol is self-regulating, therefore it does not consider baseline glucose value nor condition (e.g., diabetes).
all records on BGL. The first BGL measured directly after ICU admittance was excluded from the final analysis for further calculation, because they are hardly influenced by any ICU regimen. Admitted patients who had in total more than two BGL measurements, including admission BGL, were included in the final analysis.

2.5. Intervention

The intervention was carried out in three phases.

The glucose regulation protocol was implemented in early 2002 and was last revised in 2005 [8]. This nurse-driven protocol was in use and available on both paper and the hospital intranet in 2002. In phase 0 in this study the glucose control protocol was still only available on paper and the hospital intranet. In this phase, lasting for 8 months, we prospectively collected the data that formed the baseline for the consequent phases.

In phase 1 of the study a patient non-specific CDSS was used for 8 months. Every 5 min the system checked for new BGL measurements. Only when there was a new BGL measurement the CDSS showed a snapshot of the protocol in a pop-up window. This non-specific reminder appeared only if the ICU nurse was logged in at the bedside computer and worked in the PDMS. The pop-up window showed the whole BGL protocol including the general timing and pump position advice.

In phase 2, with duration of 10 months, the CDSS also checked for new BGL measurements every 5 min. When a new BGL measurement was encountered the CDSS calculated the time for the next measurement according to the protocol and the patient’s former BGLs. The time for the next expected measurement was then recorded in a database. The CDSS gave a reminder about 10 min before the next expected measurement was due. The pop-up window showed the planned time of measurement and reminded the ICU nurse to measure the BGL and to follow the protocol. The system showed a message only if the expected BGL was not timely performed and only if the ICU nurse was logged in at the bedside computer and worked with the PDMS.

2.6. Outcome measures

Delay in blood glucose monitoring was the primary outcome measure. Other common performance indicators were selected as secondary outcome measures to show the quality of glucose regulation [9]. These indicators are described in Table 2.

2.7. Statistical process control (SPC)

SPC uses statistical methods to identify periods of time during which a process goes from “in control” to “out of control.” SPC and its primary tool – the control chart – are a branch of statistics that combines rigorous time series analysis methods with graphical data presentation, often yielding insights into the data more quickly and in a more understandable way than other statistical techniques [10]. Control charts can distinguish between common and special causes of variation [11]. With common cause variation (noise), the variation is inherent in the process itself and the process is stable and predictable within certain limits. Special cause variation signifies that the process is no longer stable or predictable and has changed (either for better or worse) [12]. A control chart includes a plot of the data over time with three additional lines – the center line (usually reflecting the mean) and an upper and lower control limits, typically set at ±3 sigma from the mean. When the data points are, without any special pattern, within the control limits then the process is “in control” and stable. There are several rules that indicate when a special cause variation or a special pattern has occurred on a control chart. We used the following four widely used rules to identify a special cause variation: one or more points beyond a control limit, a run of seven or more points on one side of the center line, two out of three consecutive points appearing beyond 2 sigma on the same side of the center line, or a run of seven or more points all trending up or down.

2.8. Power analysis

Previous studies have shown that CDSS could reduce delay in measurement by about 50% [13]. Power analysis showed that at least 2000 BGL measurements were needed to demonstrate an absolute difference of 25% in delay time between baseline and the most effective intervention, with an alpha of 0.05 and beta of 0.8. Retrospective data analysis showed that at least 2 weeks of data would be needed to meet these requirements.

Table 2 – Outcome measures description.

<table>
<thead>
<tr>
<th>Outcome measures description</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol related indicators (primary outcome measures)</td>
<td></td>
</tr>
<tr>
<td>Sampling frequency</td>
<td>Represented as the mean sampling interval</td>
</tr>
<tr>
<td>Delay in blood glucose monitoring</td>
<td>Represented as the mean delay time. When the next measurement was done earlier than 10 min before the scheduled time, delay time was considered – 10</td>
</tr>
<tr>
<td>Safety-related indicators</td>
<td></td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Reported as percentage of overall BGL measurements ≤40 mg/dl (severe) and ≤63 mg/dl (moderate) and as percentage of patients with at least 1 episode of (severe) hypoglycemia. After a hypoglycemic event, to classify a subsequent BGL measurement as starting a new hypoglycemic event we require that the BGL first increase into the normal range and then drop again below the hypoglycemia threshold in a subsequent hour</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Defined as BGL &gt; 144 mg/dl, and severe hyperglycemia as BGL &gt; 180 mg/dl. These are reported as the percentage of overall BGL measurements above the given threshold</td>
</tr>
<tr>
<td>Hyperglycemia index</td>
<td>The area between the BGL curve and the 144 mg/dl (hyperglycemia) threshold divided by time. We report on the mean of this value per patient</td>
</tr>
<tr>
<td>Effectiveness/efficiency-related indicators</td>
<td></td>
</tr>
<tr>
<td>Mean BGL</td>
<td>The overall mean BGL during a defined time interval (more focus on efficiency can be obtained by shortening the interval)</td>
</tr>
</tbody>
</table>
2.9. Statistical analysis

We used the X-MR control chart [11] to plot and analyze the processes. We used the X-MR chart instead of attribute charts [14,15] due to the large subgroup size and hence the increased chance of false positive results. The quality indicators that we choose (each represents either a mean or a proportion) were calculated per month and plotted as points on the X-MR chart. The mean of the points before glucose control implementation was calculated along with the ±3 sigma limits. To determine whether a change in the process occurs further along the time axis, the mean and control limits, as calculated based on the 8 months of phase 0, were extrapolated over the entire study period. The ANOVA, Kruskal–Wallis and Chi square tests were used to assess the statistical significance of differences among pre- and post-intervention periods and to compare these results with those of the SPC analysis. All analysis was performed with Systat 12.

3. Results

3.1. Patients

In total, data of 3934 patient admissions (from 01 May 2007 to 30 June 2009) were evaluated, corresponding to 119,116 BGL measurements prospectively. Table 3 shows the patient baseline characteristics. Only the APACHE II score showed a statistically significant higher value in the intervention period compared to the “before” period.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Phase 0</th>
<th>Patient non-specific CDSS</th>
<th>Patient specific CDSS</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>1014</td>
<td>1017</td>
<td>1470</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>60 ± 15.5</td>
<td>60 ± 15.8</td>
<td>61 ± 15.9</td>
<td>0.62</td>
</tr>
<tr>
<td>Male (%)</td>
<td>36%</td>
<td>36%</td>
<td>36%</td>
<td>0.91</td>
</tr>
<tr>
<td>APACHE II</td>
<td>19.6 ± 7.8</td>
<td>21.1 ± 7.8</td>
<td>20.6 ± 7.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Surgical (%)</td>
<td>62%</td>
<td>60%</td>
<td>57%</td>
<td>0.09</td>
</tr>
<tr>
<td>ICU LOS (day)</td>
<td>4.9 ± 7.9</td>
<td>4.6 ± 6.8</td>
<td>4.4 ± 7.5</td>
<td>0.25</td>
</tr>
<tr>
<td>ICU mortality (%)</td>
<td>12%</td>
<td>11%</td>
<td>11%</td>
<td>0.73</td>
</tr>
<tr>
<td>Admission BGL</td>
<td>8.4 ± 4.5</td>
<td>8.4 ± 4.6</td>
<td>8.2 ± 4.1</td>
<td>0.70</td>
</tr>
</tbody>
</table>

All data are mean ± SD (medians).
* Phase 0 and patient non-specific; phase 0 and patient specific.

Table 3 – Patient characteristics.

Fig. 1 – Control charts of mean BGL sampling intervals and delay in BG monitoring (protocol-related indicator). Since September 2008 (introducing of phase II) and according to SPC rules (run of seven or more points on one side of the center line) all processes became out of control (here corresponding to a significant reduction). The center lines (CL), upper control limits (UCL) and lower control limits (LCL) were calculated based on the first 8 months (phase 0) and extrapolated over the entire study period.
3.2. CDSS messages

In the two intervention periods, the message was shown 41,875 times: 18,190 times in the patient non-specific phase and 23,685 times in the patient specific phase.

3.3. Protocol related indicators

Overall adherence to the part of the protocol concerning timing of measurements increased significantly. Mean interval between BGL measurements decreased significantly after introducing the CDSS in both levels of support (Table 4 and Fig. 1). However the reduction of the interval was larger when patient specific decision support was provided. The other protocol related indicator, delay in blood glucose monitoring, decreased and became “out of control,” according to SPC rules, after CDSS introduction in both specific and non-specific phases. Becoming “out of control” means that a significant change has been detected. Because this change is related to a decrease in the delay time, this is a good change signifying improvement. The reduction in the glucose measurement interval was greater in the BGL measurements that were high (hyperglycemic) and that were within target range (Fig. 1), in comparison to the measurements that were below the target range (hypoglycemic). This reduction was also significantly greater in the patient specific phase than in the patient non-specific phase.

3.4. Safety of glucose control

Control charts of safety-related quality indicators are shown in Figs. 2 and 3 (hypoglycemia, hyperglycemia, and hyperglycemic index). The percentage of hyperglycemia and hyperglycemic indices did not change after any of the interventions. The percentage of BGL measurements that were ≤40 mg/dl (severe hypoglycemia) and ≤65 mg/dl (moderate hypoglycemia) decreased after implementation of the patient specific CDSS (Fig. 1). According to SPC rules, this reduction was statistically significant for moderate hypoglycemia.

3.5. Effectiveness and efficiency of glucose control

Fig. 4 shows the quality control charts for the effectiveness/efficiency-related indicators of glucose control. Mean BGL, the percentage of BGL within locally defined targets, and time to reach targets did not change after introducing the patient non-specific and patient specific CDSS.

The results of ANOVA, Kruskal–Wallis and chi square tests on the effect of introducing glucose control and related changes on these indicators were concordant with the SPC results (Table 4).

4. Discussion

In this study we showed that a CDSS, integrated in a PDMS in both patient specific and patient non-specific levels, improved adherence to a locally developed protocol for BGL regulation in terms of reducing blood glucose monitoring delay in ICU
patients. However, the effect was greater in the patient specific CDSS. Interestingly, the improvement in adherence to protocol sampling rules did not lead to improvement in the quality of BGL regulation. We found a slight improvement in the safety aspect of BGL regulation only for the CDSS with patient-specific advice, with a decrease in the percentage of moderate hypoglycemic events.

Recent studies [3,4] showed that when BGL measurement is performed frequently and on time then the quality and safety of glucose regulation improve. There are several reasons for delays in glucose monitoring, and forgetting to perform a test is the most important one. A computerized reminder system, like the one which we developed and implemented, could be useful. There are several evaluation studies on the effect of CDSS on BGL regulation [6]. In contrast to the majority of the published studies in this field, we used an active CDSS, meaning that it takes the initiative to act, and it was integrated in the daily workflow of nurses. In our study the glucose regulation protocol was available on paper and in use for a long time before we implemented the CDSS. Other studies implemented a BGL regulation protocol and CDSS simultaneously which makes it hard to isolate the effect of the system alone [16]. In addition, to our knowledge, this is the first study that aimed to implement a protocol on sampling rules and compare two levels of support.

The CDSS used in the present study comprised of a patient non-specific active system, which is only aware of the protocol but does not interpret the patient’s data, and a patient-specific active system. Developing and integrating a patient specific CDSS is more complicated and technically demanding than a patient non-specific CDSS. Therefore, if they were equally

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**Fig. 2** – Control charts of percentage BGL ≤40 mg/dl and ≤63 mg/dl (safety-related indicators), shown respectively at the bottom and top of the figure. Since April 2009 (marked by * in the chart at the top) and according to the SPC rules (one point beyond lower control limit and two out of three consecutive points beyond 2 sigma on the same side of control line) the percentage of moderate hypoglycemia significantly reduced and the process became out of control. However, although severe hypoglycemia demonstrated reduction this was not detectable by SPC rules as a significant one. The center lines (CL), upper control limits (UCL) and lower control limits (LCL) were calculated based on the first 8 months (phase 0) and extrapolated over the entire study period.

**Fig. 3** – Control charts of mean hyperglycemia index and percentage of BGL > 144 mg/dl (safety-related indicators), shown respectively at the bottom and top of the figure. According to SPC rules all processes are stable and in control (i.e. there are no significant changes detected). The center lines (CL), upper control limits (UCL) and lower control limits (LCL) were calculated based on the first 8 months (phase 0) and extrapolated over the entire study period.
effective, the patient non-specific style would seem to be more practical and generalizable. A potential advantage of patient specific systems, however, is that the users do not need to interpret the protocol and make the mental calculations themselves, as the CDSS does this instead. This is easier and less time consuming for the clinicians and might increase the acceptance of the system by healthcare workers, thus increasing the effect of the CDSS.

In this study, the CDSS is triggered by a time-event (every 5 min) thereby assuring that for all new BGL measurements the time of next measurement is calculated in a timely manner. This also means that the reminder appears with a maximum delay of 5 min from the desired launching time (which is 10 min before due time of a measurement).

Delay in blood glucose monitoring significantly decreased after CDSS introduction. This reduction was larger in the higher (hyperglycemic) and in the target range measurements than the measurements below the range (hypoglycemic). This means that after CDSS implementation, when the BGL was above or in the target range, the nurses performed the next BGL measurement with less delay according to the protocol.

The frequency of measurements increased and the delay in blood glucose monitoring decreased but the quality of glucose regulation did not change according to the indicators used. Only a slight improvement was shown in moderate hypoglycemia events. This finding could be explained in different ways. First we note that according to the protocol, the quality of glucose regulation was already in acceptable range in our patients before using the CDSS. Hence it is fair to hypothesize that the effect of a CDSS in situations where quality of glucose regulation is worse could be much higher than in our patients. Second, the system is just one part of a wider socio-technical environment where it interacts with people [17]. Factors such as trust of nurses in the protocol may explain why quality of BG regulation did not improve. It could be the case that despite increasing the BGL measurement frequency, the nurses did not adjust the insulin pump accordingly. Third, external factors such as published negative studies [18] and meta-analysis studies [19,20] showing no benefit of tight glycaemic regulation could have indirectly affected the behavior of the nurses.

A limitation of our study is that we did not investigate if the use of this CDSS has any influence on insulin administration nor clinically relevant endpoints such as survival, length of stay and costs of treatment. However, as glucose regulation is shown to be an evidence based strategy that may decrease mortality, adherence to this strategy is commonly advocated.

5. Conclusion

Adherence to protocol sampling rules increased with the use of decision support, with a larger effect using patient-specific decision support. This led to a decrease in the percentage of hypoglycemia events and improved safety. The use of the CDSS at both levels, however, did not improve the quality of glucose control as measured by our indicators. More research is needed to investigate whether other socio-technical factors are in play.

Authors’ contributions

All authors made substantial contributions to the study design and methods. Saeid Eslami extracted data and analyzed data.
Summary points
What is already known:
- CDSSs have been identified as key for improving patient’s safety and outcomes.
- CDSSs can increase adherence to the guidelines.

What this study added to our knowledge:
- A CDSS integrated in a patient data management system in both levels, patient non-specific and patient specific, improved adherence to protocol with a larger effect at the patient specific level.
- The use of the CDSS at both levels, however, did not improve the quality of care as measured by our indicators. More research is needed to investigate whether socio-technical factors are at play.
- Statistical process control is a useful tool for monitoring the effect over time and captures within-institution significant and stable changes.

and drafted the manuscript. All authors interpreted the results and were involved in revising the final manuscript.

Competing interest
None of the authors has any conflict of interest in the manuscript. There were not any financial or other relations with relevant parties that could have affected the results and conclusions of the study.

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