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Review Article

Hospital Hyperglycemia: Status Investigation and Effect of a Real-Time Glycemic Alert System

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Abstract

Hospital hyperglycemia is common and associated with potential adverse outcomes. A Hospital-wide Mobile Phone Alert (HMA) system was built to achieve real time glucose monitoring with warnings for glucose excursions. This study investigated the status of glucose control and evaluated the impact of HMA system on inpatient glycemia management. Inpatients with hyperglycemia hospitalized between 1 January, 2017 and 31 December, 2018 were identified excluding those < 18 years of age. The HMA system was activated on 1 October, 2017. It sent real time cellphone warning messages to the patient's designated team physician whenever glucose levels > 10 mmol/L or < 3 mmol/L were detected. A serum glucose > 7.8 mmol/L was defined as Hospital Hyperglycemia (HH), and > 10 mmol/L was defined as Significant HH (SHH). Glucose excursions before and after the HMA system was instituted were compared. The incidence of HH, SHH and hypoglycemia was 26.1%, 12.8% and 2.5%, respectively. With the HMA system, the monthly glucose related consultation rate for all inpatients increased 65.9%. The rate of HH glucose amount/ total glucose amount improved with the HMA system, being lower than pre HMA system activation for the surgical wards (15.8±4.7% *vs*. 21.1±6.1%, p<0.05). In conclusion, one third of inpatients were noted to experience hyperglycemia. Real time cellphone warning messages to the patient's designated team physician can improve consultation utilization for blood glucose excursions. The alert system was found to reduce the incidence of hyperglycemia on surgical wards.

Keywords: Blood glucose monitoring; Hyperglycemia; Inpatients; Alert system; Patient care management; Information technology

Introduction

The prevalence of hyperglycemia in hospitalized patients is common and in our study varied from 12% to 50% of all inpatients at our facility [1-3]. Episodes of hyperglycemia were associated with several reasons, to include: history of Diabetes Mellitus (DM), newly diagnosed diabetes mellitus and stress-related hyperglycemia [4,5]. Inpatient hyperglycemia has been associated with various adverse outcomes to include a higher mortality, longer hospital stay, increased infections, and complications [5,6]. In clinic practice, the achievement of blood glucose goal in inpatients with hyperglycemia is not satisfied and a number of barriers can prevent the achievement [7,8]. The physician's omissions of hyperglycemia and impaired medication timing due to hospital system are important reasons that impact the management of hospitalized patients [7,8]. While there have been numerous publications on how to improve the management of glucose excursions in hospitalized patients, available systems to date appear to have fallen short of achieving optimal results [9-13]. Although diabetes management guidelines for inpatient diabetes advise the development and use of inpatient blood glucose monitoring systems, no gold standard models or systems presently exist.

We established a hospital-wide inpatient glucose management model for glucose monitoring and response to clinically relevant glucose excursions including: a Glycemic Care Team (GCT), Standard Operation Procedures (SOP), and Glucose Care Information system (GCI). The GCI was integrated with our Electronic Medical Record (EMR), and was developed to provide an alarm message whenever noting hyperglycemia (>7.8 mmol/L) or hypoglycemia (< 3 mmol/L) in a patient. This system was named the Hospital-wide Mobile Phone Alert (HMA) with it being developed to achieve real time warnings and resultant timely response for glucose excursions with the intent of improving overall glucose control. The study aimed to evaluate the impact of the system HMA on inpatient hyperglycemia control.

Research Design and Methods

Patients

We searched our facility's EMR database in order to identify all adult patients hospitalized in our facility between January 1, 2017 through December 31, 2018 and found that 47,093 inpatients (99.5% of total adult inpatients) who had been admitted were tested for blood glucose levels. The study did not include transplant patients. There were 12,292 inpatients (26.1%) who experienced hyperglycemia > 7.8 mmol/L and 1,175 inpatients (2.5%) that experienced hypoglycemia < 3 mmol/L. Their demographic data, diagnosis, treatment, and laboratory test were analyzed.

Study design

This study was reviewed and approved by the Ethics Committee of Beijing Tsinghua Changgung Hospital and Beijing Tshinghua Changgung Hospital Fund (Grant No. 12017C1002). The HMA system was activated on October 1, 2017. The HMA system was

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set to send real time warning messages to the patient's immediate team physician mobile phone when hypoglycemia (<3 mmol/L) or hyperglycemia (>10 mmol/L) was detected. HMA alert messages were set not to repeat until 72 hours had passed. The alert would be activated by results from either point of care POC or serum glucose testing. Hospital Hyperglycemia (HH) was defined as random blood glucose > 7.8 mmol/L, whereas a blood glucose > 10 mmol/L was defined as Significant HH (SHH). The HH and SHH rates were defined as HH amount/ total tested glucose amount % and SHH amount/ total tested glucose amount %, respectively, and used as indicators for glycemic control. The patients hospitalized before the HMA system was activated acted as the baseline group and with those patients monitored with the HMA system being labelled as the HMA group.

Statistical analysis

Continuous variables were analyzed using the Student's t-test and reported as the mean-standard deviation. Categorical variables were analyzed using the chi-squared test and Fisher's exact test and reported as frequency, percentages and standard errors. Statistical analyses were conducted using SPSS 22. All enrolled patients were assigned a unique identifier in the form of a participant number as to ensure anonymity.

Results

The status of diabetes and hospital hyperglycemia: The rate of pre-existing diabetes history in adult inpatients was 17.7%. Excluding the inpatient Endocrinology ward, Cardiac Surgery (42.9%), Nephrology (36.7%) and Neurology (35.5%) were noted to have the highest rates of DM history, while the Plastic Surgery (4.5%), Gynecology (4.4%), and Intensive Care Unit (ICU) (2.6%) wards had the lowest rates. The incidence of HH and SHH based on serum glucose testing was 26.1% and 12.8%, overall. In non-intensive care unit inpatients, the rates of HH and SHH were 20.7% and 10.8%, respectively. Excluding the Endocrinology inpatient ward, the ICU had the highest incidence of hyperglycemia (HH-73.6% and of SHH- 30.6%) being followed by Cardiac surgery (HH- 48.6% and SHH-34.3%) and Cardiology + CCU (HH- 36.5% and SHH- 22.5%). On the other hand, Plastic surgery (HH and SHH- 0%), Obstetrics (HH- 1.9% and SHH - 0.7%), and Gynecology (HH - 2.9% and SHH - 1.3%) had the lowest incidences (Table 1).

Before HMA activation, Neurology required the largest amount of glycemic related consultations (16.4/month) followed by Cardiology + CCU (12.7/month) and Orthopedics (5.8/month). Thoracic Surgery, Gastrointestinal Surgery, Cardiac Surgery, and General Practice had requested no more than one consultation per month (Table 1).

The status of hypoglycemia

There were 1,175 inpatients (2.5%) that experienced hypoglycemia < 3 mmol/L. There were 263 patients confirmed by venous blood, and the remainder were confirmed by fingertip glucose monitoring. Hepatobiliary medicine had the highest rate through fingertip glucose monitoring of 8.3%. In addition, obstetrics, nephrology, gastroenterology and gynecology were more prone to hypoglycemia, with rates of 5.7%, 4.0%, 4.0% and 3.6%, respectively.

Effect of HMA on inpatients management

The total amount of HMA messages for adult inpatients was 9539 during the 15-month test period. Within the Internal Medicine wards (excluding Endocrinology) the HMA rate was: Neurology (93/month), Cardiology + CCU (55/month), and Nephrology (52/month), these being the top three departments in receiving HMA warning messages while Hepatobiliary Surgery (85/month), Vascular Surgery (37/month), and Orthopedics (36/month) were noted as the top three surgical wards receiving HMA alerts (Figure 1).

The glycemia related consultation (number per month) of all adult inpatients increased by 65.9% in the period of HMA monitoring. The consult rates for the Gastrointestinal Surgery (476%) and Gastroenterology (446.7%) wards increased by more than fourfold, while the rates for Cardiac Surgery (200%) and Hepatobiliary Medicine (218%) were doubled. In contradistinction, a decrease in glycemia related consultations were noted for the Cardiology + CCU (20%) and Neurosurgery (16.4%) wards (Figure 2).

The glycemia excursions between baseline and HMA group

There were no significant differences noted between the two groups in occurrence of either HH or SHH rate amongst all inpatients or patients admitted to internal medicine wards, while the HH rate for surgical wards decreased significantly (HMA group *vs.* baseline = 15.8 ± 4.7% *vs.* 21.1 ± 6.1%, $p<0.05$) (Table 2).

The incidence of hypoglycemia did not have significant difference throughout the hospital. However, the incidence of hepatobiliary medicine department declined from 8.3% to 1.2%. And gastroenterology department dropped from 4% to 2%.

Discussion

Hospital hyperglycemia which is defined as random blood glucose > 7.8 mmol/L with or without diabetes history occurs frequently in inpatients [14-16]. Inpatient hyperglycemia has been associated with an increase in mortality, complications, hospital stay length, and overall hospital cost [17,18]. Previous reports have indicated that the inpatient hyperglycemia incidence is around 32.2% of ICU patients and 32% of patients admitted to non-ICU wards in the U.S. [19]. The reported incidence of hyperglycemia was 45.7% in China [20]. In our study, 26.1% of total adult inpatients were noted to experience hyperglycemia (> 7.8 mmol/L) with 12.8% having a significant episode of hyperglycemia (> 10 mmol/L). The HH and SHH prevalence of ICU inpatients are as high as 73.6% and 30.6%, respectively. Meanwhile, there are 20.7% of non-ICU inpatients with HH and 10.8% with SHH. The inpatient wards with higher hyperglycemia rates can be divided into two categories: the first category is those who tend to admit more patients with pre-existing diabetes history who are at risk for developing excursions in blood glucose control, such as the Cardiology ward; the second category consists of patients without a history of diabetes but who experience illness, stress, and/or medication related hyperglycemia. Surgical and ICU wards typically represent patients falling into the latter category [21,22]. As is known, medications other than glucocorticoids can induce hyperglycemia, such as lipid-modifying agents, antidepressants and estrogen [23-26]. In our hospital, patients following craniocerebral operations who are admitted to the Neurosurgery ward regularly receive dexamethasone therapy. However, episodes of hyperglycemia were low which appeared to be related to intensive glucose monitoring whenever glucocorticoid therapy was prescribed. This finding seems

Table 1: The baseline of pre-existing diabetes history, hyperglycemia and consultation in different inpatient wards before HMA activation (1/2017 - 9/2017).

Department	Total Inpatients (N)	Pre-existing diabetes inpatients (N)	HH inpatients (N)	SHH inpatients (N)	Consultation (N/month)	DM prevalence (%)	HH incidence (%)	SHH incidence (%)
ICU	1134	29	835	347	3 (<1/m)	2.6	73.6	30.6
Cardiac Surgery	35	15	17	12	4(<1/m)	42.9	48.6	34.3
Cardiology+CCU	1069	332	497	240	114(12.7/m)	31.1	46.5	22.5
Nephrology	447	164	167	95	13(1.4/m)	36.7	37.4	21.3
Hepatobiliary Surgery	821	129	304	142	29(3.2/m)	15.7	37	17.3
Hepatobiliary Medicine	108	28	35	15	10(1.1/m)	25.9	32.4	13.9
General Medicine	356	114	115	59	26(2.9/m)	32	32.3	16.6
Respiration	261	62	79	38	17(1.9/m)	23.8	30.3	14.6
Gastrointestinal Surgery	688	48	206	86	5(<1/m)	7	29.9	12.5
Urology	1300	149	336	129	30(3.3/m)	11.5	25.8	9.9
Neurology	828	294	196	105	148(16.4/m)	35.5	23.7	12.7
Thoracic Surgery	140	10	28	12	5(<1/m)	7.1	20	8.6
Vascular Surgery	469	113	93	47	29(3.2/m)	24.1	19.8	10
Hematology and Oncology	398	69	78	40	17(1.9/m)	17.3	19.6	10.1
Orthopedics	1217	189	238	109	52(5.8/m)	15.5	19.6	9
Hepatobiliary Intervention	92	9	16	8	0(0/m)	9.8	17.4	8.7
General Surgery	562	80	94	44	14(1.6/m)	14.2	16.7	7.8
Neurosurgery	722	59	119	45	28(3.1/m)	8.2	16.5	6.2
Radiotherapy	21	6	3	3	1(<1/m)	28.6	14.3	14.3
Rehabilitation Medicine	415	113	37	14	20(2.2/m)	27.2	8.9	3.4
Gastroenterology	349	51	29	15	9(1/m)	14.6	8.3	4.3
Ophthalmology	414	80	23	12	11(1.2/m)	19.3	5.6	2.9
O-HNS	1016	85	43	16	47(5.2/m)	8.4	4.2	1.6
Gynecology	1142	50	33	15	13(1.4/m)	4.4	2.9	1.3
Obstetrics	858	134	16	6	7(<1/m)	15.6	1.9	0.7
Plastic Surgery	22	1	0	0	2(<1/m)	4.5	0	0
Total adult inpatients	15350	2760	4013	2001	666(74/m)	17.7	26.1	12.8

HH, hospital hyperglycemia (serum random glucose > 7.8 mmol / L); SHH, significant hospital hyperglycemia (blood glucose > 10 mmol / L); CCU, cardiac intensive care unit; ICU, intensive care unit; O-HNS, Otolaryngology-Head and Neck surgery.

to support the belief that intensive monitoring of blood glucose is of benefit for inpatient glycemic control [9,27,28]. Illness associated stress which occurs in 12 -22% of inpatients has been reported to induce hyperglycemia which a resultant increase in both morbidity and mortality [5,22,29-31]. Stress-induced hyperglycemia is felt to be related to over activation of the hypothalamic–pituitary–adrenal axis and/or the sympathetic autonomic nervous system thereby causing insulin resistance followed by hyperglycemia [32]. Sleep loss, which is common in inpatients, is considered as an independent risk factor which can disrupt glycemic homeostasis [33,34]. Our study also indicates that thoracic surgery is unique in character as the rate of mild hyperglycemia (7.8-10mmol/L) is nearly three times higher than the rate of pre-existing diabetes history. This association may be related to the fact that many thoracic surgery cases were for a malignant tumor, and both lung cancer itself and its treatment have been associated with the development of hyperglycemia [35-37].

Traditional inpatient glycemic care is typically passive in nature and not very efficient [14,20,38]. Lack of timely reaction to glucose excursions, delayed treatment, and undiagnosed new onset diabetes or pre-diabetes have all been identified as common factors related to poor inpatient glycemic control [39]. Our facility developed an alert system for glucose excursions which sent real time cellphone message

Table 2: The HH and SHH rates of adult inpatients between baseline and HMA group.

	Baseline	HMA group	*p*
HH rate (%)	21.9±0.8	22.6±1.6	0.222
Internal Medicine wards	23.8±9.6	26.7±7.0	0.456
Surgical wards	21.1±6.1	15.8±4.7	<0.05
SHH rate (%)	9.7±0.5	10±1	0.279
Internal Medicine wards	12.6±5.1	14.5±5.2	0.417
Surgical wards	9.3±6.6	9.7±4.8	0.878

HH, hospital hyperglycemia; SHH, significant hospital hyperglycemia; HMA, Hospital-Wide Mobile Phone Alert System.

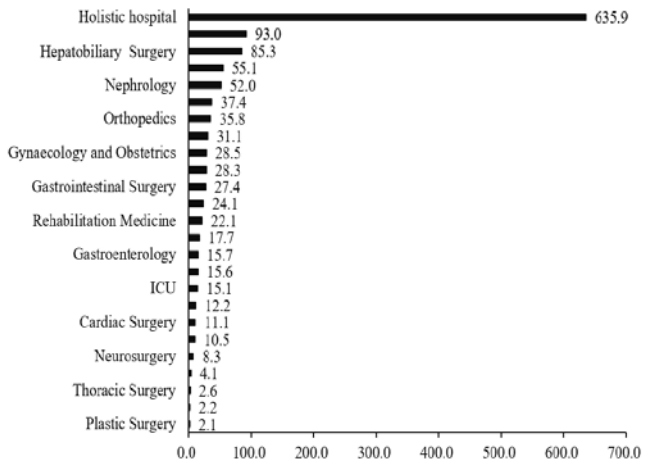

Figure 1: The average monthly HMA message amount for different inpatient wards (10/2017 - 12/2018). HMA- Hospital-wide Mobile Phone Alert System; Otolaryngology-Head and Neck surgery; CCU- Cardiac intensive Care Unit; ICU- Intensive Care Unit; Holistic hospital - all adult inpatients.

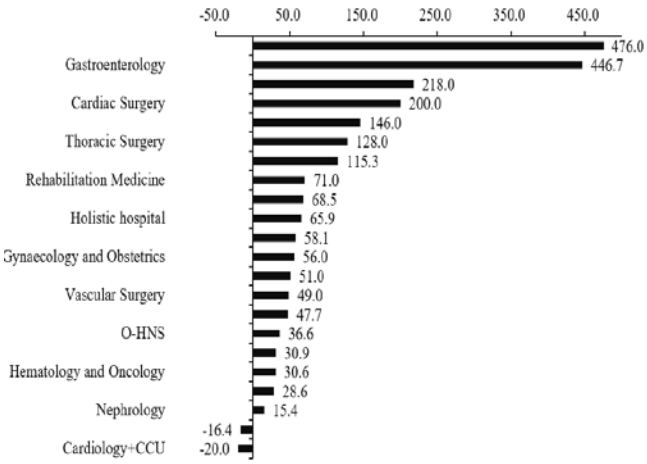

Figure 2: Percentage of average monthly consultation amount change between baseline and HMA group. HMA- Hospital-Wide Mobile Phone Alert System; O-HNS, Otolaryngology-Head and Neck surgery; CCU- Cardiac intensive Care Unit; ICU- Intensive Care Unit; Holistic hospital- all adult inpatients.

to the hospitalized patient's designated inpatient team physician with the aim of improving the reaction time and intervention for episodes of hypo- or hyperglycemia. Previously studied glucose alert systems have shown improvement of inpatient glycemic control [40,41]. With the HMA system, the monthly glycemia related consultation rate for all inpatients increased nearly 66%. While the HMA system was not noted to reduce the rate of total inpatient hyperglycemic episodes, the HH rate for the surgical wards was decreased. These findings indicate that the effect of HMA system on utilization of formal consultations for blood glucose excursions varied by the specialty service of the ward. The surgical wards actively utilized the alert by requesting endocrinology team consultation. It should be noted that two kinds of endocrinologist consultation are performed in our hospital: 1) individual endocrinology consults and 2) Glycemic Care Team (GCT) assessments. The former is the traditional way to deal glucose excursions in Chinese hospitals, and is performed during a single visit by an endocrine physician to the inpatient with recommendations being provided to fulfill the consultation requirement. The GCT is composed of a nurse, a diabetes educator, nutritionist and an endocrinologist. The endocrinologist who takes the initiative to follow-up the patient during the period that glucose excursions are occurring leads GCT assessment. In order to cover the entire complement of hospitalized patients, the GCT would require a large number of endocrinologists, which presently is beyond the capacity of our facility. Therefore, at present, GCT assessments are only available to a select number of inpatients in our hospital. The GCT glucose assessments were noted to correlate with a reduced rate of hyperglycemia and a shorter length of hospital stay, while individual endocrinologist consults were noted to decrease the average length of hospital stay and medical care expenses for inpatients experiencing hyperglycemia [42]. However, the HMA system was found to reduce the HH rate for the surgical wards even when just individual endocrinologist consultations were utilized. Within internal medicine wards, a quite different response to HMA alerts was noted. Nephrology was the fourth highest ward receiving HMA alerts but the third lowest ward in increased utilization of endocrinologist consults. The glycemia related consultation rate for Cardiology + CCU ward even declined by 20%. There is rare previous report describing the relationship between inpatient ward response to glycemic alert, hyperglycemia episodes and glycemia related consultations. We postulate that the less active response to the glucose excursions alerts may lead to suboptimal glycemic control secondary to a delay in endocrinologist consultation, or possibly that individual endocrinologist consults were not felt to be effective enough for internal medicine wards patients with more complicated glucose control issues. Future investigation is warranted as to determine the exact causes for variations in utilization of consultations for HMA alerts.

The prevalence of inpatient hypoglycemia differed from 2.8% to 22% in previous study [43]. The incidence of hypoglycemia varied greatly among different departments in our hospital. Hepatobiliary, obstetrics, nephrology, gastroenterology and gynecology were the most common departments with higher hypoglycemia rate. Our HMA alerts did not improve the overall incidence of hypoglycemia, but it might benefit some individual departments. The lower incidence of hypoglycemia in our study might due to two causes: first, we defined hypoglycemia < 3mmol/L, compared to 3.9mmol/L in other studies; second, Second, a lot of patients had only take serum blood test once or twice without continuous blood glucose monitoring, which may lead to undetected of some mild hypoglycemia and asymptomatic hypoglycemia.

In conclusion, inpatient hyperglycemia which is associated with inferior outcomes and longer hospital stays is commonly encountered in hospitalized adults, and real time glycemic alert systems for inpatients hold the potential to improve glycemic control thereby reducing complications, morbidity and mortality related to excursions in glucose from either hyper- or hypoglycemia. This study revealed the prevalence of hospital hyperglycemia at 26.1% overall, 20.7% in non-ICU inpatients, and 73.6% in ICU inpatients. It is noted that real time glycemic alert cellphone messages to the team physician who is directly responsible for the inpatient with the

glucose excursions can increase the glycemia related consultation rate overall and also appears to decrease hyperglycemia episodes in patients on the surgical wards.

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Author contributions

C. C. procured the funding, led the trial, collected and analyzed the data, and wrote the manuscript. V. B. reviewed and edited the manuscript. Z. L. and C. L. contributed to data collection and data management. C. B. was responsible for all data collection and data quality. Z. S. and H. L. were responsible for data quality and data management. J. X. contributed to clinical trial design and oversight, led and supervised all aspects of the trial, reviewed and edited the manuscript. J. X. and C. C. are the guarantors of this work and, as such, had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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