Glucommander

A computer-directed intravenous insulin system shown to be safe, simple, and effective in 120,618 h of operation

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OBJECTIVE — Intravenous insulin is now the recommended method of diabetes management in critically ill persons in the hospital. The published methods for administering the insulin are complex and are usually limited to intensive care units with a low patient-to-nurse ratio.

RESEARCH DESIGN AND METHODS — A computer-directed algorithm for advice on the delivery of intravenous insulin that is flexible in blood glucose timing and advises insulin dosing in a graduated manner has been developed. This software program, known as the Glucommander, has been used extensively by our group. The data were analyzed for this study.

RESULTS — The data from 5,080 intravenous insulin runs over 120,683 h show that blood glucose levels can be safely stabilized in a target range without significant hypoglycemia by nonspecialized nurses working on any unit of a general hospital. The mean glucose level reached <150 mg/dl in 3 h. Only 0.6% of all glucose values were <50 mg/dl. The prevalence of hypoglycemia <40 mg/dl was 2.6% of all runs. No hypoglycemia was severe.

CONCLUSIONS — This computer-directed algorithm is a simple, safe, effective, and robust method for maintaining glycemic control. It has been extensively studied and is applicable in a wide variety of conditions. In contrast to other published intravenous insulin protocols, which have been limited to intensive care units, Glucommander can be used in all units of any hospital.

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A large, randomized, controlled trial of patients admitted to a surgical intensive care unit in Leuven, Belgium, and reported by Van den Bergh et al. (1) showed that regulation of blood glucose levels to <110 mg/dl using an intravenous insulin protocol improved clinical outcomes. In the Leuven study, intensive insulin therapy reduced intensive care unit (ICU) mortality by 34% and also reduced sepsis, the need for dialysis, prolonged ventilator support, and the duration of ICU stay.

Strict glycemic control has been demonstrated to be beneficial in other settings as well, with intravenous insulin in preference to the subcutaneous route in many clinical situations, including diabetic ketoacidosis and the nonketotic hyperosmolar state (2), critical care illness (1), myocardial infarction or cardiogenic shock (3–5), and the postoperative period after cardiac surgical procedures (6). Other indications for intravenous insulin infusion therapy include use in patients with diabetes who are receiving nothing by mouth, general perioperative care, total parenteral nutrition, or high-dose corticosteroid therapy; in patients who have had a stroke; in women during labor and delivery; as a dose-finding strategy in anticipation of initiation of subcutaneous insulin; and in prevention or treatment of infection.

Based on the emerging clinical evidence, there are widespread efforts to maintain very strict glycemic control in critically ill patients. However, achieving this goal requires extensive nursing efforts, including frequent bedside capillary glucose monitoring and the implementation of complex intravenous insulin protocols generally limited to an ICU. The fear of hypoglycemia also inhibits the widespread acceptance of intensive blood glucose level management. There is a generalized need for a safe, simple method to achieve normoglycemic control in hospitalized patients.

A review of the literature failed to find an intravenous insulin protocol that is robust enough to control glucose levels in sick patients and simple enough to be used throughout the hospital without close expert supervision.

The tool for blood glucose management presented in this article is known as the Glucommander. It is a computer-based algorithm for advising on the delivery of intravenous insulin. The Glucommander was invented by the authors in 1984. Numerous physicians have used the Glucommander for 21 years in our hospitals and also throughout the American Healthways Systems units in >100 hospitals nationwide. This is the first peer-reviewed report on the Glucommander.

In this article, the heretofore unreported safety and efficacy data seen with Glucommander will be highlighted.

RESEARCH DESIGN AND METHODS — The inspiration for Glucommander is a simple control system stemming from an article published in 1982 by White et al. (7). The article presented a complex set of orders for determining the basal insulin requirement in pediatric patients with insulin pumps. When data were graphed, it was obvious that a linear regression with an intercept of 60 and a slope, or multiplier, of 0.02 can reduce the complexity of the orders of White et al. to a single formula: (blood glucose – 60) × 0.02 = insulin dose/h.

However, when this equation is used for a wide variety of patients with insulin resistance, stress responses, and confounding pharmacological effects, this multiplier is not appropriate for most patients. In our later analysis of all patients who had used the Glucommander for
intravenous insulin protocol developed by the authors in 1982 used the formula: insulin dose/h = (blood glucose − 60) × multiplier (8). The multiplier was started at 0.02. Whenever the multiplier did not correct the glucose to the targeted range, it was progressively changed until the insulin dosing formula controlled glucose in the target range. Although this was relatively simple, it was associated with many errors in application of the adjustment and timing rules and the failure to repeat scheduled glucose measurements promptly.

In 1984, the insulin drip orders were programmed into a bedside TRS-80 computer directly connected to an Auto-Syringe AS-2C pump, the first Glucommander (9). Since 2000, the system has been used in a Windows-based computer and more recently in a personal digital assistant. To initiate the system, a bedside fingerstick blood glucose value is entered, and the initial insulin infusion rate is calculated by the Glucommander, i.e., (blood glucose − 60) × 0.02. Based on the rate of change of the glucose level, the computer will notify the nurse when the next blood glucose value is needed, which may be in from 20 to 120 min. The system continues recommending the intravenous insulin infusion rate until it is discontinued by the health care provider.

Statistical analysis
The use of a computerized device allowed for expedient data collection. The data presented here are from the period 1984–1998 or until Boehringer Mannheim and MiniMed started their clinical study for presentation to the Food and Drug Administration (10).

Information collected and analyzed included the temporal relationship between all blood glucose values, insulin doses, and factors necessary to convert the glucose level to the desired insulin dose. All clinical data are expressed as means ± SD.

RESULTS—For the initial Glucommander setting, the high target for blood glucose level is usually selected as 120 or 140 mg/dl, the low target is usually 80 or 100 mg/dl, the multiplier is usually 0.01 or 0.02, and the maximal duration of time between glucose measurements is usually 120 min. The frequency of blood glucose monitoring is set at an interval predicted to prevent the blood glucose level from dropping to <60 mg/dl. When blood glucose values are stable, the interval between blood glucose level monitoring will be increased to the preset maximum interval. Our data analysis shows that the Glucommander has been able to achieve a targeted glucose level in 3–6 h that is then stable for as long as the Glucommander run continues.

The principles of the Glucommander are extremely simple. They are shown graphically in Fig. 1. A typical run on a person with type 1 diabetes is illustrated in Fig. 2. The entire database from 1984 to 1998 has been analyzed (Fig. 3). All runs were preformed at two Atlanta hospitals where the authors practiced. The runs were ordered by both the authors and others. The data were captured automatically in the computer memory. No other hospitals provided data.

During the study period, Glucommander was prescribed by a score of different physicians. All runs were in the era before the Leuven data were published; thus, values were sometimes targeted to what would now be considered very high levels. However, for the past 5 years, after the period of data collection, the most experience has been with a target blood glucose level set in the range of 80 to 120 mg/dl. The physicians prescribing Glucommander were in community hospitals and did not have house officers as backup. The prescribing physicians were endocrinologists, internists, family physicians, obstetricians, and anesthesiologists. The protocol has been administered by nurses in ICUs, operating room, delivery suites, and emergency rooms, but mostly on general medical and surgical floors.

In analysis of our extensive data, we observed that the initial multiplier can be at any level, and the self-correcting nature of the algorithm will seek and find the appropriate level. When the initial multiplier was 0.01, 50% of values are to target in 4.6 h and 90% in 10.5 h. With an initial multiplier of 0.02, these values are 3.2 and 8 h. With an initial multiplier of 0.03, these values are 3.0 and 7.5 h.

Of all glucose values, only 0.6% were <50 mg/dl. There was no severe hypoglycemia because of early recognition and treatment. The percentage of runs with at least one glucose value <60 mg/dl was 16.5%. All episodes of hypoglycemia were recognized within 20 min, because of the nature of the algorithm. Insulin was held 30 min and until the glucose level was >60 mg/dl. Only 2.6% of runs were characterized by a glucose value <40 mg/dl.

The efficacy of the correction of hypoglycemia by the Glucommander was analyzed in 886 hypoglycemic events when the blood glucose level was <60 mg/dl. The mean ± SD of all low glucose values was 49 ± 10 mg/dl, and the follow-up value in an average of 33 min was 83 ± 10 mg/day (P < 0.001). As a further
safeguard against hypoglycemia, a protocol for treating hypoglycemia was initiated in 1995. The authors incorporated an intravenous glucose formula into the Glucommander program for correction of hypoglycemia with 50% glucose levels \( \times 0.2 \text{ g} \). This procedure immediately corrected hypoglycemia. In a separate study, this procedure has been shown to correct blood glucose to the target range in 98% of patients when rechecked in 30 min (11).

An analysis of all data on runs that exceeded 10 h and therefore were presumed to have reached a stable multiplier shows that the glucose level corresponds very closely to the targeted glucose level \( (R^2 = 0.90) \).

**CONCLUSIONS** — Three recent major studies have demonstrated the benefit of intravenous insulin therapy to normoglycemia (1,3,6). All three of them are based on use of intravenous insulin during the initial care of ICU patients. All three studies showed convincing evidence that the administration of intravenous insulin was associated with markedly reduced morbidity and mortality. The DIGAMI (Diabetic Patients with Acute Myocardial Infarction) study shows that 24 h of intravenous insulin followed by 3 months of intensive insulin therapy, whether in persons with known diabetes or in persons with newly recognized diabetes resulted in up to 51% improved mortality 5 years later (3).

The study of Furnary et al. (6) comparing intravenous insulin to conventional diabetes management after coronary artery bypass grafting showed the virtual elimination of death from infection and dramatically reduced death from cardiovascular events when the average glucose level was maintained at \(<150 \text{ mg/dl}\). Their work demonstrated a
94% reduction in mortality when the average postoperative blood glucose level was reduced from 250 to 150 mg/dl.

The most impressive evidence for normal glucose control is that from Van den Berghe et al. (1). Their study showed a 34% reduction in mortality and a 3-day shortening of ICU stay by maintaining glucose levels at 110 mg/dl compared with the control group who had average glucose levels at 150 mg/dl.

A major problem in each of these studies is that the intravenous insulin protocols associated with these studies are extremely complex and are used only by very highly trained nurses in ICUs under the supervision of physicians involved with the specific studies. The Leuven protocol leaves the nurses with great responsibility in selecting doses of insulin and timing of blood glucose measurements. In contrast, use of the Glucommander is very directed.

Some of the current published protocols for management of intravenous insulin were compared with the Glucommander using the recommended insulin doses being given for an identical and typical series of blood glucose levels. We have analyzed our Glucommander data and, with this publication, the Glucommander has now been more extensively reported than any other intravenous insulin management system, we propose that it could be used as a standard. Many of the other protocols differ markedly in their recommendations.

With Glucommander as the standard, the set of other protocols show little agreement during the first 5 hours of treatment of a patient who is very hyperglycemic and is typical of patients seen clinically (1,3,6,8,12–20). This analysis is presented as Fig. 4. Only one of these other algorithms gives values in the same range as the Glucommander. Not surprisingly, it is the intravenous drip orders from which Glucommander was developed. A close match is the intravenous insulin protocol of Markovitz et al. (16).

What these three protocols have in common is that they have early aggressive dosing of insulin, the insulin doses decrease in parallel with the decreasing glucose level, all end with a similar dose of insulin, and the total insulin dose given over the 5 hours is moderate and similar.

With the Glucommander, hypoglycemia has been minimized. Van den Berghe et al. (1) defined hypoglycemia for patients in the ICU as glucose level <40 mg/dl. Their prevalence of hypoglycemia was 5.2%. The prevalence achieved with the Glucommander is reduced by one-half to 2.6%.

A primary disadvantage of most intravenous insulin protocols is that the blood glucose levels are required on a variable schedule and are difficult to reproduce without a timing and alarm mechanism. The principles of the timing for the Glucommander are that blood glucose measurement is required every 60 min unless the last two blood glucose levels can be projected to reach a level that is approach-
ing 60 mg/dl before another 60 min, in which case the time interval is shortened. When glucose control has been stabilized and levels have been in the target range for 4 h, the interval to the next requested blood glucose level is increased to the maximum interval programmed. When the blood glucose level drifts out of the target range, the time interval reverts to 60 min. If the blood glucose level is <60 mg/dl, a follow-up blood glucose level is requested in 30 min.

As is true with all published protocols for intravenous insulin, the patient cannot take intermittent meals of carbohydrate because this titrates up the insulin dose, which then carries on beyond the availability of substrate. This limitation can be coped with by giving a 1-h step-up of intravenous insulin of 1 unit/10 g of carbohydrate initiated immediately after a meal. Another option is to give 1 unit of a rapid-acting analog subcutaneously for every 10 g of carbohydrate consumed.

The Glucommander has been used to treat individuals with out-of-control diabetes, ketoacidosis, a hyperosmolar nonketotic state, gastroparesis with intractable nausea and vomiting, septic conditions, gastrointestinalitis, pancreatitis, and hyperalimentation; critically ill patients in the ICU; individuals after myocardial infarction; individuals receiving steroid therapy; and women during labor. It has also been used for perioperative glucose management and for establishing the degree of insulin sensitivity.

From projections of the data of Van den Bergh et al. (1), a reduction in ICU mortality of >60% and an annual savings of >$300 million of ICU costs in the U.S. could be realized immediately by the generalized use of the Glucommander. Furrnary et al. (21) projected savings related to use of an intravenous insulin protocol for cardiovascular surgery of $456 million annually in the U.S.

There is general agreement that a closed-loop system based on continuous glucose monitoring is what is needed for ideal in-hospital blood glucose management. The closed-loop system continues to be beyond our reach. Meanwhile we now have irrefutable proof that normal glucose levels will save lives and money. With the Glucommander, we have evidence that the necessary degree of glucose control can be achieved for all patients in all sections of all hospitals.

The authors anticipate that this article will generate interest in using the Glucommander technology at other institutions. As this article goes to press, we are still finalizing how Glucommander will be made available to interested parties.

Our personal desire and interest are to continue to work to improve the Glucommander. To this end, we are organizing a Computerized Hospital Insulin Project (CHIP) consortium. The CHIP consortium is to be open to hospitals that desire to use and further the development of computer systems to support the control of hyperglycemia in hospitalized patients.

Institutions that join and support the CHIP consortium will immediately have access to the version of the Glucommander described in this article. They will also participate in a multicenter quality improvement process by submitting their results to a central database that can track glucose control outcomes. Algorithms will be refined as new information and devices (e.g., continuous glucose monitors) become available. As refinements are implemented, members will be offered the option of adopting the new systems. Information about the Glucommander and how to obtain it can be found at our web site, www.glucommander.com.

In addition to the use of the database in the quality improvement process, a limited dataset, stripped of protected health information, will be created. This dataset will be analyzed, and results will be published periodically to describe the consortium’s progress.

In summary, the Glucommander is a simple, safe, and effective method for maintaining glycemic control. It has been extensively studied as a standardized treatment method applicable in a wide variety of conditions. In contrast to the other published intravenous insulin protocols, which have been mostly limited to ICUs, the Glucommander is a safe and robust method to significantly improve clinical outcome in all units of all hospitals.

References

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