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EDITORIAL

Technology to Treat Hyperglycemia in Trauma

David C. Klonoff, M.D., FACP

Innovative technology is being developed to treat hyperglycemia in trauma patients. The current status of the link between technology and therapy of trauma hyperglycemia is that: (1) trauma may lead to hyperglycemia; (2) morbidity and mortality of trauma hyperglycemia are related to blood glucose (BG) concentrations; (3) intensive insulin therapy (IIT) corrects trauma hyperglycemia and improves outcomes; and (4) future IIT will use continuous glucose monitoring (CGM), computerized insulin delivery, closed loop control, and physiological monitoring.

The relationship between trauma or burns and hyperglycemia has been observed since the Viet Nam war.[1] Hyperglycemia because of insulin resistance may occur because of elevated levels of counterregulatory hormones, release of inflammatory cytokines, intravenous dextrose support, and corticosteroid therapy.[2] Even people without a history of diabetes can become hyperglycemic and approximately 25% of trauma patients without a history of diabetes can present with hyperglycemia.[3,4]

The current approach to treating intensive care patients is to tightly control the hyperglycemia that frequently accompanies acute illnesses. This trend was triggered by a landmark article in the *New England Journal of Medicine* in 2001 first-authored by Greet Van den Berghe, which reported that IIT to maintain BG levels at 80-110 mg/dl reduced morbidity and mortality in a series of intensive care unit (ICU) surgical and trauma patients.[5] A handful of subsequent surgical and medical studies also reported on outcomes of intensive insulin therapy compared to usual intensive care therapy in which blood glucose levels were treated at above 180-200 mg/dl , but these reports utilized nonstandardized protocols and aimed for nonstandardized BG targets.[6] The current consensus is that IIT to control hyperglycemia in surgical and trauma ICU patients is probably warranted, but the optimal target may be as low as 80-110 mg/dl or as high as 140-150 mg/dl.[7]

Five technologies are expected to be used in intensive insulin therapy of trauma hyperglycemia: (1) subcutaneous (SC) CGM; (2) intravenous CGM; (3) computerized insulin dosing; (4) closed loop control of glycemia; and (5) physiological monitoring. Important concerns have been frequently raised about potential problems with using SC CGM in intensive therapy patients. There can be a lag between dynamic shifts in blood glucose levels and interstitial fluid glucose levels. Hypotension, which is common in an ICU, can decrease skin perfusion and prolong the lag between blood and interstitial fluid analytes. Vasoconstrictor drugs can increase the aforementioned lag. False positive nocturnal hypoglycemia results have been reported with the CGM device.[8] Finally, the accuracy of CGM devices in the hypoglycemic range is less than in the euglycemic range, which decreases their appeal as hypoglycemia detection systems.[9] Despite these concerns, in three trials of using SC CGM in intensive care units, the devices performed well with adequate accuracy. [10-12]

Trauma patients with burns may undergo diffuse skin changes even beyond the burn site that persist after the stress hyperglycemia resolves.[13] Such patients may not be candidates for SC CGM.[14]

Intravenous CGM products are not currently on the market, but several such systems are being investigated. They will involve handing blood samples by withdrawing an aliquot

Author Affiliation: Mills-Peninsula Health Services, San Mateo, California

Abbreviations: (BG) blood glucose, (CGM) continuous glucose monitoring, (ICU) intensive care unit, (IIT) intensive insulin therapy; (SC) subcutaneous

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Corresponding Author: David C. Klonoff, M.D., FACP, Diabetes Research Institute, Mills-Peninsula Health Services, 100 South San Mateo Drive, Room 3124, San Mateo, CA 94401; email address dklonoff@yahoo.com

J Diabetes Sci Technol 2007; 2:151-152

through an indwelling catheter, measuring the specimen outside the body, discarding the specimen, and finally flushing the intravenous line with crystalloid. Handwritten insulin orders may be complicated and require switching back and forth from multiple scales, also known as multiples, which represent ratios of insulin-to-be-administered to the magnitude of elevated blood glucose elevation above target. As the patient's insulin sensitivity changes, the appropriate scale may change, and for any given scale, the amount of insulin needed per hour may change.[15]

Mistakes may occur when busy intensive care nurses are asked to carry out complex handwritten or printed intensive orders for insulin therapy. There has been interest in computerizing this type of treatment. New software is being currently developed and tested for dosing intravenous insulin in an intensive care unit.[16] This type of software calculates the: (1) proper ratio of insulin dosage to the blood glucose concentration; (2) duration of intravenous insulin delivery at each rate before the BG must be retested; and (3) minimum frequency of blood glucose testing. The software can also trigger an alarm for missed or overdue blood glucose tests.

Closed loop control of glycemia requires a continuous glucose sensor, an insulin delivery system, and a controller, which are all linked. No such system is currently approved. Adoption of any such system will require satisfactory demonstration of its safety, effectiveness, and economic impact. The algorithm must protect against severe hypoglycemia to prevent morbidity, product recalls, and lawsuits. The degree of improved outcomes and the costs of these outcomes are currently unknown.[17]

Physiologic monitors to noninvasively measure multiple organ systems are being developed by industry, the U.S. Army, and National Aeronautics and Space Administration. Hypoglycemia, the greatest risk of IIT, provokes autonomic nervous system responses, which could possibly be measured qualitatively by such a monitor.[18] Once the glucose data are obtained, telemedicine technology will eventually transmit the information wirelessly to a central server that stores hospital data and can potentially send the data to caregivers by way of wireless transmission to cell phones or by way of the Internet.[19]

For trauma hyperglycemia, we know what the problem is; we know what the solutions are; and we know what the best technologies are to solve the problem. This is the time for hospitals to provide IIT with existing technologies and upgrade to additional technologies as they become fully developed.

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