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INVITED COMMENTARY

The Adjectives of Inpatient Glycemic Management

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There is currently much confusion regarding the issue of inpatient glycemic management. Following publication of the Leuven study in the *New England Journal of Medicine* in 2001, there was a rush to extend the results observed with intensive insulin therapy (IIT) in this primarily surgical patient population to all critically ill patient populations as a way of improving patient outcomes and reducing mortality [1]. The rationale for this approach was based on the significant reductions observed in intensive care unit (ICU) length of stay (LOS), sepsis, need for antibiotic therapy, time on the ventilator, need for hemodialysis, and mortality in the group randomized to glycemic targets of 80 to 110 mg/dL [1]. The fact that this was associated with significant reductions in cost was viewed favorably in an era of cost containment [2]. Similar findings from nonrandomized longitudinal studies investigating patient outcomes before and after implementation of intensive glycemic management programs lent additional support to the creation of guidelines recommending glycemic targets of 80 to 110 mg/dL in all critically ill patient populations [3, 4]. Many hospitals invested significant resources in developing and implementing protocols to achieve these glycemic goals.

Subsequent trials in medical ICU (MICU) patients with sepsis or in mixed MICU/surgical ICU patient populations were unable to reproduce the favorable results of the 2001 study [5–7]. Furthermore, these later studies called attention to the sixfold increase in risk for severe hypoglycemia observed with protocols targeting glycemic ranges of 80 to 110 mg/dL [8]. This resulted in revision of prior guidelines and in some cases revocation of programs targeting inpatient glycemic control. Statements from reputable organizations recommending against IIT in medical and surgical inpatients contributed to confusion where in fact none exists [9, 10].

Recommendations against intensive glycemic management are based on systematic reviews in which investigators found no consistent evidence to support strict glycemic control, defined as a target blood glucose range of 80 to 110 mg/dL [2, 10]. The increase in risk for hypoglycemia has been demonstrated in some studies to result in an increased risk for hospital complications and mortality [3]. Although other investigators have demonstrated that insulin-induced hypoglycemia is not associated with adverse outcomes, this remains an undesirable outcome in hospitalized patients with acute illness [11, 12].

It is well established that hyperglycemia, defined as glucose levels above 180 mg/dL, is associated with adverse outcomes in hospitalized patients and that attention to glycemic control in improves outcomes [3, 13, 14]. Protocols targeting glucose values less than 150 mg/dL have been repeatedly associated with near elimination of sternal wound infections in patients following open heart procedures [3, 13]. Where confusion lies is in using adjectives rather than specific glycemic

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targets to define the parameters and goals of a glycemic management program.

Terms such as "tight" or "strict" glycemic control and "intensive" or "conventional" insulin therapy do not provide clear information as to what glycemic targets are reasonable. Nor do they provide information as to what targets are associated with a low risk of hypoglycemia or what methods are best used to achieve these targets. The term "conventional" insulin therapy is misleading as there really is no established standard for inpatient glycemic management. If conventional is defined as usual care, then sliding scale insulin (SSI) regimens unfortunately continue to be used by many institutions as an ineffective method for achieving glycemic control [15–17].

If adjectives are to be used as a way of describing inpatient glycemic management programs, we recommend that the term "rational" be used as a way of describing recommendations for glycemic target ranges and methodologies for how to achieve these targets. This approach was recently presented in a consensus statement from the American Diabetes Association and the American Association for Clinical Endocrinologists [18]. Recommendations from this group advocated target blood glucose levels of 140 to 180 mg/dL for the majority of critically and non–critically ill hospitalized patients, as safe and achievable without an increase in the risk for hypoglycemia [7]. Glycemic targets of 140 to 180 mg/dL also serve to avoid adverse effects associated with glucose levels above 180 mg/dL, which have been demonstrated to increase risk for infections, prolong LOS, and increase mortality.

These glycemic targets can be achieved by rational use of insulin in the hospital setting. This is further explored by Drs. Mesotten and Van den Berghe [19] in the critically ill patient population and by Drs. Pichardo-Lowden and Gabbay [20] in hospitalized patients in preparation for surgical procedures. Several protocols have been published guiding inpatient insulin therapy, each of which has been associated with a low risk for hypoglycemia [21–24]. Many institutions are now turning to computerized protocols as described in the manuscript by Drs. Wei and Wexler [25] that guide clinicians in safely ordering basal-bolus insulin regimens [26, 27].

There are several caveats to use of insulin in the hospital. One is that patients who are treated with scheduled insulin therapy as an outpatient will almost always require scheduled insulin therapy as an inpatient. Discontinuation of a preadmission insulin regimen with initiation of SSI is an irrational approach that increases risk for both hyperglycemia and hypoglycemia [15, 17, 21]. Modification of the preadmission insulin regimen is often required depending on the efficacy of the home regimen, the severity of the admission diagnosis, or the ability of a patient to eat regular meals. A patient for whom all nutritional intake is withheld may require only basal insulin with a long- or intermediate-acting insulin in conjunction with correctional (supplemental) rapid- or short-acting insulin administered at defined intervals every 4 to 6 h. Patients who are eating will require scheduled prandial insulin doses if they were on this at home.

Another caveat of inpatient glycemic management relates to those patients who were treated with oral agents prior to admission or those who have newly recognized hyperglycemia. Except in the most stable of patients who are admitted for a brief elective hospitalization, oral hypoglycemic agents and non–insulin-injectable agents are not recommended for use in the hospital [18]. For patients not previously treated with insulin, it is rational to institute bedside capillary blood glucose (CBG) monitoring with use of correction insulin to treat CBG ≥140 mg/dL for the first 12 to 24 h to determine whether or not scheduled basal-bolus insulin therapy is required.

Medical nutrition therapy is an often overlooked component of rational glycemic management in the hospital setting. This important issue is nicely addressed by Drs. Gosmanov and Umpierrez [28], who discuss the application of carbohydrate counting for adjusting insulin doses in patients who are eating and apply principles of rational insulin therapy to patients receiving enteral or parenteral nutrition.

The medical definition of the adjective "intensive" is instituting treatment to the limit of safety. "Tight" is defined as affording little or no extra room or fitting too closely. Neither of these terms is suitable for an inpatient glycemic management program. However, the term "rational," which is defined as having or exercising sound judgment or good sense, is suitable for glycemic management and provides the correct adjective upon which to base an inpatient glycemic management program.

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