In Response to Carter and Heinemann: Insulin Concentration in Vials Randomly Purchased in Pharmacies in the United States: Considerable Loss in the Cold Supply Chain

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Carter and Heinemann1 recently reported that human insulin acquired from retail pharmacies averaged concentrations of ~40 U/ml, rather than the minimum 95 U/ml mandated by the Food and Drug Administration, with regular human insulin averaging <25 U/ml and NPH ~55 U/ml. We have serious reservations about the reported results and question whether they accurately describe the actual potency of pharmacy-obtained insulin.

The number of samples studied is very small (18 vials total), and the methodology for sample handling and preparation is minimally described. More important, there are serious concerns about whether the results match real-world experience and whether appropriate testing methods were used.

The results are inconsistent with our experience of using pharmacy-obtained insulin in controlled clinical studies, where the potency is clearly in line with the labeled 100 U/ml. Such alterations in potency would clearly be evident to patients, especially those frequently checking their blood glucose levels or using continuous glucose monitoring. Clinically we rarely receive complaints other than during extremes in temperature when insulin stability will be problematic.2 A more quantitative physiologic approach to assess potency would be to perform euglycemic clamp studies to assess insulin action with different insulin vials.

We also question the test methodology (their reference 2). Originally designed to identify modified insulins in plasma, it faces difficult challenges as a quantitative method and has not been validated for measurement of the large amount of insulin in commercial vials. Insulin self-aggregates, sticks to container and column surfaces, and is not very soluble in organic solvents, reducing recovery. It would be important to compare freshly manufactured and cold supply chain samples using the authors’ method, manufacturers’ methods, dual antibody immunoassays, protein content, and lyophilized weight.

We have reviewed and confirmed the quality control procedures that are strictly adhered to and documented by each manufacturer to meet FDA standards to ensure the safety, potency and efficacy of insulin throughout the supply chain. It seems highly unlikely that the insulin could degrade by any significant amount, certainly not the 75% degradation consistently found by Carter and Heinemann for regular human insulin.

The safety and reliability of commercially available insulin is of vital concern to the more than 7 million Americans who use insulin,3 and this report is understandably causing alarm. We fear that there is significant risk of harm, either in the form of patient anxiety or of outright noncompliance or misuse if patients incorrectly believe that their insulin’s potency is substantially less than it is supposed to be.

To address this concern, the American Diabetes Association is planning to work with the Juvenile Diabetes Research Foundation and the Helmsley Charitable Trust to commission an independent laboratory analysis of samples obtained from manufacturers and from retail pharmacies. We will assess insulin concentration using several laboratory methods, including that used by the authors. We hope to determine whether these findings represent a real problem in the potency of insulin available at the retail level, or if the reported results are in some way erroneous.

Declaration of Conflicting Interests

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