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ORIGINAL ARTICLES

Analysis of Studies That Compare the Dose Accuracy of Prefilled Insulin Pens

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Abstract

Multiple industry-sponsored studies have been published about the accuracy of insulin delivery using prefilled insulin pens. Although the study by Weise and colleagues in this issue of *Journal of Diabetes Science and Technology* found that the Novo Nordisk device was slightly more accurate than the Sanofi-Aventis device, one can anticipate a Sanofi-Aventis-funded study that may find the opposite, because no internationally acceptable, publicly funded, unbiased scientific organization exists to perform head-to-head comparisons of drugs and devices in an evidence-based manner. Currently, clinicians are left on their own to determine whether a study on this topic was conducted in an accurate, unbiased manner. A fundamental redesign of clinical research could reinvigorate and revolutionize the process by which innovations travel from the bench to the bedside. As we anticipate changes in healthcare in the future, it is imperative that the approval and postmarketing surveillance process is revised to support the practice of true evidence-based medicine.

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Insulin pens help overcome barriers to insulin administration. Potential benefits include improved access to supplies, less interference with day-to-day activities, ease of use, social acceptability, eliminating improper filling of syringes, discreetness of insulin delivery, and helping to overcome injection anxiety. Type 1 diabetes patients have accepted the insulin pen as a convenient means of insulin delivery, often as a step on the path toward the insulin pump. As insulin use earlier in the course of type 2 diabetes is now preferred, the potential for many type 2 patients to use insulin pen devices is great.

Multiple industry-sponsored studies have been published comparing the accuracy of insulin delivery using prefilled insulin pens.[1,2] Clinicians and patients must be able to trust the accuracy and precision of the devices, and therefore it is important that comparative studies are published assessing the accuracy of delivery. Previous studies have looked at the accuracy of such devices as the Novo Nordisk FlexPen® and the Sanofi-Aventis OptiClik® and SoloSTAR® along with Eli Lilly pen devices such as the Luxura™. Abstracts and published studies have shown that the OptiClik device is the least accurate of these pens (and therefore clinicians should discourage its use).

The study by Weise and colleagues[3] in this issue of *Journal of Diabetes Science and Technology* compared insulin delivery between the new insulin-delivery device from Novo Nordisk, the Next Generation FlexPen®, and the Sanofi-Aventis SoloSTAR (marketed as a replacement for the OptiClik). The study was conducted using a device to measure the mass of the insulin delivered with the volume then calculated from the known density of each insulin. Only insulin glargine (Sanofi-Aventis) and insulin detemir (Novo Nordisk) were studied.

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Although this study found that the Novo Nordisk device was slightly more accurate than the Sanofi-Aventis device, one can anticipate a Sanofi-Aventis-funded study that may find the opposite. The good news is that both devices performed within the International Organization for Standardization limits. The bad news is that we may have to wait a long time before an internationally acceptable, unbiased scientific organization with no conflicts of interest that is funded by public money emerges to perform head-to-head comparisons of drugs and devices in an evidence-based manner.

A number of proposals have been made since the late 1990s to redesign the process for drug and device development, including extending drug or device exclusivity if postmarketing safety studies are completed or if head-to-head (nonindustry) studies show the drug or device to have a therapeutic advantage over other similar or "me-too" drugs or devices.[4–7] In Wood's example,[4] this could lead to an "economic Darwinism," in which markets act as selection vehicles. As firms compete, unsuccessful companies fail to make a profit.[8] In this model, drug or device manufacturers would recognize the need to complete safety and postmarketing surveillance studies to lengthen the duration of exclusivity or face earlier generic versions of their drug or device, thus reducing profit. (The current process gives no economic advantage to those few drug or device manufacturers who actually complete the safety or postmarketing surveillance studies.)

The current state is that clinicians are left on their own to determine if the study handed to them by the drug or device representative was done in an unbiased manner. A fundamental redesign of clinical research, such as the National Clinical Research Enterprise,[9] could reinvigorate and revolutionize the process by which innovations travel from the bench to the bedside (see the following discussion). This project will require overcoming four challenges that are currently facing clinical research: (1) enhancing public participation in clinical research; (2) developing information systems; (3) developing an adequately trained workforce; and (4) attracting sufficient funding. This project would derive its budget from all healthcare stakeholders and would lead to systemwide improvements that would benefit the public.

Revamping the Food and Drug Administration's approval process and postmarketing surveillance also would prevent the need for the clinician to be on the lookout continuously for the sometimes subtle bias often present in industry-sponsored studies. The economic benefit to the public would be the availability of unbiased comparative studies with results that would lead to lower rates of prescribing less safe or higher-priced, less efficacious "me-too" drugs or devices. As we anticipate changes in healthcare in the future, it is imperative that the approval and postmarketing surveillance process is revised to support the practice of true evidence-based medicine.

The National Clinical Research Enterprise was first developed by an Institute of Medicine Clinical Research Roundtable with cross-spectrum input over a four year period. A public–private partnership funded by 0.25% of the budgets of all healthcare stakeholders with strong advocacy for increased funding for the National Institutes of Health, the National Clinical Research Enterprise invites public participation in the development and prioritization of research initiatives; promotes recruitment, training, and retention of clinical research trainees; mentors, promotes intersociety collaboration, promotes development and maintenance of an information technology infrastructure; and creates incentives for individuals, clinics, and hospitals to practice evidence-based medicine.[9,10]

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