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Breaking Down the Bionic Pancreas: A Device for Dosing Decisions for T1D

Dr. Buse:
Is there a way for patients with type 1 diabetes to avoid having to measure carbs and monitor their blood sugar levels? Can a bionic pancreas take care of that for them? This new device could save time for patients who have to make dosing decisions multiple times a day every day for the rest of their lives.

Welcome to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse. And here today to talk about the latest research on the bionic pancreas for type 1 diabetes is Dr. Steven Russell. Dr. Russell is an Associate Professor of Medicine at Harvard Medical School at the Massachusetts General Hospital.

Steven, thanks for speaking with me today.

Dr. Russell:
Thank you, John. It's a pleasure to be here.

Dr. Buse:
So, first, can you review the landscape of so-called sensor-augmented pump therapy? And where does this terminology, bionic pancreas, conceptually belong in that spectrum?

Dr. Russell:
Certainly. So, there is a wide range of what is considered a sensor-augmented pump. On the one end of the spectrum, there's a pump that will allow you to see CGM data, see your glucose and, perhaps, see a graph the glucose over time, but it doesn't use that information to do anything. You're still totally in control of insulin dosing. The next step would be a predictive low-glucose suspend where you control all the insulin dosing unless the blood glucose is predicted to be below a certain level, within a certain time in the near future, and the system will temporarily suspend insulin delivery to try and prevent lows. Next would be a hybrid closed-loop system in which the system can increase dosing of insulin within some sort of guardrails or decrease dosing of insulin to prevent hyperglycemia or treat hyperglycemia on the one hand and to try and prevent hypoglycemia on the other hand. And those systems, in particular, all have certain characteristics. They still have to have a set of insulin-dosing parameters programmed into them, usually at the recommendation of a healthcare provider, like a basal rate profile, carbohydrate ratio, correction factor, and then those dosing parameters are updated by the healthcare provider at intervals. Users have to count carbohydrates for meals, enter those carbohydrates, and then the dose of insulin they get is dependent on the carbohydrates entered and the carbohydrate ratio that they have programmed for that time of the day, and then the user still has to initiate correction boluses. Although the system may give partial correction boluses at intervals, to really get the best glucose control, they have initiate boluses.

And so the bionic pancreas is different in many respects. First of all, it does use the CGM information to dose insulin, but it does that starting with only the patient's weight for initialization. There's no insulin regimen programmed into it. And that weight just gives an initial dose scaling, and then the system adapts continuously and autonomously to the individual insulin needs. And the only setting is a glucose target, which is just set as usual, lower or higher. And we can get back to that a little bit later. And then there's no carbohydrate counting for meals. Meals are just announced as a breakfast, lunch or dinner. And then the meal size is "usual for me," "less" or "more," and then the system learns what amount of insulin is needed for a "usual for me" breakfast, for instance, and it will give three-quarters of the insulin it predicts as needed and then add any additional insulin automatically. So the person doesn't have to carb count.

Dr. Buse:

Fabulous. So now that we have an idea conceptually of what the bionic pancreas does, tell us about the trial. What were the key design features, and what were some of the key findings?

Dr. Russell:
Sure. Well, first of all, one of the key design elements is that it was a randomized controlled trial, meaning that people who were enrolled in the trial were randomly assigned to either continue with their usual method of insulin therapy or to go on the bionic pancreas for 13 weeks, and that usual kind of insulin therapy could be really anything. It could be multiple daily injections with a CGM or without a CGM, it could be a pump with or without a CGM, and it could be any FDA-approved predictive low-glucose suspend or hybrid closed-loop system. And if they were assigned to the control group, they would continue using that during the trial under the recommendations of their own healthcare provider, or they could go on the bionic pancreas.

In terms of the results of the study, our primary outcome was hemoglobin A1c, so we measured it at baseline and then after 13 weeks. And then we also looked at things like mean glucose and time and range and time with a CGM glucose less than 54 mg/dL or less than 70 mg/dL. And what we found at the very top line was that for people randomized to the standard of care group, meaning any insulin delivery therapy including hybrid closed-loop, their A1c at baseline was 7.7 percent, and it stayed 7.7 percent at 13 weeks. In other words, it didn't change. Not too surprising because we didn't change their method of therapy.
By chance, the group that was randomized to the bionic pancreas had a little higher A1c at baseline, 7.9 percent, and at the end of the trial, it was 7.3 percent. And when we adjusted for differences in the cohorts and calculated a baseline adjusted group difference, it was a reduction for the average A1c of -0.5 percent, and that was highly statistically significant. And we found that that reduction was the case in children—they had an average reduction of 0.5 percent—and in adults, who also had an average reduction of 0.5 percent. And if we looked according to the baseline hemoglobin A1c, what we found is that the higher the baseline A1c the larger the reduction in A1c, so people who had an A1c of less than 7 had very little difference in their A1c at the end of 13 weeks in the bionic pancreas group, but people who had their A1c be significantly higher. For instance, in children, if they had a baseline A1c of greater than 9 percent, they had a reduction of more than 2 percent in their A1c. And then we were able to do that without increasing the amount of hypoglycemia, so the time less than 54, was no different between the people who continued on the standard of care group and the people who were randomized to the bionic pancreas, so we were able to reduce A1c and also, by the way, reduce mean glucose and increase time and range but without increasing hypoglycemia.

Dr. Buse:
Wonderful. Were there any signals regarding safety issues or adverse events?

Dr. Russell:
So there was no DKA events. There were severe hypoglycemia events in both arms of the trial, so both in the standard of care and the bionic pancreas arm. There was no statistically significant difference in the number of events between those 2 arms, and the rate of events was actually lower than what the T1D Exchange has found as the population rate of severe hypoglycemia events.

Dr. Buse:
Wonderful. For those just tuning in, you're listening to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse, and today I'm speaking with Dr. Steven Russell about the research he and his team published on the bionic pancreas in type 1 diabetes recently in The New England Journal of Medicine.

Now, as you mentioned, at the end of the trial, the mean A1c was 7.3 percent. How do you feel about that? Is that, you know, is that what you were hoping for? Does it relate at all to the device targeting a particular level of glucose?

Dr. Russell:
Sure. So, you know, obviously, we would like to have gotten everyone in the bionic pancreas group to have an A1c of less than 7 percent or to meet goal for therapy, but we just don't think that that is realistic with a bionic pancreas that just delivers insulin, and that's kind of consistent with what has been shown in other trials of hybrid closed-loop devices. The most analogous one is the trial of the Control-IQ system, which also used a randomized controlled design, and they saw a similar final hemoglobin A1c in their intervention group. They actually had a little bit lower A1c at baseline than our cohort did, and they saw a 0.3 percent reduction in hemoglobin A1c, whereas we saw a 0.5 percent reduction in hemoglobin A1c. So, we actually saw a larger reduction despite the fact that our system requires less input from the healthcare provider and the user. We see that as a positive thing.

In order to get even better glucose control than that, we think it's going to be important to add an additional drug, and that is glucagon. So we've done pre-pivotal studies where we tested a different version of the bionic pancreas that uses both insulin and glucagon. And in that context we can be a little bit more aggressive with dosing insulin, whereas we find in our pre-pivotal studies that we can get about 40 to at most 50 percent of people meeting goal for therapy, with the bihormonal bionic pancreas. Using glucagon we can get more like 90 percent of people with an A1c less than 7 percent. And so we are planning to do a large pivotal study of the bihormonal configuration

of the bionic pancreas in the future.

Dr. Buse:
Thank you. What's next for this insulin-only bionic pancreas? How close are we to having clinical application?

Dr. Russell:
Well, Beta Bionics, the company that is producing and developing the iLet Bionic Pancreas clinically, has submitted the data from the pivotal trial to the USFDA in what's called a 510(k) application, and that is currently under review. So based on when the FDA makes a final decision that will determine the timing of the availability of the bionic pancreas for people with diabetes.

Dr. Buse:
Well, fingers crossed. Before we close for the day, any final thoughts you'd like to leave with our audience?

Dr. Russell:
Well, one thing I would say, we appreciate your help with this study. We talked about the clinical sites, and you were kind enough to lead one of the clinical sites, so we really appreciate that. We also appreciate the help of all the people living with diabetes who volunteered for the trial and participated in the trial. And we're very much looking forward to being able to let folks who use the device in the trial use it again because many of them expressed a desire to do that, and to make it available for a larger population of people with diabetes who might appreciate what it offers.

Dr. Buse:
Yeah. Well, thank you for those kind words. You know, the participants in these trials really enjoyed the study, and are looking forward to the bihormonal trial coming up, and I just comment that in general, many patients found it so liberating not to have to do so much math in their head, and just say small, medium, or large meal.

With those interesting thoughts in mind, I'd like to thank my guest, Dr. Steven Russell, for being here to explore the potential role of the bionic pancreas in managing type 1 diabetes. Steven, it was great speaking with you today.

Dr. Russell:
Thank you very much for having me, John.

Dr. Buse:
For ReachMD, I'm Dr. John Buse. To access this episode and others from our series, visit ReachMD.com/DiabetesDiscourse where you can be Part of the Knowledge. Thanks for listening.