

Paediatric diabetes care 100 years after insulin discovery – closer to closing the loop but still yearning for the cure

Cukrzyca u dzieci i młodzieży 100 lat po odkryciu insuliny – coraz bliżej zamknięcia pętli, ale wciąż z utęsknieniem czekamy na wyleczenie

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When more than 25 years ago I started to work with children with type 1 diabetes I hoped (or at some moments even believed!) that at the 100th anniversary of insulin discovery there would be a cure for them and insulin will not be necessary any more. One of the reasons for that I thought so was that during several months of my internship in Paris in 1995, I had the opportunity to see children with type 1 diabetes participating in a promising study in which cyclosporine was tested (we hoped it would stop autoimmune destruction of pancreatic β cells), and later me myself (not having diabetes), together with several other young colleagues from Professor Jerzy Bodalski's team from Lodz, we received subcutaneous insulin in an initial part of a French study testing the usefulness of insulin in pre-diabetes (the idea behind was to initiate immune tolerance). Years passed, and despite the fact that also in the next decades therapies designed to protect insulin secretion (sophisticated, like anti-CD-3 antibodies or T-regulatory cells and more simple, including the very early use of oral insulin), poly-therapies combining drugs with different mechanisms of action, as well as stem cell-derived beta cells have been extensively studied and some of them seemed to be promising, still today in a hospital room, when talking to a parent of a child with newly diagnosed type 1 diabetes I am forced to say that for their small one we do not have any other effective medicine apart from insulin administered by pen or pump [1–3]. Of course, I immediately point out that researches are ongoing worldwide and we are still waiting with great hope for an effective therapy, which should appear, but... Insulin still remains with us.

Parallel to this thread, in my opinion, as an activity ancillary to the search for diabetes cure (and if we were to look at it in perspective of a paediatric diabetologist practicing in 1990s somehow surprisingly), there has been work going on to technically improve the way of insulin use. And this attempts succeeded earlier. The clinical use of insulin pumps started in the 1970s–1980s and they have been very much improved over the next decades. Later we witnessed the development of continuous

glucose monitoring (CGM) systems and their broad incorporation into clinical practice in 21st century. It turns out that today we are at the stage when it is still insulin, together with sophisticated technological solutions that improve the treatment effects and quality of life of many people with type 1 diabetes and their families. Insulin still remains with us, however its formulations were greatly improved. For young generation of physicians animal insulin preparations (bovine or pork) belong to the annals of medical history. Now, we have modern, long acting insulin analogues available and regular (i.e. short acting) human insulin preparations have been more and more willingly replaced with rapid acting insulin analogues as they more effectively control postprandial glucose levels [4]. In the last years, also ultra-rapid insulin analogues entered the market. Rapid acting and ultra-rapid insulin formulations seem to be especially welcome in the context of new technological solutions, as they have been to some extent a prerequisite for the exploitation of the present capabilities of insulin pumps and in particular of the systems at various stages of the artificial pancreas development.

Besides waiting for a cure, we are therefore benefiting for our patients, as broadly as possible, from what is nowadays offered by CGMs, insulin pumps, related software, as well as by “closed loop” systems that connect them (i.e. “artificial pancreas” – type devices). I appreciate not only the advanced hybrid closed loop systems (which unfortunately are not available for everyone) but also the predictive low glucose suspend and low glucose suspend devices. Also CGM systems, especially these with real-time alerts, have their very significant position here and, as shown in this issue by Kowalczyk *et al.*, in respect to glucose control measures, may be beneficial especially for the youths with inadequately controlled diabetes (with $HbA_{1c} > 7\%$) [5].

These mentioned above devices, in particular advanced hybrid closed loop systems, which control glucose levels not only adapting basal insulin delivery but also delivering automated correction boluses, when embraced well by users, ease their

lives, and for many may enable to reach life with less diabetes-related burden. This is especially due to experiencing less episodes of hypoglycaemia and more sleepy nights, together with less fright about chronic complications in the future because time in glucose range (TIR), HbA_{1c} and glycaemic variability improve [6, 7]. However the users of these systems and/or their caregivers still need thorough specialized education. They have to learn and practice how to operate these sophisticated device/s and dedicated software and they still need to count carbohydrate content of meals and enter them into the pump (at least for the systems that are publicly available today). They have to know what is the correct timing for meal insulin boluses (also when more rapid insulin formulations are used), how and when to modify the device settings or how to prepare for physical activity. They still have to be very familiar with a conventional blood glucose meter and remember how to prevent and treat hypoglycemia. Moreover it is very important that they know how to operate the pump using only its basic functions (i.e. what to do to prevent and manage low or high glucose levels without pump cooperation with real-time CGM), how to troubleshoot technical problems in case of the pump or other elements malfunction (including problems with wireless communication between the system units), how to calculate insulin doses for meals (and for hyperglycaemia) and how to use simple pen injectors (how to operate them to set and inject correct insulin doses). Education must be implemented initially, when any artificial pancreas system is started and then it should be continued as an ongoing diabetes education, like for patients who use more conventional therapies. Such education and care should be provided by diabetes therapeutic team members including diabetes educators/nurses, dietitians, psychologists and physicians, who often cooperate also with social workers and other specialists. Education and ongoing support, also psychological, may play a role in correct embracement of

any diabetes technologies into daily life and publications like the one by Kowalczyk *et al.* [5] may prompt us that technology itself is not enough and patients and caregivers should still pay attention to the conventional elements of the diabetes management “puzzle”: healthy eating, estimating carbohydrate content of meals, correct timing of insulin boluses in relation to meals, and even carrying glucose tablets always with oneself. Introduction of any new diabetes technology in a particular patient should not be an excuse for her/him for not doing so.

In Poland paediatric diabetologists and their patients are privileged compared to the diabetologists caring for adult people with type 1 diabetes – most of the children and many young adults (by age 26) may get a “simple” insulin pump for free and reusables for pumps and (under several conditions) also for CGMs are at least partly reimbursed for many of them. We and our young patients are in this respect really lucky! Though there is still a lot of work to be done to remove diabetes-related burdens with a really closed glucose-insulin loop, one has to admit that diabetes technologies that are available now, when compared with glucose meters and pen injectors or conventional insulin pumps used in the preceding decade, changed lives of our patients and their caregivers a lot.

Therefore we can all – people who are with diabetes every day i.e. patients and their family members and people who are close to these with diabetes most of the days i.e. diabetes therapeutic teams’ members – consciously enjoy what was already achieved in diabetes care in Poland and what we already have for our disposition now. Many thanks to those who have accomplished this! Yet we still have in the back of our minds that the available technical solutions are just another step in the quest to conquer type 1 diabetes. I think that as a lot was already done in respect to artificial pancreas within the last decade, a meaningful medication/s or a cure for type 1 diabetes must also come soon and this let be our hope for the next decade.

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