



Normoglycaemic control with a selfmade fully closed-loop insulin delivery system during emergency surgery: an extemporaneous stress test

Andreas Holstein¹ · Bruno Bolli²

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Dear Editor,

Hybrid closed-loop insulin delivery systems have entered clinical use and progressed from supervised safety trials [1] to free-living home studies [2]. In 2017, the Federal Drug Administration (FDA) approved the first hybrid closed-loop system [3] making the “Artificial Pancreas” a realistic therapeutic option for an eligible proportion of people with type 1 diabetes mellitus (T1DM). Hybrid closed-loop insulin delivery systems are characterized by continuous glucose monitoring and algorithm-directed insulin pump delivery providing automatically the basal insulin requirement. However, in contrast to a fully closed-loop approach, prandial insulin boluses need still to be carried out by the patient himself.

Generally, affected people are frequently impatient with the progress of medical developments, completion of clinical trials or final regulatory approvals. Some individuals try to improve and advance medical technology more rapidly by themselves. In particular, there is an increasing worldwide community of people with T1DM who provide an internet-based open source to make closed-loop technology more widely available and to empower people to build their own system [4]. Cautiously, it can be estimated that there are approximately 3,000 people worldwide using such selfmade hybrid closed-loop systems.

To the best of our knowledge, we report the first case in which a patient used a selfmade fully closed-loop insulin delivery system on his own responsibility and without medical supervision within the framework of an emergency surgery. This male 57-year-old self-employed designer with a 36-year history of uncomplicated T1DM performed therapy with CSII for over 16 years. In October 2017, he built his own fully closed-loop insulin delivery system comprising a real-time glucose sensor (modified FreeStyle Libre® with XDRIP software and a MiaoMiao-Transmitter), an insulin pump (ACCU-Chek Spirit Combo®), and a standard enjoyed mobile phone device containing the control algorithm (Software Android-APS). Basal insulin requirement as well as meal-related insulin boosts—after previous input of prandial glucose amount—were automatically delivered. The pre-set glucose threshold was 90 mg/dl (5.0 mmol/l). According to his self-disclosure, he did not experience any events of hypoglycaemia (<70 mg/dl; <3.9 mmol/l) and in particular no severe episodes.

In an early evening in December 2018, the patient suffered from acute, increasingly severe pain in the epigastrium. Four hours later, he was admitted to the hospital. Initial pain management with piritramid intravenously was necessary. Clinical and laboratory findings showed significant pressure pain in the right upper abdomen and elevated biomarkers of inflammation: leucocytes of 17.0 /nl and C-reactive protein of 4.6 mg/dl (reference <0.5 mg/dl). The current HbA1c was 5.9% (reference <6.0%). Abdominal ultrasound revealed multiple gallstones with criteria of acute cholecystitis. Thus, approximately 15 h after the onset of pain, an early laparoscopic cholecystectomy was performed also confirming histologically the diagnosis of acute ulcerous gangrenous cholecystitis. The postoperative course was unremarkable and the patient was discharged from the hospital after 4 days.

Managed By Antonio Secchi.

✉ Andreas Holstein
Andreas.Holstein@klinikum-lippe.de

¹ First Department of Medicine, Lippe-Detmold Hospital, Röntgenstr. 18, 32756 Detmold, Germany

² WeAreNotWaiting / User of closed loop with AndroidAPS, Corneliusstr. 2a, 32791 Lage, Germany

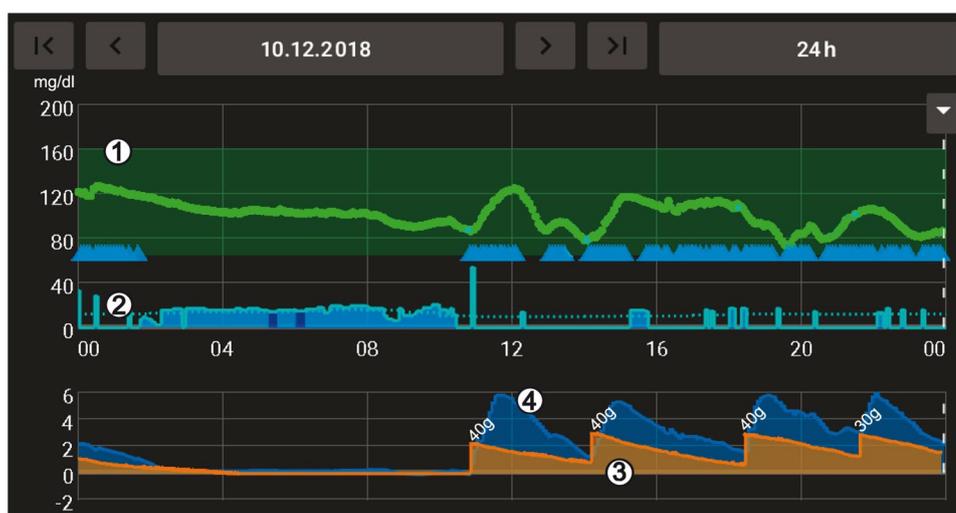
Severe intercurrent illnesses or the perioperative state, respectively, represent a thorough testing for any diabetes therapy. Therefore, the extemporaneous perioperative use of a fully closed-loop insulin delivery system was a stress test for this technology. Completely relying on his system, the patient was carrying all the risks of his self-experiment.

In everyday life, the normal basal insulin rate consisted of 22.9 I.E. insulin lispro per 24 h with an additional meal-related requirement of approximately further 23 I.E. (Fig. 1). After onset of pain and during the day of emergency surgery, there was no oral carbohydrate intake at all. Nevertheless, the automatic basal insulin delivery was increased by 14.6 I.E.–37.5 I.E./24 h (+ 157%). Temporarily, the basal insulin amount was even raised up to 500% which is the maximal deliverable basal insulin amount of this particular insulin pump. Figure 2 demonstrates the blood glucose control as well as the automatically delivered amounts of insulin over

the pre- and perioperative course. The mean blood glucose concentration was 128.1 ± 16.3 mg/dl (7.1 ± 0.9 mmol/l), and the time in target range was 99%. During abdominal surgery, the insulin infusion set had to be placed at the thigh. Perioperatively, close blood glucose monitoring was also carried out by the anaesthesiologist via an Accu-Chek® Inform II System providing a laboratory accuracy. All these measured values were also in the normoglycaemic range and comparable to the results of the continuous glucose monitoring.

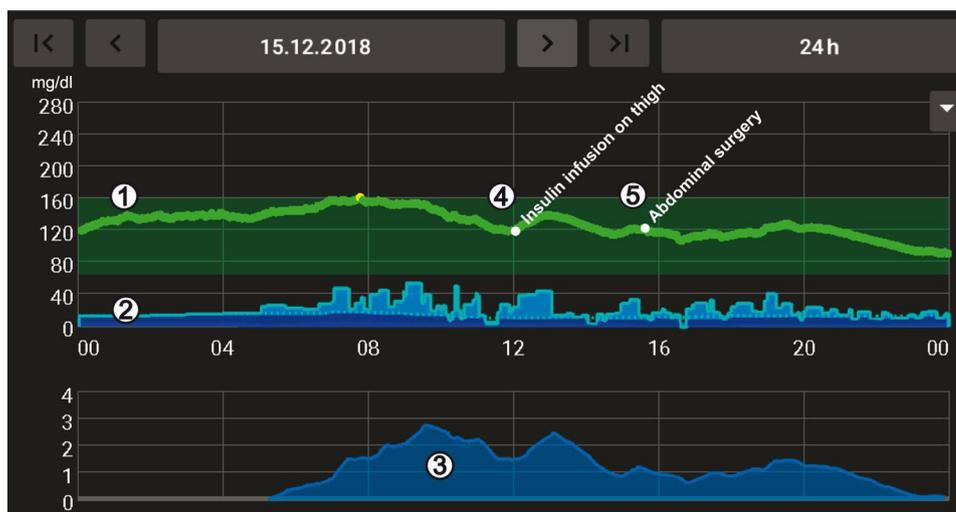
So far, fully closed-loop insulin delivery systems have not been approved. Furthermore, we have no published data about the extemporaneous use of this technology in the context of emergency procedures or the perioperative setting. To date, there is only a single randomized controlled study conducted on general wards in tertiary hospitals evaluating the glycaemic control and safety of hybrid closed-loop insulin

Fig. 1 Insulin requirement, carbohydrate intake and glycaemic control before surgery under everyday conditions using a selfmade fully closed-loop insulin delivery system. (1) Blood glucose concentration measured by continuous glucose monitoring (CGM-xDrip). (2) Basal insulin delivery of 22.9 I.U./24 h. (3) Carbohydrate intake. (4) Corresponding prandial insulin boluses



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Fig. 2 Glycaemic control and insulin requirement in the perioperative setting and during abdominal surgery using a selfmade fully closed-loop insulin delivery system. (1) Blood glucose concentration measured by continuous glucose monitoring (CGM-xDrip). (2) Basal insulin delivery. (3) Additional insulin requirement after onset of pain and during the day of emergency surgery. (4) Switch of the insulin infusion set from abdomen to the thigh. (5) Abdominal surgery (laparoscopic cholecystectomy)



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delivery systems in patients with T2DM receiving non-critical care. Compared with conventional insulin therapy, the use of a closed-loop system resulted in a significantly better glycaemic control [target ranges 65.8% versus 41.5%; mean glucose levels 154 mg/dl (8.6 mmol/l) versus 188 mg/dl (10.4 mmol/l)] without increasing the risk of hypoglycaemia [5].

Irrespective of the successful and safe application of a fully closed-loop insulin delivery system in the context of perioperative setting, our case raises serious general concerns. At first, these do-it-yourself (DIY) systems are not approved by any regulatory authorities. Consequently, the assumption of treatment costs remains open. Furthermore, malfunctions can cause life-threatening metabolic disturbances, in particular severe hypoglycaemia or diabetic ketoacidosis. Last but not least, if the worst case scenario with serious physical harm occurs, who will be considered to be criminally responsible and will bear the subsequent costs? What is the role of the treating diabetologist?

Undoubtedly, further register data are required to summarize systematically benefits and risks of uncontrolled application of these selfmade systems. Nevertheless, whether we like it or not, we have already progressed into a new era in which people with diabetes themselves are important pioneers in advancing the technology of “Artificial Pancreas”.

Compliance with ethical standards

Conflict of interest The authors declare no duality of interest.

Human and animal rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent The patient gave his signed consent for the material presented in the publication.

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