Original Work

TL;DR – Insulin Pumps and A Case of Mistaken Insulin Identity

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The pharmacotherapy department at SSM Health-Monroe Clinic Medical Group was established in 2007 and is an independent department of pharmacists, residents, and medical assistants working under a collaborative practice agreement to manage a wide range of chronic disease states including but not limited to: anticoagulation, diabetes, hypertension, lung disease, and pain management. Based in Monroe, Wis., they serve many patients living in rural areas in both Wisconsin and Illinois.

Overview of Insulin Pump Management and Definitions

Insulin pumps are one of many insulin delivery devices available for patients with diabetes mellitus. They are most often used by patients with type-1 diabetes but are also occasionally used by patients with type-2 diabetes. Insulin pumps provide a continuous delivery, or basal rate, of rapid-acting insulin such as insulin aspart (Novolog™ or Fiasp™) or insulin lispro (Humalog™). Additionally, they provide mealtime or prandial insulin in the form of bolus doses of the same type of insulin. Medtronic® and Tandem® are two of the most popular manufacturers of insulin pumps in the United States. Both have models that function as a pseudo-artificial pancreas when connected to a continuous glucose monitor (CGM). This means the insulin pump will adapt and predict the patient's insulin needs based on their sensor glucose readings provided by the CGM device. This technology has significantly advanced the field of insulin pump management and pharmacists are well-positioned to be able to manage these patients with their strong foundational knowledge of insulin pharmacokinetics and attention to detail. See Table 1 below for additional terminology that is used through the remainder of this case report.

Meet the Patient

A 73-year-old with type-1 diabetes and hypoglycemia unawareness was seen in office for routine follow-up. The patient uses a Medtronic MiniMed 770G™ insulin pump with a Medtronic Guardian™ continuous glucose monitor (CGM) and the Auto Mode feature to adjust basal rates.

TABLE 1. Terms and Definitions for Insulin Pump and Diabetes Management

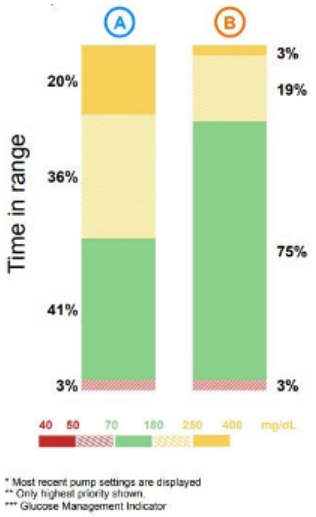
Term	*Definition*
Basal rate	Continuous insulin delivery of rapid-acting insulin via an insulin pump
Bolus dose	A programmed or scheduled dose of insulin administered immediately prior to mealtime (e.g., units/hour)
Continuous glucose monitor (CGM)	A sensor that inserts a small microfilament under the skin to measure glucose concentrations in the interstitial fluid. Readings are connected via Bluetooth to a device to collect and analyze trends.
Carbohydrate ratio	The grams of carbohydrate consumed that are treated by 1 unit of insulin
Correction factor	The amount of glucose (measured in mg/dL) corrected by 1 unit of insulin, sometimes referred to as insulin sensitivity
Active insulin	The amount of insulin presently at work in the body, often estimated using an assumed end point based on kinetics of the insulin (commonly 4 hours)
Manual insulin delivery	Basal insulin delivered at a pre-determined rate (units/hr) during specified periods of time (e.g., between 8 a.m. and 11 a.m). Referred to as Manual Mode by Medtronic.
Automated insulin delivery ("smart" basal)	An algorithm taking several variables into account (e.g., insulin sensitivity, active insulin time, current sensor glucose and rate of change, etc.) to establish or adjust basal insulin delivery. Referred to as Auto Mode in our case report.
Bolus calculator	A pump feature that supplies a bolus suggestion for patient-entered carbohydrate consumed, current sensor or blood glucose, and pump-estimated active insulin. Referred to as Bolus Wizard™ throughout our case report.
Glucose Management Indicator (GMI)	The A1c value associated with a given average sensor glucose. Analogous to A1c and estimated average glucose.
Time in Range (TIR)	A percentage of time spent within target range for sensor glucose (70-180 mg/dL); American Diabetes Association guidelines recommend a TIR > 70% for most patients.

Their pump is synced via cell phone to the clinic's CareLink™ account, which is a browser-based software for handling pump and sensor data. Historically, the patient has had a controlled A1c for their goal of less than 7.5% and spends over 70-80% of time in their target range (70-180 mg/dL). They also spend between 2% and 8% of time low (<70 mg/dL) and no time below 50 mg/dL. At this visit, the patient did note their glucose control had slightly worsened with no clear etiology. The patient felt their sugars were not responding adequately to bolus doses; therefore, insulin sensitivity and carbohydrate ratio pump settings were adjusted. A routine follow-up was scheduled months out, given the patient's history of good A1c control. Approximately two weeks later, however, the patient called to report ongoing elevations starting after breakfast. Available sensor data was reviewed online, and a trend of recurring early morning hypoglycemia is also noted. The patient was offered a telehealth appointment the next day to address these concerns.

Sensor Glucose Trends & Identifying the Culprit

To prepare for the telephone visit, the patient's chart, prescription fill history, and online CGM and pump report were reviewed (see Figure 1). According to CareLink™, the patient's total insulin requirements had increased over 50% from an average of 20.9 units per day to 36.8 units per day. Additionally, the patient's time in range had decreased from 75% to 41%, further supporting evidence of worsening sensor glucose control. The patient's lack of response to their bolus dose was apparent and worsening despite the adjustments that were made to the carbohydrate ratio and correction factor weeks prior. They were experiencing frequent overnight and early morning hypoglycemia in the preceding 14 days, which normally indicates heavy-handed basal rates; however, use of Auto

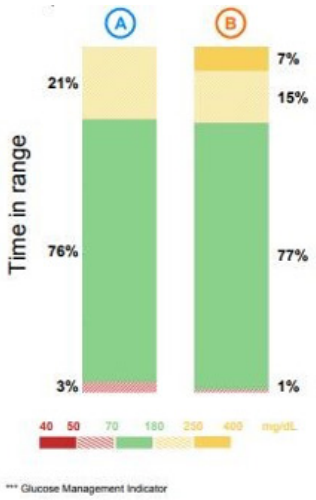
FIGURE 1. Initial Carelink Report
Time in Range, Auto Mode Summary, and Insulin Requirements from telemed visit. Blue (A) results are most recent, red (B) is his baseline (months prior).



Auto Mode Exits	A	B
No Calibration	• 1	0
High SG Auto Mode Exit	+ • • • • • 10	1 •
Auto Mode max delivery	• • • • 4	0
Auto Mode min delivery	• 1	1 •
BG required for Auto Mode	• 1	0
Sensor Algorithm Underread	• • • • 4	0
Sensor Updating	0	0
No SG values	• • 2	2 • •
Sensor Expired	0	0
Auto Mode disabled by user	0	0
Alarms	0	0
Pump Suspend by user	0	0
Auto Mode Warm Up	0	0
Unidentified	0	0

Statistics	A	B
Auto Mode (per week)	92% (6d 10h)	99% (6d 22h)
Manual Mode (per week)	8% (14h)	1% (02h)
Sensor Wear (per week)	96% (6d 17h)	98% (6d 20h)
Average SG ± SD	187 ± 66 mg/dL	146 ± 48 mg/dL
GMI***	7.8%	6.8%
Coefficient of Variation (%)	35.5%	33.2%
Low / High SG Alerts (per day)	3.1 / 6.5	3.4 / 1.7
Average BG	217 ± 69 mg/dL	181 ± 55 mg/dL
BG / Calibration (per day)	13.6 / 3.4	9.5 / 3.6
Total daily dose (per day)	36.8 units	20.9 units
Bolus amount (per day)	17.7U (48%)	11.4U (55%)
Auto Basal / Basal amount (per day)	19.1U (52%)	9.5U (45%)
Set Change	--	--
Reservoir Change	Every 2.2 days	Every 5.0 days
Meal (per day)	9.6	7.4
Carbs entered (per day)	214 ± 61 g	150 ± 42 g
Active Insulin time	4:00 hrs	4:00 hrs

FIGURE 2. Follow-up Carelink Report
After patient had resumed utilization of insulin aspart in their pump. Blue (A) results are most recent, red (B) is his baseline (months prior).



Auto Mode Exits	A	B
No Calibration	0	0
High SG Auto Mode Exit	0	3 • • •
Auto Mode max delivery	0	1 •
Auto Mode min delivery	0	0
BG required for Auto Mode	0	0
Sensor Algorithm Underread	0	0
Sensor Updating	0	0
No SG values	0	1 •
Sensor Expired	0	0
Auto Mode disabled by user	0	0
Alarms	0	0
Pump Suspend by user	• 1	0
Auto Mode Warm Up	0	0
Unidentified	0	0

Statistics	A	B
Auto Mode (per week)	10% (17h)	98% (6d 21h)
Manual Mode (per week)	90% (6d 07h)	2% (03h)
Sensor Wear (per week)	98% (6d 20h)	98% (6d 21h)
Average SG ± SD	139 ± 43 mg/dL	152 ± 49 mg/dL
GMI***	--	--
Coefficient of Variation (%)	--	--
Low / High SG Alerts (per day)	2.0 / 0.3	1.0 / 2.0
Average BG	161 ± 49 mg/dL	196 ± 74 mg/dL
BG / Calibration (per day)	6.9 / 3.0	8.9 / 4.0
Total daily dose (per day)	20.9 units	20.8 units
Bolus amount (per day)	11.4U (55%)	12.5U (60%)
Auto Basal / Basal amount (per day)	9.5U (45%)	8.3U (40%)
Set Change	--	--
Reservoir Change	Every 3.0 days	Every 5.0 days
Meal (per day)	5.3	7.9
Carbs entered (per day)	147 ± 30 g	168 ± 29 g
Active Insulin time	4:00 hrs	4:00 hrs

Mode typically prevents this by pausing administration of insulin.

The final piece of the puzzle fell into place upon review of their prescription fill history. The clinic uses Epic® electronic health record software, and data on fill history is available via Surescripts™. The patient's last refill for their pump insulin, insulin aspart (Novolog™), was almost six months prior. Interestingly, the patient's backup insulin, insulin detemir (Levemir™), had been filled twice in the past couple of months. This was immediately suspicious, as the patient had not reached out to the clinic to report any recent insulin pump failures. This information, along with the glucose trends, would seem to support the possibility that insulin detemir was being used in the insulin pump instead of insulin aspart.

During the telephone call, the patient was asked to read off the label of the insulin they used to fill their pump. They confirmed they had used insulin detemir and had no insulin aspart at home. Education was provided to the patient regarding the difference between the types of insulin and how this related to their current glucose readings. The pump manufacturer was contacted for advice on transitioning the patient's insulin safely back to insulin aspart and how to re-initiate Auto Mode.

The patient was advised to pick up a new prescription for insulin aspart and conduct a complete set change (tubing, reservoir, and infusion site). Next, the patient was instructed to suspend delivery of insulin until the following morning (about 24 hours) because they still had active basal insulin in their system in the form of insulin detemir. For mealtime bolus doses, the patient was instructed to resume insulin only while the bolus infused and then suspend again.

The patient was advised to wait until the next day to resume basal insulin delivery using manual mode for at least six days; this recommendation was provided by the Medtronic representative. This was to allow the pump time to re-learn the patient's basal insulin needs. As an additional safety measure to prevent hypoglycemia, the patient was instructed to turn on the "suspend before low" setting, which is normally deactivated while using Auto Mode. Teach-back was utilized to gauge patient understanding of these complicated instructions given via a telehealth visit.

The patient was contacted the next day to ensure they had successfully resumed delivery of basal insulin. By that time, sensor glucose trends had already significantly improved (see Figure 2). Daily insulin requirements had returned to baseline of 20.9 units/day, and time in range had improved from 41% the day prior to 76%. At the time of this writing, the patient has not contacted the department with any issues and is planning to follow up as previously scheduled.

Discussion and Recommendations

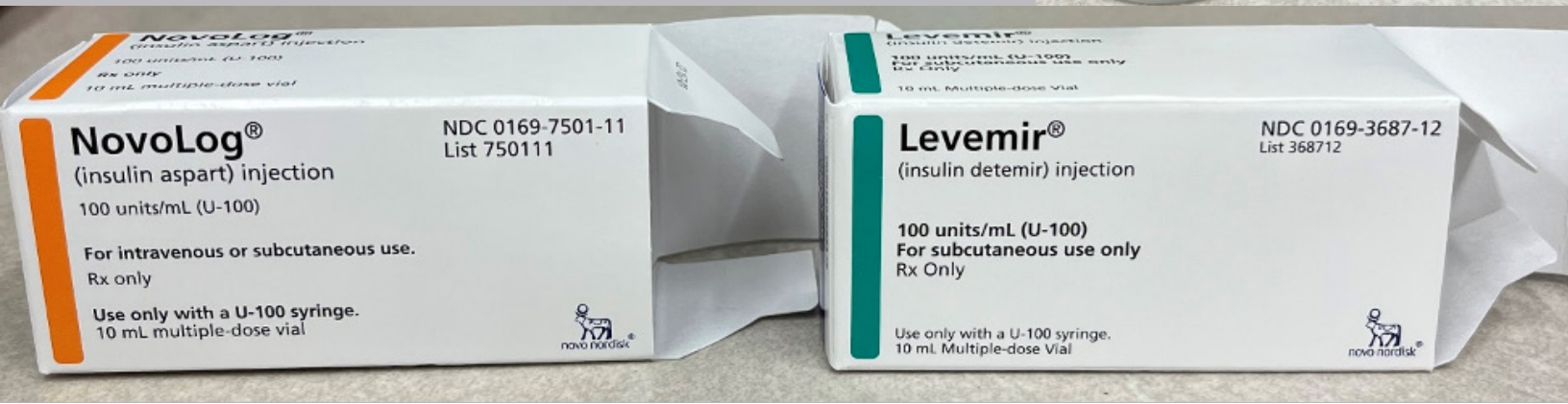
While working up the case, case reports or guidance on accidental use of long-acting insulin in an insulin pump were not readily found. This case offers good examples of the clinical features with which a patient using long-acting insulin in their insulin pump with "smart basal" may present. A patient with glucose readings slow to respond (or unresponsive) to boluses and recurring hypoglycemia despite pauses in basal insulin should prompt inquiry about the type of insulin they are putting into their pump.

This case also illustrates the importance of clear communication among providers, pharmacies, and patients. This patient has been managing their insulin with the same insulin pump for many years. This begs the question, "What went wrong in this case that can be prevented in the future?" It is important not to point the finger at any one person for this outcome. Instead, let us look at the layers of errors and anomalies that aligned to allow this to occur.

First, Levemir™ and Novolog™ are made by the same company, Novo Nordisk®, and have nearly the same packaging except for color-scheme, as seen in photos to the right and below. Unfortunately, color was not enough of a distinguishing factor for our patient to identify the difference in this case. Additionally, both of this patient's insulins were prescribed in vials. If insulin detemir pens had been utilized instead, the patient would have had to take additional steps to be able to put this insulin into his pump, and it would have provided a visual difference between the two types of insulin.

Right: *Novolog® vs. Levemir® Vials (Image source: Author)*

Below: *Novolog® vs. Levemir® Packaging (Image source: Author)*



Another consideration with this approach is the added benefit of providing five different back-up treatments per package, whereas a vial of insulin (even if only used once) should be discarded if the contents are not used within a month.

If cost is a limitation to prescribing insulin pens, clues can still be provided in prescription instructions and on the prescription label itself. Prescribers are encouraged to clearly indicate the rapid-acting insulin is "for use in insulin pump" to help pharmacies identify a pump patient. For long-acting insulins, including the phrases "In case of pump failure" and "Not for use in insulin pumps" on the label may also deter accidental use by this route. Technicians who have identified a pump user may wish to verify what type of insulin the patient is requesting when they ask for their generic "insulin" refill.

In conclusion, insulin pump management is very complex and requires careful coordination among providers, dispensing pharmacies, and patients to ensure safe and effective insulin therapy. The authors hope that through sharing their experiences, a future similar event may be prevented.

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PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Disclosure: The authors declare no real or potential conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts and honoraria.

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