



Commentary

Unexpected Hyperglycemia? Check the Pen and Needle! An Opportunity to Prevent Injection Technique Errors and Find Causes and Possible Solutions

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Abstract

The clinical case presented demonstrates how a person living with type 2 diabetes and treated with insulin reuses the same pen needle several times to save money and performs an incorrect maneuver while screwing the needle, which breaks, remains stuck at the end of the pen, and causes loss of insulin during subsequent use. The findings in this case study are observed in many others in clinical practice but have only been sporadically published. Who is responsible for incorrect injections? Indeed, health workers, diabetic patients, and all the other actors involved in diabetes care and insulin utilization share responsibility. Recommendations and guidelines are not enough to fill this gap. Moreover, not all healthcare providers (HCPs) know or adhere to them. It is observed daily that more than half of insulin users make mistakes that affect glycemic control, increase the risk of complications, and reduce the quality of life of people living with diabetes, who, by a rough estimate, make up a population of over 100 million in the world. This case study offers us the opportunity to briefly review the literature on the most common errors made during insulin injection technique and, therefore, consider how necessary it is to promote structured and coordinated actions among various actors to promote the culture of therapeutic education.

Keywords: diabetes; errors in insulin administration; injection technique; education



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1. Premises

The compelling goal of insulin treatment is to achieve optimal glycemic control. To achieve this, current standards use various insulin preparation strategies designed to mimic hormone secretion as closely as possible. However, despite making available products increasingly close to "physiology", fast-progressing technology is not enough for treatment to be effective. Indeed, to administer insulin correctly and manage the disease effectively, people with diabetes (PwDs) must learn a complex sequence of actions. Despite this, data from the literature documents that at least half of PwDs perform injections inadequately and sometimes make significant technical errors, causing a series of harmful health effects, including ecchymoses, lipodystrophies, and skin infections [1–4].

Although recommendations on correct injection techniques are available [2,3], and in recent years, many researchers have published clinical trials, case series, case reports, reviews, and meta-analyses on this topic, the frequency of cutaneous lipodystrophies

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continues to suggest that this literature has not had a real impact on clinical practice. Indeed, injection errors continue to exist with harmful consequences for health, including wide glycemic variability and unpredictable hypoglycemia [1,4].

In light of this scenario, the following questions arise: (i) Is knowledge of correct injection techniques effectively transmitted by healthcare providers to PwDs? (ii) Who are the professional figures responsible for educating PwDs on correct insulin handling? (iii) Who checks, and when, that PwDs have truly understood the indications received and can apply them? (iv) How do PwDs experience the moment of injection? (v) What are the most frequent injection errors?

Starting from this last point and reporting a clinical case of an injection technique error, we extend the investigation from types of errors, as explored in our recent case study on insulin-treated PwDs, to verify whether, in the absence of careful and regular checks, unexpected injection errors occur even in PwDs who are followed up by a care team who are convinced of their educational skillfulness. We then searched the literature for examples of injection errors—reporting the most frequent ones—and the documented abilities of the actors involved in treating PwDs, realizing that there is still a strong need for improved knowledge, attitude, and behavior toward injection techniques. Finally, we reported some statements expressing emotions felt by PwDs at the beginning of insulin therapy, with the intention of describing the previously ignored emotional burden that patients experience during the initial disease acceptance phase after diagnosis. All this aims to promote the interest of professionals caring for PwDs, in an effort to prevent injection technique errors by encouraging more substantial personal involvement and mitigating psychological reactions that affect the cognitive ability of people living with a challenging chronic disease.

2. Clinical Case

We report the case of a 72-year-old man living with type 2 diabetes (T2D) for 15 years. His BMI was 25.8 kg/m^2 , HbA1c 9.4%, fasting C-peptide 0.4 ng/mL, and serum creatinine 1.0 mg/dl. After starting on basal-bolus intensive insulin treatment (a fast-acting meal analog three times a day and bedtime insulin glargine), he had to progressively increase his daily dose from 30 IU/day to 62 IU/day (up to 0.82 IU/kg) because of persistent, high fasting and post-meal blood sugar levels (>320 mg/dl) with 9 kg of weight loss experienced in the last six months. Having thoroughly educated the subject on insulin handling and injection since the beginning, and after finding him anti-insulin-antibodies-negative, we initially found no plausible reason behind his persistent hyperglycemia. We checked the injection sites during the last visit, one month after the patient started insulin. We also asked the subject to show the action sequence implemented to perform the injection. When examining the insulin pen used, we found a needle stump stuck in the upper rubber end of the pen and realized that it was coming from a previously used, inadvertently broken needle embedded in the rubber (see Figure 1). When asked about it, the patient revealed having noticed the presence of fluid leaking from the pen during each injection.

After that, the subject was re-educated on the correct injection technique and, more specifically, how to handle the needle. The insulin dose was prudently reduced by 20%, and within just over a month, the fasting and post-meal blood sugar levels achieved a more adequate range (i.e., 120-140 mg/dL in the fasting state and 170-220 mg/dL postprandially) with minimal dose adjustments.

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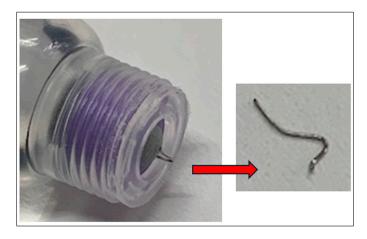


Figure 1. A picture showing the pen with a needle stuck into the rubber and the needle stump.

3. Comments

This story documents how a trivial movement error made when screwing the needle onto the pen (which must align without angling the former onto the latter) can cause incomplete insulin administration and, therefore, prevent glycemic control despite steadily increasing insulin doses.

Such a finding prompted us to pay closer attention to the role of continuous education and taught us that healthcare providers (HCPs) should regularly check injection techniques throughout the entire action sequence carried out daily by insulin-treated PwDs [5,6].

4. Epicrisis

We then systematically checked all the devices used by people receiving insulin in the six months following this observation. Out of the 160 insulin-treated subjects, we found 2 similar cases with a needle stump stuck into the pen rubber (1.8%) and 14 cases of missing drug flow (8.7%) resulting from unexpected needle bending as a consequence of an angled screwing maneuver (Figure 2).

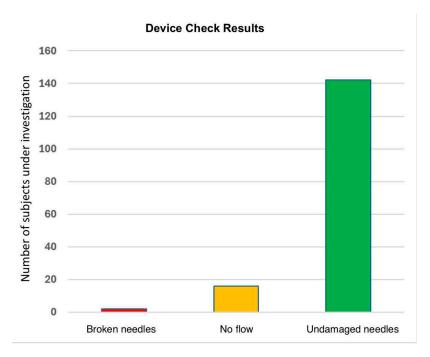


Figure 2. Results from device check performed in 160 consecutive insulin-injecting PwDs.

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Case Considerations and an Overview

As shown by the brief analysis of insulin-treated patients from our clinic, the clinical case we just described is certainly not an isolated one, despite the considerable effort our team has invested into structured education since treatment initiation, which involves periodic, at least annual refreshers, in line with ADA indications [7].

Indeed, although apparently simple, the act of injecting insulin is complex and presents several pitfalls that can lead to errors capable of canceling out entirely or partially the effect of insulin, i.e., the most potent remedy we have to combat hyperglycemia.

Any inexperienced person suddenly thrown into the mostly unknown world of insulin has to face the significant stumbling block of understanding that the medication dose is expressed in international units rather than milliliters. Then, they have to become fully aware of the difference between long-acting ("basal") and fast-acting ("bolus") insulin and accept that this kind of drug is not taken orally but through subcutaneous injections. Finally—perhaps even more complex—they must carefully observe the educator's movements to memorize how to perform the injection, thereby prioritizing a whole series of actions that represent when, where, and how much insulin to inject. The emotional aspect of undertaking such a compelling new treatment path, taking responsibility, and becoming an active participant rather than passively undergoing treatment cannot be underestimated [8].

Such an engaging and emotional aspect represents a significant hurdle to fully understanding and appropriating all the elements of a correct treatment method. As such, this is when care providers have to be patient and keen to ease anxiety, explain and, if necessary, re-explain what and how to perform a correct insulin injection. After that, they should place the pen or syringe in the patient's hands and ask them to perform a test injection directly under their watchful eyes with a few units of insulin, according to the patient's glycemic level at the time.

Let us try to analyze step by step the entire sequence of necessary actions needed to inject insulin appropriately, and understand exactly what a PwD has to pay attention to from the beginning: the patient sees a pen for the first time and, when handling it, learns that (i) it consists of a reservoir for insulin, a wheel to set the dose, a window to read the dose, a piston to press for drug injection, a mobile rubber that changes position inside the reservoir when insulin is injected and an upper rubber that fits the back of the needle; (ii) insulin has a clearly recognizable odor when flowing out of the needle; (iii) to inject insulin a needle has to be screwed onto the end of the pen; (iv) the needle is contained in a casing covered by external waterproof protection and a second internal rubber protecting the tip that must also be removed; (v) there are a number of areas of the body where insulin can be injected and patients should use their full body surface by constantly rotating between sites; (vi) the pen should be held firmly in the fist and the thumb used to press the plunger letting insulin flow from the pen into the skin and held down for a few seconds to allow the entire dose to pass through a thin needle.

The number of lines used to describe this sequence will allow the reader to perceive how much the PwD must learn to perform an activity that they have never even thought of before correctly and understand that all this requires competence and time availability from HCPs. Yet, the real question is the following: Does this reflect what happens in real-world clinical settings?

In 2013, our working group conducted a survey asking people with type 1 diabetes to describe their feelings at their first insulin injection. Eighty consecutive PwDs aged 7 to 37 years with type 1 diabetes for less than one year (20 from each of four diabetes centers in different regions of the country) were asked to respond to the following single question: "Describe the emotions you felt when you received your first insulin injection."

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Fifty-seven people were adults (average age 22 ± 4 years), fifteen were between 12 and 17 years old (14 ± 1 years), and the remainder were under 12 years old (8 ± 1 years). The written responses were analyzed by two psychologists, whose opinions were compared and found to agree in 96% of cases. A total of 95% of the subjects had experienced the first insulin injection with fear and apprehension, and only five adult males had accepted the injection since the beginning.

The answers were marked mainly by resigned passivity and acceptance, but, in some cases, were indicative of a deep discomfort. The most engaging ones were recited by professional actors and temporarily published by voice on the website "Diabete Italia", a non-profit association that brings together patient volunteer associations, scientific societies, and experienced operators in the world of diabetes that were never published in scientific journals. We provide some of the most significant findings. Maria, 7 years old, stated the following: "In a way, self-injecting insulin was like hurting yourself voluntarily...". Ludmilla, 30 years old, stated the following: "The first time I had to inject insulin myself I was 10 years old and ... I didn't do it! After more than an hour of trying to do it, I ran to my room crying. Then, little by little and with my mother's help, I started to do it myself." Antonio, 27 years old, stated the following: "The first time I injected insulin myself my hand was shaking, and I had to use both of them and then I pressed the pen against my skin so hard that I got bruises." Luigi, 40 years old stated the following: "When I saw the syringe for the first time, I thought << My God, this iron must be going into my skin every day and several times a day! How am I going to do it?>> Then, little by little, I started and then the shorter needles and the pens arrived and everything went better." Paola, 36, stated the following: "I was 5 when my diabetes arrived and I found angels in white uniforms in the hospital who taught me everything". There are many more statements, but these examples speak for themselves.

5. Errors

After searching the literature for cases similar to those observed by us, we reported the most common errors as examples, without intending to conduct any in-depth systematic research or meta-analysis.

Indeed, we found various examples of errors that patients commit while injecting insulin. Some errors seem incredible and uncommon, but all are the consequences of insufficient education (either completely lacking or approximate and hastily given information) linked to doctors' and nurses' lack of time dedicated to therapeutic education or even knowledge, attitudes, or behaviors, as explained in another paragraph of this paper.

For example, in a diabetes care clinic, four patients had to increase their insulin or other injectable diabetes medication doses with no improvement in glycemic control. One case depended on switching formulations in an ill-educated cognition-impaired subject, and another case experienced suboptimal drug absorption due to lipohypertrophy. Three of these cases resulted in multiple instances of hypoglycemia, and all patients exhibited markedly improved glycemic control after correcting the injection error. Their clinical pharmacist was essential in identifying and correcting errors [9].

An emblematic case is that of a patient with a reused pen needle stuck in the right arm after a non-dominant hand injection [10], which migrated distally before being surgically removed [10]. Overall, a wealth of reports in the literature include cases of incorrect injection technique errors [11–15].

6. Nurses

The insulin injection knowledge, attitudes, and behavior of doctors and nurses are crucial not only at the beginning of insulin therapy but throughout the entire disease process

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for people living with diabetes, regardless of hospital type [16]. In 2023, Chinese researchers evaluated these aspects among 19,853 nurses from 82 hospitals in 15 cities in China using a self-administered questionnaire, observing that only 22.3% of nurses demonstrated good knowledge, 75.9% had good attitudes, and 92.7% exhibited good behavior, considering various confounding parameters [17]. Other Chinese researchers further confirmed these data in a subsequent analysis involving 10,694 PwDs, 2643 physicians, and 2816 nurses [18].

7. Physicians

When analyzing glucose diaries or downloads, physicians consider the type and amount of administered insulin more than other elements, despite drug administration modalities being at least as important as the insulin dosage itself [19].

Indeed, insulin delivery is a complex factor that involves patient and HCP interactions at multiple levels. This includes the selection of injection sites as a function of insulin delivery, the choice of needle length based on subcutaneous thickness, the adoption of the best injection or infusion technique to ensure consistently effective SC delivery, the precise and systematic rotation of delivery sites, the examination of injection sites for lipohypertophy (LH), and minimized or null needle reuse and the safe disposal of exploited sharps to avoid risks to the community [20–24].

Physicians must be aware of LH. In 2021, 499 physicians from hospitals in 13 cities in China completed questionnaires addressing awareness, knowledge, and behavior concerning LH in clinical practice [25]. They displayed an unsatisfactory general level of awareness, knowledge, and behavior overall, i.e., primary, secondary, and tertiary hospital levels were investigated, and independent of medical status, such as being a senior, attending, or resident physician, the most satisfactory results were obtained by older medical employees. Only 38.7% of doctors could successfully identify all the hazards associated with LH; however, more doctors from tertiary hospitals were able to do so compared to those from secondary and primary hospitals. This suggests that physicians have an inadequate understanding of LH, especially in primary hospitals.

Even when device use seems easy, such as with pens, a lack of proper injection technique can cause dangerous mistakes [21], which surprisingly occur at one or more of the following several steps: preparing for injection, drawing up insulin (syringe users), priming (pen users), preparing correct doses, and injecting insulin. As such, occasionally, HCPs need to ask patients to administer an injection under their supervision [22]. As such, reported cases of failure to remove the inner pen needle shield, causing death, could also be prevented [23,24].

Also, other research highlights the need to increase the level of knowledge of doctors regarding correct injection techniques and the prevention of lipohypertrophy (LH), which is the most widespread type of complication due to incorrect injection techniques [25–29].

8. Pharmacists

Optimal diabetes control is crucial in preventing complications that contribute to the economic burden. Pharmacists are well-positioned within communities to provide the vital care necessary for patients with diabetes and possess a unique skill set that has demonstrated clear benefits in both clinical and non-clinical outcomes [30]. Fortunately, the appropriate management of insulin-treated people with diabetes (PwDs) has proven to be cost-effective and improved outcomes. Pharmacists can provide counseling on glucose monitoring, managing out-of-range levels, and developing an action plan for when blood sugar levels drop too low [31,32].

Such activities are instrumental in primary care, especially in the telemanagement developed during the SARS-CoV-2 pandemic and continuous glucose monitoring (CGM)

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systems [33]. The pharmacist is ideally positioned to educate patients during this delicate transition phase, preventing rehospitalization due to medication errors and helping to enhance adherence [34,35]. Pharmacist education at hospital discharge is beneficial and has a significant impact on medication adherence, diabetes follow-up, and, ultimately, disease control [36].

Pharmacists can also take care of high-risk patients and provide education. In a survey of Sudanese community pharmacists during Ramadan, most professionals were able to identify patients who should stop fasting and suggest ways to avoid hypoglycemia and hyperglycemia [37]. In a similar survey conducted in Norway, community pharmacists proved willing to provide diabetes risk-assessment services but required some guidance on recruiting and identifying patients who were best-suited to this service [38]. Surveys from English community pharmacists, primary care physicians, and nurses show that all other professionals were very comfortable with the transitioning aspects of diabetes care from healthcare professionals (HCPs) to community pharmacists. They suggested that improved education for technicians and primary care providers was the best way to enhance the program [39]. Taken together, these studies suggest the significance of pharmacists' comfort level in caring for complex patient populations.

However, despite such positive evaluations of pharmacists' role in collaborating with medical personnel for diabetes treatment, some problems persist.

Despite pointing to a good momentum in service improvement, Chinese authors examining 737 surveys from pharmacists [32] reported their ability to only meet basic rather than clinical needs with a moderate understanding of diabetes care requirements. The respondent pharmacists considered low patient self-management levels and a funding shortage as the main barriers, leading the authors to conclude that efforts are still needed to expand pharmacists' scope of practice and reduce patients' reluctance through education (see Table 1).

Table 1. The errors made by the different actors involved in insulin injection.

The Patient	The Diabetes Team	The Pharmacist
Does not remove the inner pen needle cover	Does not know enough about injection techniques	Gives the patient inadequate needles that are too long
Does not press and keep down the pen piston at the end of the injection	Does not know enough about lipohypertrophy	Provides the patient with pen-incompatible threading
Does not press down enough on the pen piston due to hand problems	Has knowledge of lipohypertrophy but not its mechanisms	Gives the patient lancets non-compatible with the lancing device
Holds the pen incorrectly, so that the hand weakens and the injection is incomplete	Does not know how to manage lipodystrophies	Tells the patient to keep the drug in the refrigerator without saying that the daily pen has to be kept at room temperature
Injects into the nodules	Has poor communication skills	Offers little or no collaboration in therapeutic education
Does not rotate the injection sites	Is not aware of all possible errors made by patients during injection	Provides information different from or even contradictory to that coming from colleagues
Tends to reuse needles	Does not check injection sites systematically	Provides poor counseling on hypoglycemia prevention and care

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Table 1. Cont.

The Patient	The Diabetes Team	The Pharmacist
Does not remove the needle from the pen after the injection	Does not monitor patients while injecting insulin	Provides poor counseling on hyperglycemia prevention and care
Uses long needles without inching the skin (pens or syringes)	Dose not check the pen used by the patient	Provides poor nutritional counseling
Injects ice-cold insulin	Does not teach patients how to manage hyperglycemia	
Makes mistakes when selecting the dose on the pen	Does not teach patients how to manage hypoglycemia	
Dose not dispose of the needles after use	Does not teach patients how to dispose of needles after use	
	Exchanges pens in promiscuous environments	
	Do not have enough time for therapeutic education	
	Provides information different from or even contradictory to that coming from colleagues	

9. Injection Technique Training and Clinical Outcomes

A multi-centre prospective interventional study on insulin-treated PwDs showed that even a simplified education significantly reduced detectable LH, with mean HbA1c values decreasing by over 0.5% and considerably lower rates of unexplained hypoglycemia and glucose variability while the mean daily insulin dose (TDD) decreased by 5.6 units from a 71.6 units/day baseline level [40].

In a controlled, multi-centre, prospective study, patients with LH [41] were informed of the presence of LH and encouraged once to avoid injections into lesions (control group; CG) or underwent repeated instructions to shift injections to non-LH areas, rotate correctly within injection sites, avoid needle reuse, and switch to 4 mm needles to facilitate rotation without increasing the risk of intramuscular (IM) injections besides intensive education on many of the issues summarized in this review (intervention group; IG),

Both groups displayed a significant decrease in HbA1c (up to 0.5%). The IG showed a ~5-unit TDD decrease from baseline (P = 0.035), and a substantial percentage of patients improved their injection habits. The authors concluded that any intervention was effective, but intensive education led to faster and better outcomes.

Three groups of patients with type 1 or type 2 diabetes, with two groups receiving structured insulin treatment training and one (the control group) group receiving no training or needles, were followed for 6 months in a randomized interventional study [42]. HbA1c reductions of ~1% and an evident decrease in LH and needle reuse occurred only in the two trained groups.

In our experience, an intensive and structured educational program can significantly reduce the clinical (with a reduction of about 50% in hypoglycemic events and glucose variability) and economic impact (4- to 6-time-fold reduction in health and social costs for serious hypoglycemic events related to injection errors) of injection errors compared to simpler, non-structured, and spotty educational interventions [5,6,43]. However, the favorable effect of structured education on correct injection techniques is short-term and requires periodic reminders to maintain correct injection performance in PwDs [6].

10. Needle Reuse

A further issue is the repeated use of the same needle. In the real world, patients commonly reuse needles, primarily due to convenience and cost savings. However, several studies have linked extensive needle reuse to LH [2,4,44–47], possibly due to the hope of avoiding injection pain [48,49]. Bacterial growth occurred on reused needles, and inflammatory changes (skin redness) were apparent at the injection sites of patients who reused needles [50,51]. Although local infections or abscesses have not been documented with needle reuse, FITTER recommendations advise against reusing needles [2], which regulatory agencies label for single use. A worldwide expert panel reaffirmed these indications in a recent update of recommendations on correct injection techniques [52].

A meta-analysis of 25 studies was unable to produce a compelling conclusion regarding the acceptability of needle reuse [53]. Indeed, despite several studies being unable to provide clear scientific evidence against the reuse of needles for subcutaneous insulin injections, our present case suggests that people living with diabetes should be on alert for complications caused by the reuse of needles (1 needle = 1 injection) [52,53]. Disposable injection needles are thin and sharp, coated with a lubricating silica gel layer that reduces friction and pain during acupuncture and injection. Reuse may lead to the bending and deformation of the needle tip, which can increase injection pain and cause local hyperemia (LH) and the induration of subcutaneous tissues, potentially affecting the accuracy of insulin injection [54,55].

Furthermore, many factors affect insulin pharmacokinetics (PK), such as variable drug uptake, including delivery into subcutaneous fat or muscle. Needles that are too long pose a substantial risk of intramuscular injection, which releases insulin slightly faster than an SC injection at rest but variably and substantially increases with light or more intense exercise, leading to erratic uptake [56].

11. Conclusions

We interpreted the reported clinical case as confirmation that unexpected and unpredictable situations can affect the outcome of insulin therapy, even in settings where healthcare workers operate. Thus, significant attention needs to be paid to educational training on injection techniques. This is why we decided to verify whether other cases of unrecognized errors occur among our PwDs. We were interested to find out that, in a consecutive series of 160 insulin-treated subjects, two more patients had a piece of broken needle stuck in the rubber, with only partial insulin delivery due to fluid leakage. Furthermore, in 14 subjects (8.9%), we observed abnormal or absent insulin flow due to the incorrect screwing of a needle that had a bent rear, preventing it from piercing the cartridge fluid. This frustrating finding documents the fact that educational training must be continuous over time and include the direct control of injectable devices besides skin areas because, as we already documented elsewhere, in the absence of systematic, regularly occurring educational refreshers, PwDs progressively forget what they have learned at the start of insulin injection training [5,6,43].

Therefore, HCPs must have the knowledge, specific expertise, and ability to convey to PwDs not only all possible information but the practical skills needed with an awareness that initial training is not enough to ensure sustained success. Unfortunately, based on the high frequency of skin lesions reported worldwide, several studies highlight the need for improvement [17,18,24,25,32,37], despite the extensive guidelines and literature review available on the topic [1,4,21,44,45,55–59].

Indeed, one aspect that has been scarcely considered so far is what people think and "feel" after being suddenly forced to accept the idea of self-pricking several times a day to survive a chronic disease? Despite the rich literature on anxiety and depression affecting

PwDs, we are not aware of any studies examining the influence of emotional aspects on diabetes control and correct insulin injection habits, which our interviews showed to be highly impactful, requiring empathic assistance from healthcare workers. A drawing from a young patient of ours may be suggestive of the relevance of the abovementioned emotions: he portrayed himself as a tightrope walker balancing over nothing with a pole in his hand and oscillating between a drop of blood and a sugar cube.

It is worth highlighting some concepts now widely accepted by the scientific community, from which we can draw some conclusions.

LH is the most frequent local complication of insulin injections [57–60] and infusions [61,62], with prevalence rates of \geq 50% in multiple studies from various countries. HCPs should make it a habit to check for LH frequently (at least yearly), especially when facing high glucose variability and unexplained hypo- and hyperglycemia.

Approximately half a billion people in the world have diabetes [62]; those with type 1 diabetes and about 20% of those with type 2 diabetes use insulin. Therefore, 150–200 million PwDs are estimated to be insulin users worldwide [63,64].

These data mean that, as over 50% of insulin-treated patients have LH, some 75–100 million PwDs run a high risk of poor glycemic control and prominent glucose variability due to frequent and unexplained hypo- and hyperglycemia with consequent high rates of micro- and macrovascular complications.

Significant educational gaps have been highlighted by studies conducted in various parts of the world among HCPs of different professional levels and from diverse settings, with the obvious consequence of one or more injection errors per patient having serious clinical, economic, and quality-of-life repercussions.

Given this general picture, we encourage intensive training for doctors and nurses working in any ward due to the widespread presence of PwDs in all hospital departments and branches.

HCP training must occur through periodic postgraduate refresher courses, even at the pre-graduate level of the curriculum. Diabetic volunteers, scientific societies, professional associations, institutional bodies responsible for health protection, insulin and device manufacturers, and pharmacists should unite to promote widespread awareness-raising actions among patients and their families by implementing training courses for HCPs and educational classes for individuals living with diabetes.

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Informed Consent Statement: This study was conducted in conformance with good clinical practice standards. The study was led in accordance with the original Declaration of Helsinki and subsequent amendments. Written informed consent was obtained from the person whose story we reported in an anonymized way.

Data Availability Statement: The data reported in the current study is available from the corresponding author on reasonable request.

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Abbreviations

ADA American Diabetes Association

BMI body mass index CG control group

CGM continuous glucose monitoring

FITTER Forum for Injection Technique and Therapy Expert Recommendations

FI HCPs healthcare providers
IG intervention group
IM intramuscular
LH lipohypertrophy
TDD daily insulin dose
PwD people with diabetes

References

- 1. Gentile, S.; Guarino, G.; Della Corte, T.; Marino, G.; Fusco, A.; Corigliano, G.; Colarusso, S.; Piscopo, M.; Improta, M.R.; Corigliano, M.; et al. AMD-OSDI Study Group on Injection Techniques and Nefrocenter Research & Nyx Start-up Study Group. Insulin-Induced Skin Lipohypertrophy in Type 2 Diabetes: A Multicenter Regional Survey in Southern Italy. *Diabetes Ther.* 2020, 11, 2001–2017. [CrossRef] [PubMed] [PubMed Central]
- 2. Frid, A.H.; Kreugel, G.; Grassi, G.; Halimi, S.; Hicks, D.; Hirsch, L.J.; Smith, M.J.; Wellhoener, R.; Bode, B.W.; Hirsch, I.B.; et al. New Insulin Delivery Recommendations. *Mayo Clin. Proc.* **2016**, *91*, 1231–1255. [CrossRef] [PubMed]
- 3. Frid, A.H.; Hirsch, L.J.; Menchior, A.R.; Morel, D.R.; Strauss, K.W. Worldwide Injection Technique Questionnaire Study: Population Parameters and Injection Practices. *Mayo Clin. Proc.* **2016**, *91*, 1212–1223. [CrossRef] [PubMed]
- 4. Mader, J.K.; Fornengo, R.; Hassoun, A.; Heinemann, L.; Kulzer, B.; Monica, M.; Nguyen, T.; Sieber, J.; Renard, E.; Reznik, Y.; et al. Relationship Between Lipohypertrophy, Glycemic Control, and Insulin Dosing: A Systematic Meta-Analysis. *Diabetes Technol. Ther.* 2024, 26, 351–362. [CrossRef] [PubMed] [PubMed Central]
- 5. Gentile, S.; Guarino, G.; Della Corte, T.; Marino, G.; Satta, E.; Pasquarella, M.; Romano, C.; Alfrone, C.; Strollo, F. On behalf of the AMD-OSDI Study Group on Injection Technique, and Nefrocenter Research and Nyx Start-Up Study Group. Role of Structured Education in Reducing Lipodystrophy and its Metabolic Complications in Insulin-Treated People with Type 2 Diabetes: A Randomized Multicenter Case-Control Study. *Diabetes Ther.* 2021, 12, 1379–1398. [CrossRef] [PubMed] [PubMed Central]
- 6. Gentile, S.; Guarino, G.; Della Corte, T.; Marino, G.; Satta, E.; Pasquarella, M.; Romano, C.; Alfrone, C.; Giordano, L.; Loiacono, F.; et al. on behalf of the AMD-OSDI Study Group on Injection Technique; Nefrocenter Research and Nyx Start-Up Study Group. The Durability of an Intensive, Structured Education-Based Rehabilitation Protocol for Best Insulin Injection Practice: The ISTERP-2 Study. *Diabetes Ther.* **2021**, *12*, 2557–2569. [CrossRef] [PubMed] [PubMed Central]
- American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to glycemic treatment: Standards
 of Medical Care in Diabetes—2022. Diabetes Care 2022, 45 (Suppl. S1), S125–S143.
- 8. Aronson, R. The role of comfort and discomfort in insulin therapy. Diabetes Technol. Ther. 2012, 14, 741–747. [CrossRef]
- 9. Wei, E.T.; Koh, E.; Kelly, M.S.; Wright, L.A.; Tylee, T.S. Patient errors in use of injectable antidiabetic medications: A need for improved clinic-based education. *J. Am. Pharm. Assoc.* **2020**, *60*, e76–e80. [CrossRef] [PubMed]
- 10. Qiao, Y.J.; Xin-Yuan, Y.; Xu, R.L.; Song, X.Y.; Ye, S.; Zhen, P.; Zhou, S.H.; Zhang, H.Q. Effect of a reused insulin needle remaining in a patient's body. *J. Diabetes Investig.* **2023**, *14*, 821–823. [CrossRef] [PubMed] [PubMed Central]
- 11. Briatore, L. Insulin: Where, how, how much?, or: The most bizarre ways to (not) inject insulin. *Il G. AMD* **2015**, *18*, 197–199. Available online: https://aemmedi.it/files/Congressi/amd_2015/poster/P134.pdf (accessed on 15 March 2025).
- 12. Pozzuoli, G.M.; Laudato, M.; Barone, M.; Crisci, F.; Pozzuoli, B. Errors in insulin treatment management and risk of lipohypertrophy. *Acta Diabetol.* **2018**, *55*, 67–73. [CrossRef] [PubMed]
- 13. Saltiel-Berzin, R.; Cypress, M.; Gibney, M. Translating the research in insulin injection technique: Implications for practice. *Diabetes Educ.* **2012**, *38*, 635–643. [CrossRef] [PubMed]
- 14. Truong, T.H.; Nguyen, T.T.; Armor, B.L.; Farley, J.R. Errors in the Administration Technique of Insulin Pen Devices: A Result of Insufficient Education. *Diabetes Ther.* **2017**, *8*, 221–226. [CrossRef] [PubMed] [PubMed Central]

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15. Değer, T.B.; Çakmak, H.S.G.; Erdoğan, B.C.; Değer, M.Ö. Effect of Insulin Pen Training Using the Teach-Back Method on Diabetes Self-Management, Quality of Life, and HbA1c Levels in Older Patients with Type 2 Diabetes: A Quasi-Experimental Study. *Healthcare* 2024, 12, 1854. [CrossRef] [PubMed] [PubMed Central]

- Wu, X.; Zhao, F.; Zhang, M.; Yuan, L.; Zheng, Y.; Huang, J.; Li, Y.; Li, C. Insulin Injection Knowledge, Attitudes, and Practices of Nurses in China: A Cross-Sectional Nationwide Study. *Diabetes Ther.* 2021, 12, 2451–2469. [CrossRef] [PubMed] [PubMed Central]
- 17. Liao, Y.; Liu, X.; Huang, J.; Chen, Q.; Li, N.; Zhou, P. Insulin injection knowledge, attitude and behaviour of nurses: A cross-sectional study in Guangdong Province. *Nurs. Open* **2023**, *10*, 3754–3765. [CrossRef] [PubMed] [PubMed Central]
- 18. Guo, L.; Zhang, Q.; Xue, Y.; Ran, X.; Chen, L.; Jiang, S.; Liu, D.; Ji, Q.; Liu, J. A Nationwide Cross-sectional Survey of Knowledge and Practices of Diabetes Drug Injection Techniques of Patients, Nurses, and Physicians: The China IT Improve Study. *Mayo Clin. Proc.* 2023, *98*, 1482–1500. [CrossRef] [PubMed]
- 19. Hirsch, L.J.; Strauss, K.W. The injection technique factor: What you Don't know or teach can make a difference. *Clin. Diabetes* **2019**, *37*, 227–233. [CrossRef] [PubMed]
- 20. Spollett, G.; Edelman, S.V.; Mehner, P.; Walter, C.; Penfornis, A. Improvement of insulin injection technique: Examination of current issues and recommendations. *Diabetes Educ.* **2016**, *42*, 379–394. [CrossRef]
- Gentile, S.; Strollo, F.; Guarino, G.; Brancario, C.; Corigliano, M.; Cozzolino, G.; Improta, M.; Fasolino, A.; Lamberti, C.; Lapice, M.; et al. Why are so huge differences reported in the occurrence rate of skin lipohypertrophy? Does it depend on method defects or on lack of interest? *Diabetes Metab. Syndr.* 2019, 13, 682–686. [CrossRef] [PubMed]
- 22. Trief, P.M.; Cibula, D.; Rodriguez, E.; Akel, B.; Weinstock, R.S. Incorrect insulin administration: A problem that warrants attention. *Clin. Diabetes* **2016**, *34*, 25–33. [CrossRef]
- Institute for Safe Medication Practices. Severe Hyperglycemia in Patients Incorrectly Using Insulin Pens at Home. Available
 online: www.ismp.org/alerts/severe-hyperglycemia-patients-incorrectlyusing-insulin-pens-home. (accessed on 10 September
 2018).
- 24. Kalra, S.; Mithal, A.; Sahay, R.; John, M.; Unnikrishnan, A.G.; Saboo, B.; Ghosh, S.; Sanyal, D.; Hirsch, L.J.; Gupta, V.; et al. Indian Injection Technique Study: Injecting Complications, Education, and the Health Care Professional. *Diabetes Ther.* **2017**, *8*, 659–672. [CrossRef] [PubMed] [PubMed Central]
- 25. Shen, M.; Shi, Y.; Zheng, S.; Fan, H.; Xu, J.; Yang, T. A Systematic Survey of Physicians' Insights into Lipohypertrophy. *Front. Public Health* **2021**, *9*, 738179. [CrossRef]
- 26. Luo, D.; Shi, Y.; Zhu, M.; Wang, H.; Yan, D.; Yu, J.; Ji, J.; Liu, X.; Fan, B.; Xu, Y.; et al. Subclinical lipohypertrophy–Easily ignored complications of insulin therapy. *J. Diabetes Complicat.* **2021**, *35*, 107806. [CrossRef] [PubMed]
- 27. Guo, Z.H. *Hospital Management*; People's Health Publishing House: Beijing, China, 1990.
- 28. Zhang, W.; Deng, Z.; Evans, R.; Xiang, F.; Ye, Q.; Zeng, R. Social media landscape of the tertiary referral hospitals in China: Observational descriptive study. *J. Med. Internet Res.* **2018**, 20, e249. [CrossRef]
- 29. Frid, A.H.; Hirsch, L.J.; Menchior, A.R.; Morel, D.R.; Strauss, K.W. Worldwide injection technique questionnaire study: Injecting complications and the role of the professional. *Mayo Clin. Proc.* **2016**, *91*, 1224–1230. [CrossRef]
- 30. Orabone, A.W.; Do, V.; Cohen, E. Pharmacist-Managed Diabetes Programs: Improving Treatment Adherence and Patient Outcomes. *Diabetes Metab. Syndr. Obes.* 2022, 15, 1911–1923. [CrossRef] [PubMed] [PubMed Central]
- 31. CDC. Cost-Effectiveness of Diabetes Interventions. 2021. Available online: https://www.cdc.gov/chronicdisease/programs-impact/pop/diabetes.htm#:~:text=The%20High%20Cost%20of%20Diabeteshronic%20condition%20in%20our%20nation. &text=%241%20out%20of%20every%20%244aring%20for%20people%20with%20diabetes.&text=%24237%20billion%E2%80% A1(c)%20is,(c)%20on%20reduced%20productivity (accessed on 15 March 2025).
- 32. Wang, J.; Pei, Y.; Yu, F.; Kang, Z.; Zheng, Y. Understandings, Attitudes, and Barriers About Diabetes Care: Analysis of Factors Influencing Community Pharmacists in China. *Diabetes Metab. Syndr. Obes.* **2021**, *14*, 1999–2009. [CrossRef] [PubMed] [PubMed Central]
- 33. Woodhouse, A.G.; Orvin, C.; Rich, C.; Crosby, J.; Keedy, C.A. Diabetes outcomes before and during telehealth advancements surrounding COVID-19. *J. Am. Pharm. Assoc.* **2022**, *62*, 214–217. [CrossRef]
- 34. Fantasia, K.L.; Stockman, M.-C.; Ju, Z.; Ortega, P.; Crable, E.L.; Drainoni, M.-L.; Walkey, A.J.; Bergstrom, M.; O'BRien, K.; Steenkamp, D. Professional continuous glucose monitoring and endocrinology eConsult for adults with type 2 diabetes in primary care: Results of a clinical pilot program. *J. Clin. Transl. Endocrinol.* 2021, 24, 100254. [CrossRef]
- 35. Ulrich, H.; Bowen, M. The clinical utility of professional continuous glucose monitoring by pharmacists for patients with type 2 diabetes. *J. Am. Pharm. Assoc.* **2003**, 2021, e76–e82. [CrossRef]
- 36. Shah, M.; Norwood, C.A.; Farias, S.; Ibrahim, S.; Chong, P.H.; Fogelfeld, L. Diabetes transitional care from inpatient to outpatient setting: Pharmacist discharge counseling. *J. Pharm. Pract.* **2013**, *26*, 120–124. [CrossRef]
- 37. Abdelaziz, T.A.; Abdulraheem, M.A.; Badi, S.A.; Badawi, M.I.; Saeed, A.O.; Elobied, M.A.; Ahmed, M.H. Knowledge, attitude and practice of Sudanese pharmacist with regard to management of diabetes during Ramadan: A cross-sectional survey. *Diabetes Metab. Syndr.* 2019, 13, 122–126. [CrossRef]

38. Risøy, A.J.; Kjome, R.L.S.; Svensberg, K.; Råheim, M.; Sølvik, U.Ø. Pharmacists' experience of a diabetes risk-assessment service and analytical quality control in community pharmacies—A focus-group study. *Res. Soc. Adm. Pharm.* **2021**, *17*, 1259–1266. [CrossRef]

- 39. Katangwe, T.; Family, H.; Sokhi, J.; Al-Jabr, H.; Kirkdale, C.L.; Twigg, M.J.; Torpey, K. The community pharmacy setting for diabetes prevention: Views and perceptions of stakeholders. *PLoS ONE* **2019**, *14*, e0219686. [CrossRef]
- 40. Smith, M.; Clapham, L.; Strauss, K. UK lipohypertrophy intervention study. *Diabetes Res. Clin. Pract.* **2017**, 126, 248–253. [CrossRef] [PubMed]
- 41. Campinos, C.; Le Floch, J.P.; Petit, C.; Penfornis, A.; Winiszewski, P.; Bordier, L.; Lepage, M.; Fermon, C.; Louis, J.; Almain, C.; et al. An effective intervention for diabetic lipohypertrophy: Results of a randomised, controlled, prospective, multicentre study in France. *Diabetes Technol. Ther.* **2017**, *19*, 623–632. [CrossRef] [PubMed]
- 42. Misnikova, I.V.; Gubkina, V.A.; Lakeeva, T.S.; Dreval, A.V. A randomized controlled trial to assess the impact of proper insulin injection technique training on glycemic control. *Diabetes Ther.* **2017**, *8*, 1309–1318. [CrossRef]
- 43. Gentile, S.; Guarino, G.; Della Corte, T.; Marino, G.; Satta, E.; Pasquarella, M.; Romano, C.; Alfrone, C.; Giordano, L.; Loiacono, F.; et al. The Economic Burden of Insulin Injection-Induced Lipohypertophy. Role of Education: The ISTERP-3 Study. *Adv. Ther.* 2022, 39, 2192–2207, Erratum in *Adv. Ther.* 2022, 39, 3058. https://doi.org/10.1007/s12325-022-02147-9. [CrossRef] [PubMed] [PubMed Central]
- 44. De Coninck, C.; Frid, A.; Gaspar, R.; Hicks, D.; Hirsch, L.; Kreugel, G.; Liersch, J.; Letondeur, C.; Sauvanet, J.-P.; Tubiana, N.; et al. Results and analysis of the 2008–2009 Insulin Injection Technique Questionnaire survey. *J. Diabetes* **2010**, *2*, 168–179. [CrossRef]
- 45. Vardar, B.; Kızılcı, S. Incidence of lipohypertrophy in diabetic patients and a study of influencing factors. *Diabetes Res. Clin. Pract.* **2007**, 77, 231–236. [CrossRef]
- 46. Saez-de Ibarra, L.; Gallego, F. Factors related to lipohypertrophy in insulin-treated diabetic patients; role of educational intervention. *Pract. Diabetol. Int.* **1998**, *15*, 9–11. [CrossRef]
- 47. Strauss, K.; De Gols, H.; Hannet, I.; Partanen, T.; Frid, A. A pan-European epidemiologic study of insulin injection technique in patients with diabetes. *Pract. Diabetol. Int.* **2002**, *19*, 71–76. [CrossRef]
- 48. Misnikova, I.; Dreval, A.; Gubkina, V.; Rusanova, E. The risk of repeated use of insulin pen needles in patients with diabetes mellitus. *J. Diabetol.* **2011**, *1*, 2. [CrossRef]
- 49. Puder, J.J.; Atar, M.; Muller, B.; Pavan, M.; Keller, U. Using insulin pen needles up to five times does not affect needle tip shape nor increase pain intensity. *Diabetes Res. Clin. Pract.* **2005**, *67*, 119–123. [CrossRef]
- 50. Schuler, G.; Pelz, K.; Kerp, L. Is the reuse of needles for insulin injection systems associated with a higher risk of cutaneous complications? *Diabetes Res. Clin. Pract.* **1992**, *16*, 209–212. [CrossRef]
- 51. Thomas, D.R.; Fischer, R.G.; Nicholas, W.C.; Beghe, C.; Hatten, K.W.; Thomas, J.N. Disposable insulin syringe reuse and aseptic practices in diabetic patients. *J. Gen. Intern. Med.* **1989**, *4*, 97–100. [CrossRef]
- 52. Klonoff, D.C.; Berard, L.; Franco, D.R.; Gentile, S.; Gomez, O.V.; Hussein, Z.; Jain, A.B.; Kalra, S.; Anhalt, H.; Mader, J.K.; et al. Advance Insulin Injection Technique and Education with FITTER Forward Expert Recommendations. *Mayo Clin. Proc.* **2024**. *submitted*. [CrossRef]
- 53. Zabaleta-Del-Olmo, E.; Vlacho, B.; Jodar-Fernández, L.; Urpí-Fernández, A.-M.; Lumillo-Gutiérrez, I.; Agudo-Ugena, J.; Morros-Pedrós, R.; Violán, C. Safety of the reuse of needles for subcutaneous insulin injection: A systematic review and meta-analysis. *Int. J. Nurs. Stud.* **2016**, *60*, 121–132. [CrossRef]
- 54. Chowdhury, S.; Chakraborty, P.P. Errors of insulin therapy: Real-life experiences from developing world. *J. Fam. Med. Prim. Care* **2017**, *6*, 724–729. [CrossRef]
- 55. Kamrul-Hasan, A.; Paul, A.K.; Amin, M.N.; Gaffar, M.B.J.; Asaduzzaman, M.; Saifuddin, M.; Mustari, M.; Alam, M.J.; Shahid, M.M.; Nahid-Ul-Haque, K.M.; et al. Insulin injection practice and injection complications—Results from the Bangladesh insulin injection technique survey. *Eur. Endocrinol.* 2020, *16*, 41–48. [CrossRef]
- 56. Vaag, A.; Handberg, A.; Lauritzen, M.; Henriksen, J.E.; Pedersen, K.D.; Beck-Nielsen, H. Variation in absorption of NPH insulin due to intramuscular injection. *Diabetes Care* **1990**, *13*, 74–76. [CrossRef] [PubMed]
- 57. Blanco, M.; Hernández, M.; Strauss, K.; Amaya, M. Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. *Diabetes Metab.* **2013**, 39, 445–453. [CrossRef] [PubMed]
- 58. Grassi, G.; Scuntero, P.; Trepiccioni, R.; Marubbi, F.; Strauss, K. Optimizing insulin injection technique and its effect on blood glucose control. *J. Clin. Transl. Endocrinol.* **2014**, *1*, 145–150. [CrossRef]
- 59. Ji, L.; Sun, Z.; Li, Q.; Qin, G.; Wei, Z.; Liu, J.; Chandran, A.B.; Hirsch, L.J. Lipohypertrophy in China: Prevalence, risk factors, insulin consumption and clinical impact. *Diab Technol. Ther.* **2017**, *19*, 61–67. [CrossRef]
- 60. Gentile, S.; Ceriello, A.; Strollo, F. Insulin shot dependent lipodystrophy: Evidence, uncertainties and current terminology overlaps. *J. Diabetes Metab. Disord. Control* **2016**, *3*, 53–55.
- 61. Conwell, L.S.; Pope, E.; Artiles, A.M.; Mohanta, A.; Daneman, A.; Daneman, D. Dermatological complications of continuous subcutaneous insulin infusion in children and adolescents. *J. Pediatr.* **2008**, *152*, 622–628. [CrossRef]

Diabetology 2025, 6, 89 14 of 14

62. Pickup, J.C.; Yemane, N.; Brackenridge, A.; Pender, S. Nonmetabolic complications of continuous subcutaneous insulin infusion: A patient survey. *Diabetes Technol. Ther.* **2014**, *16*, 145–149. [CrossRef]

- 63. Centers for Disease Control and Prevention. Age-Adjusted Percentage of Adults with Diabetes Using Diabetes Medication, by Type of Medication, United States, 1997–2011. Available online: https://www.cdc.gov/diabetes/php/data-research/index.html (accessed on 21 July 2025).
- 64. Garg, S.K.; Rewers, A.H.; Akturk, H.K. Ever-increasing insulin-requiring patients globally. *Diabetes Technol. Ther.* **2018**, 20 (Suppl. S2), S21–S24. [CrossRef]

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