Evaluation of Thai Insulin-Treated Diabetics' Knowledge and Practice of Insulin Pen Storage

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Objective: To evaluate patients' knowledge of, and practices regarding, the use and storage of insulin pens for insulin-treated diabetes.

Materials and Methods: This cross-sectional study randomly recruited 152 insulin-treated diabetics using an insulin pen who were followed up at the Outpatient Department, Siriraj Hospital, between February and November 2017. Each subject underwent a structured interview conducted by the same investigator. A retrospective chart review was also performed to collect participants' diabetes information.

Results: The 152 participants had a mean age of 61±15 years, and 59% were women. Of the subjects, 59% had had diabetes for 10 years or more, 35% had used an insulin pen for five years or more, and 76% took care of their own insulin pen. In daily practice, 60% refrigerated their in-use insulin pen, 68% had never noticed a visual change in the insulin quality of the in-use pen, and half did not know the duration for which an insulin pen should be used once opened. Moreover, a third used their in-use pen longer than the manufacturer's recommendation.

Conclusion: Most longtime-use, insulin-treated, diabetic patients lacked knowledge of proper insulin pen storage and usage. Moreover, some healthcare providers appeared to be unaware of the need to impart this knowledge to their patients. Ongoing educational teaching programs are therefore needed for both healthcare providers and diabetics to improve the glycemic control and safety of insulin-treated patients.

Keywords: Insulin pen, Insulin storage, Insulin use knowledge, Diabetes education

Data is increasingly demonstrating that good glycemic control can delay and reduce chronic diabetic complications. However, only one-third of diabetics have their hemoglobin A1c within target. A study at our institute demonstrated that insulin treatment is one of the factors related to poor glycemic control[1]. Insulin therapy is the most effective treatment and has less adverse events than other options. Both insulin-treated diabetic patients and physicians are educated to pay attention to the details of insulin use, including the site of injections and the injection technique, to ensure effective absorption of the insulin. However, one of the least well-known considerations is that the proper storage of in-use insulin affects its quality. More specifically, inappropriate storage diminishes its maximum efficacy, which results in poor glycemic control in diabetics. Several studies[2,3] have shown that insulin potency and biological activity decline after storage either at a high temperature or at a room temperature beyond 28 days. Moreover, studies have demonstrated that insulin-treated diabetics and healthcare professionals have insufficient knowledge of insulin therapy[4-6]. Nowadays, insulin pens are widely used for insulin-treated diabetic patients due to the convenience of the pens, which has also improved patients' adherence. Many studies[4-6] have been conducted on the appropriate use of insulin self-administration; however, studies focusing on the use of insulin pens and the studies of their storage are still scarce. Therefore, the purposes of the present study were to evaluate patients' knowledge, use, and storage of the pens for insulin-treated diabetes.

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Materials and Methods

Study design

This descriptive, cross-sectional study was conducted at the Outpatient Department of the Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, between February and November 2017. Subjects who attended the Outpatient Department and met the inclusion criteria were recruited. The study's protocol was approved by the Siriraj Institutional Review Board (COA No. Si 043/2017), and it complied with the principles embodied in the Declaration of Helsinki. Written, informed consent was obtained from all participants.

Participants and eligibility criteria

Subjects were included if they were aged 18 years or older and had been using an insulin pen for more than three months. However, subjects were excluded if 1) they were totally dependent on others and physically unable to participate in the interview, 2) they were lost to follow-up for more than 12 months, or 3) they were unwilling to participate in the study.

Data collection

A face-to-face interview using a structured questionnaire and a retrospective chart review were conducted for each participant. The questionnaire comprised of three parts, 1) a socio-demographic profile, 2) an assessment of the subject's knowledge of, and practices regarding, the use and storage of an insulin pen, and 3) the individual's history of diabetes and glycemic control. Details of diabetes complications, recent laboratory test results, and medications were obtained from the chart review.

Sample size calculation and statistical analysis

The sample size was calculated using the estimated proportion of one group. Assuming a similar level of incorrect answers, 72%, as found in previous data[2], 104 participants were needed to achieve an acceptable confidence interval of 8.64%. For the present study based on an estimate of 10% of data missing, 115 participants were required. The data analysis was performed using SPSS Statistics for Windows, version 18 (SPSS Inc., Chicago, IL, USA). Demographic and clinical data were interpreted using descriptive statistics. Data are presented as numbers and percentages, or as means ± standard deviation. A Chi-square test, or Fisher's exact test were used to compare data between groups, as appropriate. For all analyses, a p-value less than 0.05 was regarded as being statistically significant.
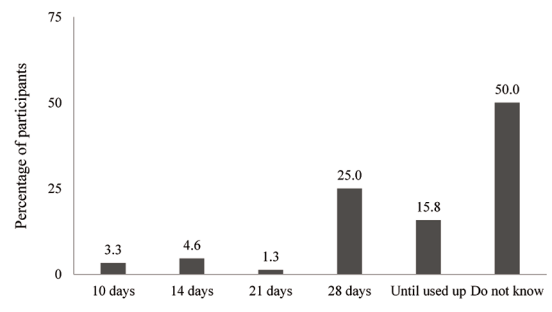

Figure 1. Participants' awareness of the duration insulin pens could be used once opened.

Results

Baseline characteristics

The present study randomly recruited 152 diabetics, 91.4% of whom lived in Bangkok city and the surrounding Bangkok Metropolitan Region. Their mean age was 61.8±15.5 years (range 19 to 94 years), and they had a mean HbA1c of 8.0±1.3% (range 5.6% to 12.7%). Most had type 2 diabetes mellitus, with 58.6% of the study cohort having been diagnosed as diabetic for longer than 10 years. One hundred of the participants (65.8%) had diabetes complications. As to insulin pens, 65.1% of the subjects had been using one for less than five years. The mean insulin dosage via the pens was 22.4±15.2 units/day (range 4 to 72 units/day), with 75.5% taking care of their own pen. Table 1 contains full details of the participants' baseline characteristics.

Assessment of the knowledge and practice of the use and storage of insulin pens by insulin-treated diabetics

Of the study cohort, 73.7% (95% CI 65.9 to 80.5) knew that an unopened insulin pen should be kept in the body of a refrigerator or cooling device. However, 24.3% (95% CI 17.8 to 32.0) stored their pens in a door shelf of their refrigerator, where the temperature might be higher due to the door being opened and closed many times. Moreover, although 86.8% (95% CI 80.4 to 91.8) of the subjects knew that sun exposure affected insulin quality, 68.4% (95% CI 60.4 to 75.7) had never noticed the appearance of their in-use insulin pen before an injection, and almost two-thirds (59.9%) (95% CI 47.6 to 64.0) refrigerated their opened insulin pens. Table 2 summarizes the knowledge and practice of the insulin-treated diabetics relating to insulin storage.

As shown in Figure 1, half of the insulin-treated diabetics did not know how long insulin pens could be reliably used once opened. Moreover, one-third

Table 1. Baseline characteristics of the participants

Data	Results n (%)
Age (years), Mean±SD	61.8±15.5
Sex	
Male	63 (41.4)
Female	89 (58.6)
Occupation	
Unemployed	85 (55.9)
Civil servants	29 (19.1)
Employee	15 (9.9)
Merchant	14 (9.2)
Others	9 (5.9)
Medical coverage	
Universal health insurance	32 (21.0)
Social security	17 (11.2)
Civil servant	81 (53.3)
Self-paying	22 (14.5)
Education level	
Uneducated	8 (5.3)
Less than bachelor's degree	99 (65.1)
Equal to, or higher than, bachelor's degree	45 (29.6)
Type of diabetes	
T1DM	10 (6.6)
T2DM	137 (90.1)
Other	5 (3.3)
Duration of diabetes (years)	
<5	35 (23.0)
5 to 10	28 (18.4)
>10	89 (58.6)
HbA1c (%), Mean±SD	8.0±1.3
Insulin dosage (units/day), Mean±SD	22.4±15.2
Duration of insulin-treatment (years)	
<5	99 (65.1)
5 to 10	27 (17.8)
>10	26 (17.1)
Number of insulin injections	
Once daily	81 (53.3)
Twice daily	53 (34.9)
Multiple daily doses	18 (11.8)
Diabetes complications (n = 100)	
Diabetes retinopathy	74 (48.7)
Diabetes nephropathy	70 (46.1)
Diabetes neuropathy	18 (11.8)
Stroke	5 (3.3)
Coronary artery disease	28 (18.4)
Type of insulin	
Long acting	76 (42.7)
Intermediate acting	25 (14.0)
Rapid acting	23 (12.9)
Premix insulin	54 (30.3)

SD=standard deviation; T1DM=type 1 diabetes mellitus; T2DM=type 2 diabetes mellitus; HbA1c=glycated hemoglobin

Table 2. Assessment of the knowledge and practice of insulin storage of insulin-treated patients

Knowledge and practice assessment	Frequency n (%)
Unopened insulin storage	
Freezer	2 (1.3)
In the body of a refrigerator or cooling device	112 (73.7)
Refrigerator door	37 (24.3)
Room temperature	1 (0.7)
Effect of direct sunlight on quality of insulin	
Yes	132 (86.8)
No	20 (13.2)
Notice the appearance of insulin before injection	
Yes	48 (31.6)
No	104 (68.4)
Place to keep in-use insulin pen	
Bedroom	40 (26.3)
Living room	15 (9.9)
Kitchen	5 (3.3)
Refrigerator	91 (59.9)
Cooler device	1 (0.7)
Can in-use insulin pen be refrigerated?	
Yes	130 (85.5)
No	22 (14.5)
Travelling	
Keep in a cooler	62 (40.8)
Keep in a suitcase	10 (6.6)
Keep in a car	7 (4.6)
Keep in a handbag	72 (47.4)
Keep in shirt pocket	1 (0.7)

(28.3%, 95% CI 21.3 to 36.2) of the participants used their pens longer than the recommended time, while almost one-third (23.7%, 95% CI 17.2 to 31.3) of responders claimed that they had never received any insulin storage recommendations from their healthcare providers. The present study showed that glycemic outcome had no association with participant who used opened insulin pen within or longer than recommended period (p=0.44). However, patients who have used opened insulin longer were found to have more knowledge in insulin storage (p=0.007).

Of the patients who used the pens for longer than recommended, the most commonly given reason was simply a lack of knowledge of the in-use period of opened insulin pens (39.5%, 95% CI 31.6 to 47.7). The second most frequent reason was the misunderstanding that the pens could be safely used

longer than the recommended time (17.8%, 95% CI 12.0 to 24.8). The perceived high cost of the pens was offered as a further reason by self-paying patients (5.9%, 95% CI 2.7 to 10.9). Lastly, 3.9% (95% CI 1.5 to 8.4) expressed concern that an insufficient number of insulin pens would be available for use during their follow-up periods if the pens were discarded at the recommended time.

Discussion

Insulin therapy is the most potent hypoglycemic medication currently available for diabetes treatment; however, the potency of insulin deteriorates if it is stored under improper conditions[7]. In spite of the critical need for correct storage, the present study identified that both diabetics and healthcare professionals do not pay sufficient attention to this. Manufacturers recommend that in-use insulin pens be stored at a temperature not exceeding 25°C to 30°C; unfortunately, in tropical countries such as Thailand, mean room temperatures are typically higher. Some authors have proposed that if insulin pens cannot be stored properly, they should be discarded within two weeks of opening[3]. The current study showed that most of the patients believed that the pens should be refrigerated; consequently, more than half of the patients were in the habit of refrigerating their pens after opening them. Another study identified that some physicians also believe that refrigerating in-use insulin pens is the ideal storage method as it reduces the risks of the pens being exposed to extreme temperatures and excessive agitation[8]. Nevertheless, the manufacturers' storage guidelines do not recommend refrigerating in-use insulin due to a lack of stability data for insulin storage under cyclic temperature conditions[9]. Studies are needed to clarify the proper storage conditions for in-use insulin pens in tropical countries. One simple step to detect insulin deterioration is to observe the characteristic of the insulin inside the pens. Surprisingly, more than two-thirds of the patients in the present study had never noticed visual changes in the insulin before injection. It follows that physicians and diabetes educators need to educate diabetics on the need to check for visual changes in pen insulin. These include changes in the insulin's color and turbidity, and the appearance of suspensions such as large aggregates and/or material adhering to the cartridge wall[10]. Moreover, in cases of insulin suspension, attention should be paid to how well-mixed the suspension is before the pen is used because poor mixing results in variations in the dose of insulin dispensed.

According to American Diabetes Association guidelines, the in-use period for insulin vials is 28 days, regardless of the formulation or brand involved. By contrast, the guidelines advise that insulin pens should only be used for 10 to 28 days after being opened. The specific period depends on the particular brand of pen, and it can be less than 28 days even if the same formulation is used in insulin vials[7,11,12]. Because insulin pens are expected to undergo more rigorous agitation and be exposed to a wider range of stressors, the pens are typically used for a shorter period than that for vials[11]. The present study established that many patients have a misunderstanding about the particular in-use period recommended for their pens. To avoid using pens beyond their suggested in-use period, the individual use-by dates should always be calculated by diabetic patients. This is especially important in the case of pediatric, type 1 diabetes mellitus, and type 2 diabetes mellitus patients who use a pen to administer a daily insulin dose of less than 15 units. Moreover, treating physicians need to ensure that enough insulin pens are prescribed to cover the full follow-up periods.

To the best of our knowledge, this was the first study to focus on the knowledge, storage, and usage of insulin pens by insulin-treated diabetics. A strength of the present study was that only one investigator conducted the structured interviews to ensure the participants clearly understood all the questions. Moreover, the study was conducted in a tertiary care hospital that had diabetes educational support for patients. However, the present study did not evaluate the knowledge and practices of the hospital's healthcare providers to ensure that the storage and usage recommendations were being correctly transferred to diabetic patients. Despite the support available at the hospital, the results of the present study confirmed that insulin-dependent diabetics generally lack knowledge of correct insulin usage and storage. However, the association between longer insulin usage and more knowledge of insulin storage found in the present study imply that the participants who used insulin longer might have more chance to get knowledge about insulin storage. Therefore, ongoing education is required to ensure that the potency of insulin is maintained and to avoid the unnecessary complications that have been reported by prior studies[13,14].

Conclusion

Most insulin-treated diabetics in the present study lacked knowledge about insulin pen storage and usage. Moreover, some healthcare providers appeared to be

unaware of the need to impart this knowledge to their patients. Therefore, ongoing educational teaching programs are needed for both healthcare providers and diabetics to improve the glycemic control and safety of insulin-treated patients.

What is already known on this topic?

Many factors affect insulin quality including insulin storage and in-use period of opened insulin. Improper storage of insulin could decrease its potency and there are misunderstanding of in-use period of opened insulin between insulin pen and insulin vial.

According to ADA guidelines, in-used insulin pen can be used for 10 to 42 day depending on the type of insulin while insulin in vial can be used for 28 days.

What this study adds?

Despite that the insulin pen is used more and more nowadays, there is a lack of studies evaluating the knowledge and practice of the insulin pen.

The findings from this study emphasize that insulin treated diabetic patients and healthcare providers have common misunderstanding about insulin pen storage and in-use validity duration.

Moreover, this study encourages the awareness of insulin storage issue and promote continuous educational program for both patients and healthcare providers.

Acknowledgement

Conflicts of interest

The authors declare no conflict of interest.

References

1. Sriwijitkamol A, Moungngern Y, Vannaseang S. Attainment of American Diabetes Association clinical practice recommendations in 722 Thai type 2 diabetes patients. J Med Assoc Thai 2011;94 Suppl 1:S159-67.
2. Saliva MA, Chuong M, Kerr S, Cabrera A. Stability of two long-acting insulin formulations after 28 days. J Pharm Pract Res 2013;43:37-40.
3. Vimalavathini R, Gitanjali B. Effect of temperature on the potency & pharmacological action of insulin. Indian J Med Res 2009;130:166-9.
4. Jasper US, Opara MC, Pyiki EB, Akinrolie O. Knowledge of insulin use and its determinants among Nigerian insulin requiring diabetes patients. J Diabetes Metab Disord 2014;13:10.
5. Basazn Mekuria A, Melaku Gebresillassie B, Asfaw Erku D, Taye Haile K, Melese Birru E. Knowledge and self-reported practice of insulin injection device disposal among diabetes patients in Gondar Town, Ethiopia: A cross-sectional study. J Diabetes Res 2016;2016:1897517.
6. Shanmugam J, Roy A. Knowledge and awareness of insulin usage among diabetic patients in Chennai. Int J Sci Res 2017;6:889-91.
7. Moslemi P, Najafabadi AR, Tajerzadeh H. A rapid and sensitive method for simultaneous determination of insulin and A21-desamido insulin by high-performance liquid chromatography. J Pharm Biomed Anal 2003;33:45-51.
8. American Diabetes Association. Insulin administration. Diabetes Care 2004;27 Suppl 1:S106-9.
9. Sanofi-Aventis Canada. Product monograph LANTUS [Internet]. 2017 [cited 2018 Nov 23]. Available from: http://products.sanofi.ca/en/lantus.pdf.
10. Shnek DR, Hostettler DL, Bell MA, Olinger JM, Frank BH. Physical stress testing of insulin suspensions and solutions. J Pharm Sci 1998;87:1459-65.
11. Grajower MM, Fraser CG, Holcombe JH, Daugherty ML, Harris WC, De Felippis MR, et al. How long should insulin be used once a vial is started? Diabetes Care 2003;26:2665-6; discussion 266-9.
12. Joffe D. Stability of common insulins in pens and vials [Internet]. 2011 [cited 2018 Nov 23]. Available from: https://www.ghdonline.org/uploads/se_insulin_stability_chart.pdf.
13. Weeraratne CL AW, Kuruppumullage RP. Knowledge on insulin therapy among healthcare professionals. J Ceylon Coll Phys 2010;41:67-71.
14. Jittsue A, Sangja mP, Treesak C, Hanlerdrit T. Assessment of knowledge and practice of patient before and after counseling in the use of the reusable insulin pen at Vachiraphuket hospital. Songkla Med J 2016;34:27-37.