Dosing Accuracy with a Novel Pen Device (SoloSTAR®) as Performed by Patients with Diabetes in a Clinical Setting

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Abstract

Background: Pen devices can help to overcome some of the barriers associated with insulin therapy. The present study evaluated the accuracy of dose delivery by people with diabetes using the novel prefilled, disposable SoloSTAR® device with insulin glargine (Lantus®) and insulin glulisine (Apidra®) (all from sanofi-aventis, Paris, France).

Methods: People with type 1 or type 2 diabetes (insulin users or insulin naive) were eligible to participate in this randomized, single-center, open-label study. Each participant delivered six separate insulin doses into a sponge using SoloSTAR (three with glargine [10, 40, and 80 units] and three with glulisine [5, 15, and 30 units]). Pens were weighed before and after each test dose to determine the dose delivered. Thresholds for dosing accuracy were calculated according to the 2000 International Organization for Standardization (ISO) recommendations (Guideline 11608-1).

Results: All doses of glargine and glulisine delivered (60 participants; 360 individual doses) were within the ISO limits. Mean (standard deviation) glargine doses delivered were 9.87 (0.24), 39.63 (0.36), and 79.02 (0.62) units for 10, 40, and 80 units, respectively. Insulin glulisine doses delivered were 4.98 (0.20), 14.87 (0.29), and 29.67 (0.34) units for 5, 15, and 30 units, respectively.

Conclusions: The SoloSTAR pen allows people with diabetes to achieve a dosing accuracy with glargine and glulisine similar to that achieved in laboratory conditions. The dosing accuracy and ease of use of SoloSTAR may provide greater confidence in the precision and accuracy of the device while titrating glargine and/or glulisine to goal.

Introduction

ALTHOUGH THE EFFICACY of insulin therapy is well established in terms of reducing the risk of diabetes-related complications,[1,2] many barriers to its successful use by patients with diabetes exist, including hypoglycemia, social acceptability, and the individual's perceived ability to self-manage his or her treatment with injections that may be difficult and painful to administer.[3]

The introduction of pen devices has increased patients' acceptance of insulin therapy, by helping to overcome the fear of injections associated with using a standard syringe.[4,5] Pens can also increase accuracy of dosing (and, therefore, glycemic control) in people with diabetes.[6–8] However, the ability of patients to accurately administer the correct insulin dose can vary between pen devices.[6]

Accurate dosing with an easy-to-use device can increase a patient's confidence in his or her ability to self-manage diabetes,[6,9] leading to improved treatment adherence.[10,11] SoloSTAR® (sanofi-aventis, Paris, France) is a disposable, prefilled insulin pen device for administration of insulin glargine (Lantus®; sanofi-aventis) or insulin glulisine (Apidra®; sanofi-aventis). Unlike other disposable insulin pens, the body of the SoloSTAR pen is color coded to aid with the correct identification of basal and bolus insulins, even in patients with impaired vision.[12] In addition, the SoloSTAR pen requires a lower injection force and can deliver a higher maximum dose than some other disposable pens.[13]

Laboratory studies have shown that using the SoloSTAR pen to deliver insulin glargine is highly accurate for three different doses,[13] according to procedures and standards defined by the International Organization for Standardization (ISO) (Guideline 11608-1).[14] However, accuracy in the lab does not necessarily reflect the real-life setting in which patients administer their own injections. Therefore, the present

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Characteristic	
Total number of patients	60
Mean ± SD age (years)	55.9 ± 13.0
Female (*n* [%])	24 (40)
Type of diabetes (*n* [%])	
Type 1	11 (18)
Type 2	49 (82)
Mean ± SD duration of diabetes (years)	14.0 ± 9.5
Diabetes therapy (*n* [%])	
Oral antidiabetic drugs	6 (10)
Oral antidiabetic drugs + insulin	22 (37)
Insulin	32 (53)
Previous insulin pen experience (*n* [%])	53 (88)
Mean ± SD duration of insulin therapy (years)	8.1 ± 6.4
Moderate motor impairment (*n* [%])	7 (12)
Moderate visual impairment (*n* [%])	9 (15)

clinically relevant doses of insulin glargine (10, 40, and 80 units) and insulin gluisine (5, 15, and 30 units).

Research Design and Methods

Study design

This was a prospective, open-label, single-center study, which was conducted over a period of 1 week at our diabetes research clinic (Forschungsintitut Diabetes GmbH, Bad-Mergentheim, Germany).

Patients

A minimum of 54 patients was considered sufficient to demonstrate validity of the study; considering that 10% of dose deliveries could be non-evaluable, the target sample size was 60 patients. Men and women 18–79 years old with

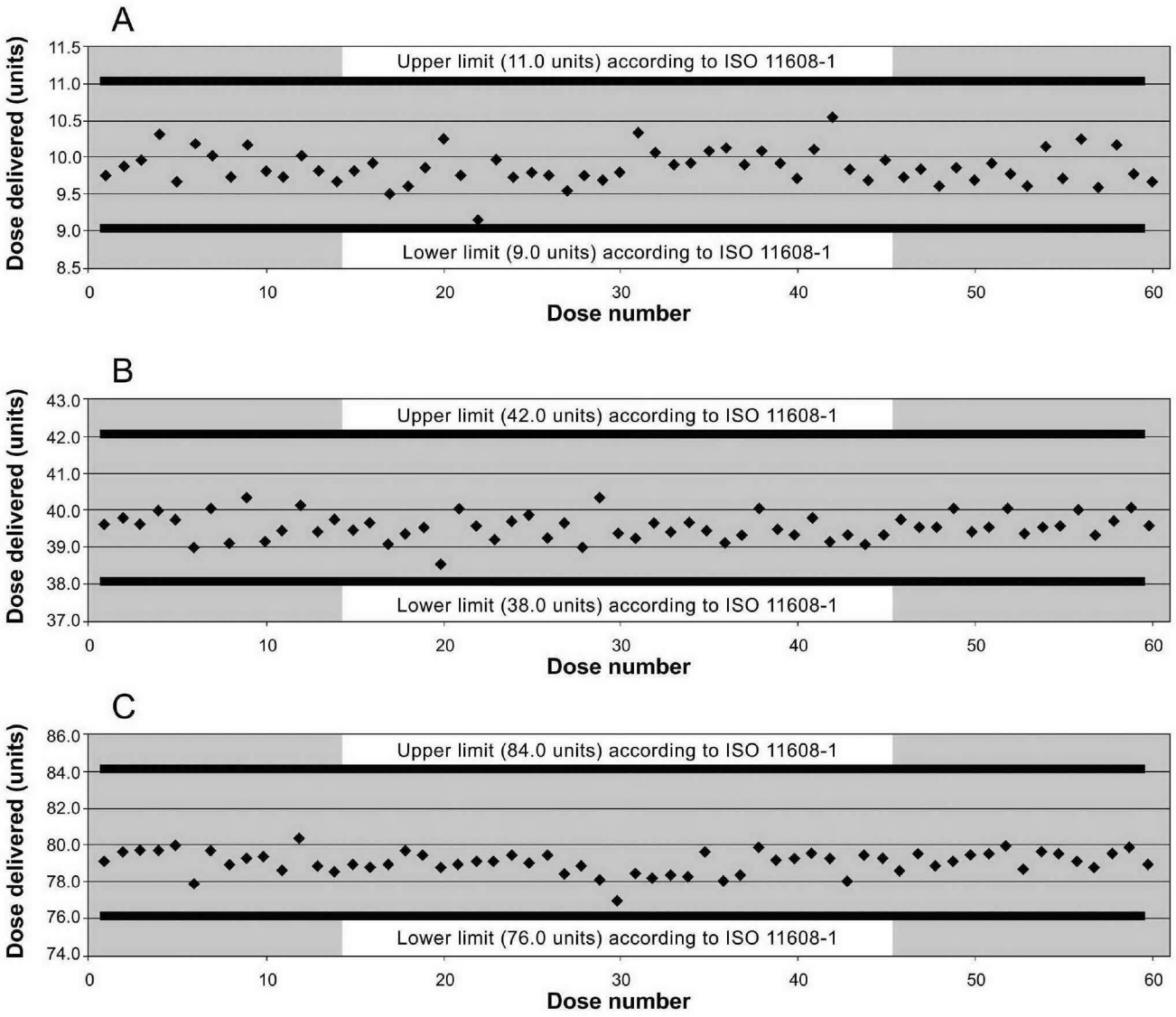

FIG. 1. Accuracy of the SoloSTAR pen when delivering (**A**) 10-, (**B**) 40-, and (**C**) 80-unit doses of insulin glargine. The upper and lower limits, as defined by the ISO standard, 11608-1, are indicated for each dose. Each data point represents the dose delivered by an individual person.

gible to participate in the study. Patients were required to be current or past users of injectable insulin or to be insulin naive and considered to be candidates for initiation of insulin therapy. Current insulin users with experience of disposable pens (including SoloSTAR) and/or reusable pens were eligible to participate in the study. Patients were required to speak and read German.

Exclusion criteria included the presence of a substance use disorder, severe visual or motor impairment, or a diagnosis of dementia, as recorded in the patient's medical files, which were reviewed after an initial screening visit. Patients with mental illnesses rendering them unable to understand the requirements and implications of the study and those considered unlikely to adhere to the study protocol were also excluded. All patients provided written informed consent prior to study entry.

A total of 63 patients participated in the study (Table 1). The majority of patients had type 2 diabetes (82%), the mean disease duration was 14 years, and 88% had previous experience with insulin pens. Seven participants had moderate motor impairment, and nine had moderate visual impairment. All participants were instructed in the use of the SoloSTAR pens prior to the study. Results from three participants were excluded. In one case, 15 units of insulin glulisine was injected twice instead of one 5-unit and one 15-unit injection, in another case, a single patient was excluded for providing a second set of measurements, and in the third case, a patient with severe motor impairment was incorrectly included.

Study design

Patients were required to deliver six separate insulin injections into a sponge. Study nurses demonstrated the use of SoloSTAR pen. Patients were asked if they had any questions regarding the use of the SoloSTAR pen. After that patients were requested to give a test injection of 10 units into a sponge.

Each participant dialed and delivered three doses with the insulin glargine SoloSTAR pen (10, 40, and 80 units) and three doses with the insulin glulisine SoloSTAR pen (5, 15, and 30 units); the order of pen usage and dose delivery was randomized. Between the study doses, the pens were primed with an insulin dose of 2 units. The randomization list was generated by the lead investigator using SYSTAT (Systat Software, Inc., Chicago, IL) before the start of the study with allocations sealed in envelopes, which were opened by the nurse during the participant's visit.

The SoloSTAR pens were weighed by the investigators following the priming doses and again following the test injections delivered by the patients, using a precision balance (P 205 DR/M, Mettler Toledo GmbH, Giessen, Germany). Pens were fitted with 0.25-mm (31-gauge) × 8-mm needles (Becton Dickinson GmbH, Heidelberg, Germany) for all tests.

Statistical analysis

Dosing accuracy was assessed by comparing pre- and post-injection weights of the SoloSTAR pens. Mean ± standard deviation (SD) of the delivered doses were calculated for each test dose for both insulins. The level of dosing accuracy was evaluated using ISO 11608-1, which is applicable for insulin pen devices, provides a set of criteria against which the dosing accuracy of an insulin pen is assessed. Results are normally presented as milliliters; for insulin formulations of 100 units/mL, results can be presented in units for easier interpretation (as has been done here).

The ISO limits are as follows:

- For doses of ≥20 units, the tolerance is ±5% (e.g., 38–42 units for the 40-unit dose; Eq. 1)
- For doses <20 units, the tolerance is ±0.01 mL (e.g., 4–6 units for the 5-unit dose), as defined in the ISO recommendations (ISO 11608-1)

Further calculations were performed according to ISO 11608-1, as shown in Eq. 2, to confirm whether the data sets were within the threshold limits. This calculation is valid for k values of 2.667, for a P value of 0.975, and with a 95% confidence interval (CI).

$$\text{Upper threshold value} = V_{set} + V_{set} \cdot 5\%$$
$$\text{Lower threshold value} = V_{set} - V_{set} \cdot 5\% \qquad (1)$$

where V_{set} = volume set (i.e., 40 units [0.4 mL]).

$$x + (k \cdot s) \leq \text{upper threshold value}$$
$$x - (k \cdot s) \geq \text{lower threshold value} \qquad (2)$$

where s = standard deviation and x = mean dose delivered. The k value was derived from a lookup table, which was based on the number of samples and a P value of 0.975 with a 95% CI (using the Clopper-Pearson method).[14] The k value used was 2.667.

A third evaluation was the proportion of doses delivered by the patients that were within the ISO ranges, with a success criterion of ≥90%.

TABLE 2. DOSE ACCURACY FOR INSULIN GLARGINE DELIVERED USING SOLOSTAR

Target dose	*Dose (units)*
10 units (ISO limit, ±1 unit: 9, 11 units)	
Observed dose	9.87 ± 0.24
Lowest dose delivered	9.15
Highest dose delivered	10.54
ISO calculated minimum[a]	9.23
ISO calculated maximum[a]	10.50
40 units (ISO limit, ±5%: 38, 42 units)	
Observed dose	39.54 ± 0.36
Lowest dose delivered	38.50
Highest dose delivered	40.33
ISO calculated minimum[a]	38.58
ISO calculated maximum[a]	40.49
80 units (ISO limit, ±5%: 76, 84 units)	
Observed dose	79.02 ± 0.62
Lowest dose delivered	76.83
Highest dose delivered	80.31
ISO calculated minimum[a]	77.35
ISO calculated maximum[a]	80.69

Values for observed dose are mean ± SD.
[a]Calculated using Eq. 2.

(Systat Software, Inc.) was used.

Results

Accuracy of doses delivered

For insulin glargine, the mean delivered dose in each test was marginally below the target dose (between −0.9 and −1.3%). For all three doses (10, 40, and 80 units), 100% of individual deliveries were within the established tolerance limits according to the ISO standard (Fig. 1 and Table 2). When the data sets were analyzed, the 95% CI (Eq. 2) for each dose was within the tolerance limits, thus passing the ISO standards.

The mean delivered dose in each test for insulin glulisine was marginally below the target dose (between −0.4 and −1.1%). For all three doses (5, 15, and 30 units), 100% of injections according to the ISO standard (Fig. 2 and Table 3). When the data sets were analyzed, the 95% CI (Eq. 2) for each dose was within the tolerance limits, thus passing the ISO standards.

The predefined success rate of ≥90% of delivered doses within the ISO ranges was also achieved for both insulin glargine and insulin glulisine.

Discussion

The results of this study are consistent with those reported previously in a clinical setting, when used by patients with diabetes, and also in a laboratory setting, when delivered by trained technicians. As required for regulatory approval, and as previously demonstrated,[13] in a laboratory setting with doses delivered by technicians, the SoloSTAR device

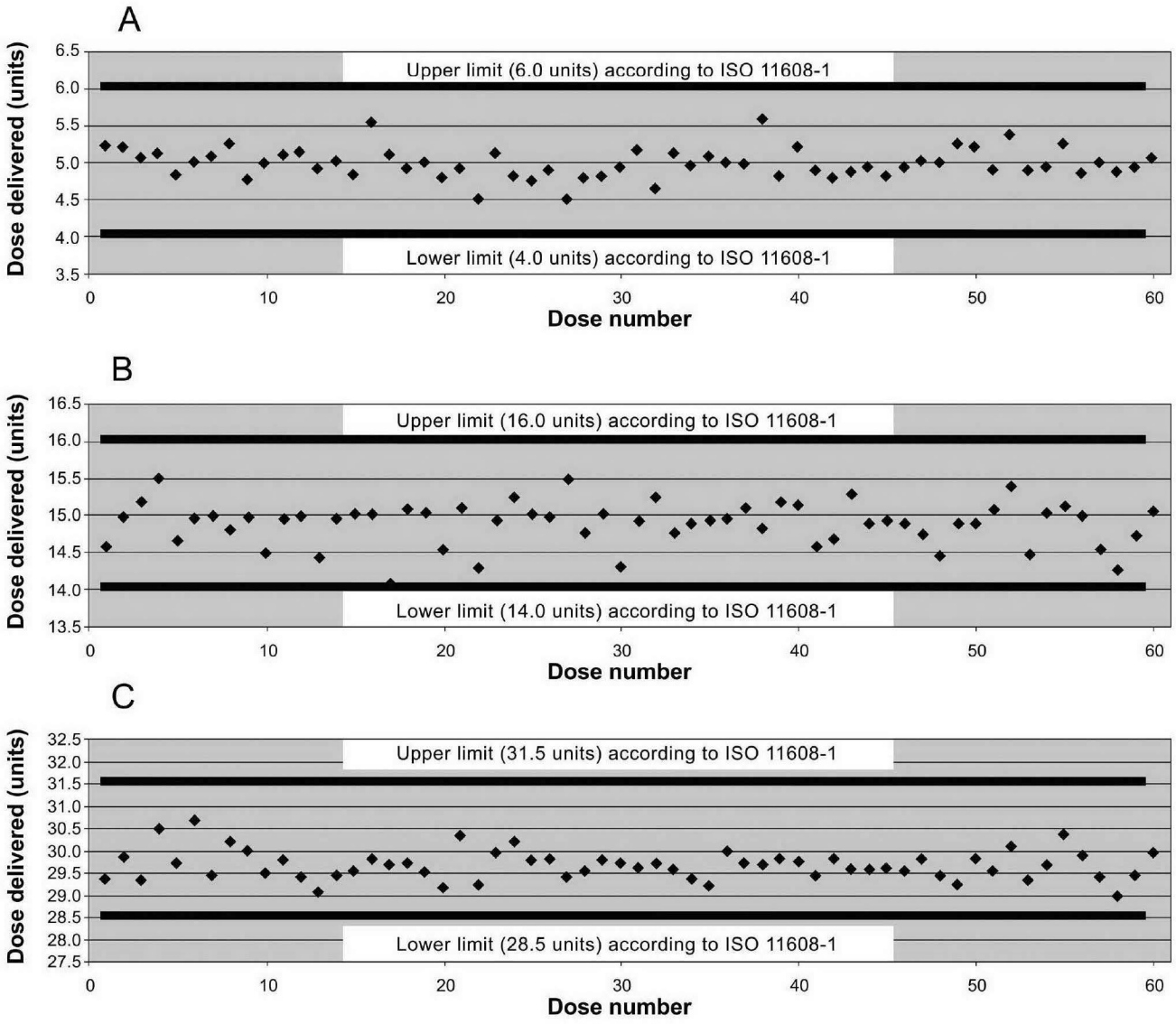

FIG. 2. Accuracy of the SoloSTAR pen when delivering (**A**) 5-, (**B**) 15-, and (**C**) 30-unit doses of insulin glulisine. The upper and lower limits, as defined by the ISO standard, 11608-1, are indicated for each dose. Each data point represents the dose delivered by an individual person.

Target dose	*Dose (units)*
5 units (ISO limit, ±1 unit: 4, 6 units)	
Observed dose	4.98 ± 0.20
Lowest dose delivered	4.50
Highest dose delivered	5.55
ISO calculated minimum[a]	4.44
ISO calculated maximum[a]	5.52
15 units (ISO limit, ±1 unit: 14, 16 units)	
Observed dose	14.87 ± 0.29
Lowest dose delivered	14.07
Highest dose delivered	15.48
ISO calculated minimum[a]	14.09
ISO calculated maximum[a]	15.65
30 units (ISO limit, ±5%: 28.5, 31.5 units)	
Observed dose	29.67 ± 0.34
Lowest dose delivered	28.93
Highest dose delivered	30.69
ISO calculated minimum[a]	28.76
ISO calculated maximum[a]	30.57

Values for observed dose are mean ± SD.
[a]Calculated using Eq. 2.

achieved repeated doses and accuracy well within the ISO standards. In the clinical setting, people who had not previously used an insulin pen device were able to accurately deliver repeated doses of insulin glargine with the SoloSTAR pen.[15] The majority of participants in the present study were experienced in the use of insulin pens; therefore, this may be considered a true test of dosing accuracy rather than usability of the SoloSTAR device.

In the present study, we evaluated the inter-subject variability in dose accuracy. For future studies, it would also be of interest to evaluate the intra-subject variability to confirm whether people with diabetes can consistently deliver the required dose. In addition, future studies could also evaluate the dose accuracy of SoloSTAR compared with alternative pen devices or the vial and syringe, to investigate if other devices achieve the same standards when used by patients as shown here for SoloSTAR.

This study confirms that people with diabetes can achieve a level of accuracy with the SoloSTAR device similar to that of technicians in a controlled lab environment that is consistently within ISO standards across the dosing range of the pen.

Conclusions

When considered together, the dosing accuracy and ease of use associated with the SoloSTAR device[16,17] may encourage patients and healthcare professionals alike to strive for optimal glycemic control with greater confidence in the precision and accuracy of the device while titrating insulin glargine and/or insulin glulisine to treatment goals.

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