Functional Evaluation of the Reusable JuniorSTAR[®] Half-Unit Insulin Pen

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Abstract

Background: The functional performance of the JuniorSTAR[®] (Sanofi, Paris, France) half-unit insulin pen was evaluated through a series of specific objective tests to assess the dose accuracy, pen weight, injection force, and dialing torque. **Method:** Pens (n = 60) were tested under standard atmospheric conditions with 3 different types of insulins manufactured by Sanofi (insulin glargine, insulin glulisine, and biphasic insulin isophane). The dose accuracy was tested according to the ISO 11608-1:2012 standards. Injection doses of 0.010, 0.155, and 0.300 ml were evaluated. For mean weight evaluation, the pens without the cartridge were weighed on precision balances. The injection force was measured using a texture analyzer and the dialing torque was measured using a torque meter. **Results:** JuniorSTAR met the ISO 11608-1:2012 criteria for dose accuracy as all the delivered doses were within the predefined limits for all types of insulin tested. The mean weight of the JuniorSTAR pen was 33.4 g (SD = 0.075). The mean injection force was 6.0 N (SD = 0.8), 4.3 N (SD = 0.4), and 5.1 N (SD = 0.6) for insulin glargine, insulin glulisine, and biphasic insulin isophane, respectively. The mean dialing torque was 5.09 Ncm (SD = 0.29) and 5.88 Ncm (SD = 0.53) for setting and correcting a dose, respectively. **Conclusions:** Together with results from a previously reported usability survey, these results show that the JuniorSTAR reusable, half-unit pen is a lightweight and accurate device for insulin delivery with a dialing torque and injection force suitable for young people with type 1 diabetes.

Keywords

dose accuracy, half-unit, injection force, insulin pen, JuniorSTAR[®], weight

The introduction of insulin pens has revolutionized the treatment of both type 1 (T1D) and type 2 diabetes.¹ Pens are now used by >60% of insulin users worldwide¹ and by 80–90% of users in Europe.² Overall, the use of insulin pens has been associated with reduced dosing errors and hypoglycemic events,^{3–6} as well as improved treatment adherence compared with the conventional method of delivery (vial and syringe).^{1,6,7} Possibly the most significant improvement is the superior dosing accuracy, particularly for dosing <5 U.^{6,8}

The vast majority of insulin pens facilitate dosing in 1 U increments. However, half-unit dose accuracy may be particularly important in the young T1D population. As per the American Diabetes Association (ADA) guidelines, young and prepubertal children require lower insulin doses.⁹ Furthermore, children with newly diagnosed T1D may require an initial dose of 0.5–1.0 U/kg/day and during this honeymoon period, requirements may even fall below this dose.⁹

To address these needs, specific insulin pens have been designed that facilitate 0.5 U dosing increments. While the impact of half-unit insulin variations on glycemic control and incidence of hypoglycemia has not been definitively proven in rigorous studies, the improved accuracy of insulin

dosing using a half-unit pen should help reduce dosing variability. This is one of the factors affecting successful management of blood glucose concentration.⁸ An insulin pen targeted at the pediatric population with a 0.5 U dosing precision may also aid in facilitating treatment compliance, and help children and adolescents gain autonomy in self-injection and diabetes treatment.

JuniorSTAR[®] (Sanofi, Paris, France; manufactured by Haselmeier, Stuttgart, Germany) is a reusable, half-unit pen with an injection dose range between 1 and 30 U. It can be used with all insulins manufactured by Sanofi (insulin glargine

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[Lantus[®]], insulin glulisine [Apidra[®]], and biphasic insulin isophane [Insuman[®]]; Sanofi, Paris, France). The pen is also available in 3 different colors (blue, red and silver), enabling users to restrict a type of insulin to a specific color. While all JuniorSTAR colored-variations can be used with any Sanofi insulin, the user can select a different colored pen for each insulin depending on their own preference. This will be advantageous to the users administering multiple insulin types, as facilitating differentiation might help prevent injection of the wrong insulin type.¹⁰ An easy dial-back process is also an important feature,¹¹ which may prevent any dose dialing errors.

This study evaluated the functional performance of JuniorSTAR. A series of specific objective tests was conducted to assess the dose accuracy, pen weight, injection force and dialing torque of the half-unit pen. Specifically, dose accuracy of the pen was tested to determine whether the ISO criteria 11608-1:2012¹² (the international standard for dose accuracy of needle-based injection systems for human use) was met.

Methods

A total of 60 JuniorSTAR pens were preconditioned in a climate chamber for a minimum of 4 h under standard atmospheric conditions (room temperature $23 \pm 5^\circ\text{C}$, relative humidity $50 \pm 25\%$)—as defined by the ISO 11608-1:2012 standard.¹² Each test was performed by 1 technician and the majority of the tests were performed in a single session and under standard atmospheric conditions (measured conditions were between 21.3°C and 26.3°C and between 47.7% and 67.5% humidity).

Dose Accuracy

The evaluation of dose accuracy was based on the guidelines of the 2012 ISO (ISO 11608-1:2012).¹² Three dose settings were tested (0.010 ml [1 U], 0.155 ml [15.5 U], and 0.300 ml [30 U]), each with the 3 types of insulin: insulin glargine, insulin glulisine, and biphasic insulin isophane, all at a concentration of 100 U/ml and in standard 3 ml cartridges. Biphasic insulin isophane was thoroughly mixed prior to testing, as outlined in the instructions for use.¹³ Prior to the accuracy test, the pen was primed and the pen needle (BD Microfine Ultra 31 G $\times$ 8 mm; Becton, Dickinson and Company, Franklin Lakes, NJ) was carefully wiped to remove any drops. Next, the specific dose was set and expelled fully into a beaker of silicon oil, with the button held for 10 s. The volumes of the expelled doses were calculated from the measured beaker weights and statistically analyzed according to ISO 11608-1:2012.¹²

Pen Weight

Each pen without the cartridge was weighed individually on a precision balance.

Injection Force

The mean (SD) injection force of the half-unit pen plunger with the 3 different insulins was measured using a texture analyzer (Texture Analyser TA.XTplus, Stable Micro Systems Ltd, London, UK) and a 31-gauge needle (BD Microfine Ultra 31 G $\times$ 8 mm).

To reduce any variability in measurements that might occur at the extreme settings of the pen due to the limitations of the texture analyzer machine and to take into account the half-unit increments, injection force was measured as the plunger was moved at a constant speed of 3 mm/s from 29.5 U to 1.5 U (a distance of 31 mm). The limitations of the texture analyzer signify that an increased force may be required to initiate plunger movement when set to the maximum at 30 U; therefore 29.5 U was selected instead. Similarly, at the lower limit, 1.5 U was selected, as excess force may be recorded when the plunger reaches 0 U, which may occur if a setting of 0.5 U is chosen. The single injection speed used was as a reference point to evaluate the effects of different cartridges and insulins as at the low injection speed any differences are most apparent. Measurements were repeated 3 times per pen.

To test injection force using insulin cartridges, the half-unit pen was primed with an injection of a 2 U dose. Following this, a simulated injection of the maximum dose (30 U) was performed before measuring injection force whilst depressing the plunger from 29.5 U to 1.5 U (dispensing 28 U).

Injection force of the half-unit pen without the cartridge was recorded as a control so that potential differences in the testing conditions and pens used could be excluded. For the test without an insulin cartridge, each pen was prepared by performing 3 simulated injections of the 30 U. Injection force was then measured whilst depressing the plunger from 29.5 U to 1.5 U.

Dialing Torque

The test was performed with an automated torque meter (Motor-Cap MC5G-L; Mecmesin GmbH, VS-Schwenningen, Germany). The dialing torque for both setting a dose and correcting a dose was measured. For the dose-setting torque, the starting point was 0 U and for the dose correction it was 30 U. Each was measured for 2 rotations (angular rotation 720°) per minute and the maximum dialing torque of each test was documented.

Statistical Methods

The mean and associated SD values were calculated for all outcome measures. For pen weight and dose accuracy, the minimum and maximum values for weight/dose delivered were also recorded. Distribution of delivered volumes was used to assess the adherence of the half-unit pen to the ISO standard (ISO 11608-1:2012).¹² To meet the ISO criteria for dose accuracy, there should be 95% confidence that at least

Table 1. Mean, Minimum, and Maximum Doses of Insulin Glargine, Insulin Glulisine, and Biphasic Insulin Isophane Delivered Using the JuniorSTAR® Reusable, Half-Unit Insulin Pen for Each Target Dose Tested (n = 60).

Target dose, ml (U)	Mean dose delivered, ml (SD)	Minimum dose delivered according to ISO 11608-1:2012, ml	Minimum dose delivered, ml	Maximum dose delivered according to ISO 11608-1:2012, ml	Maximum dose delivered, ml
Insulin glargine					
0.010 (1 U)	0.0109 (0.0007)	0.0091	0.0093	0.0127	0.0133
0.155 (15.5 U)	0.1553 (0.0016)	0.1510	0.1524	0.1596	0.1600
0.300 (30 U)	0.3015 (0.0021)	0.2958	0.2970	0.3072	0.3068
Insulin glulisine					
0.010 (1 U)	0.0092 (0.0009)	0.0067	0.0070	0.0116	0.0111
0.155 (15.5 U)	0.1541 (0.0017)	0.1497	0.1511	0.1586	0.1596
0.300 (30 U)	0.2991 (0.0022)	0.2932	0.2938	0.3051	0.3046
Biphasic insulin isophane					
0.010 (1 U)	0.0097 (0.0009)	0.0072	0.0082	0.0121	0.0118
0.155 (15.5 U)	0.1549 (0.0015)	0.1508	0.1510	0.1589	0.1576
0.300 (30 U)	0.3005 (0.0024)	0.2941	0.2960	0.3069	0.3078

97.5% (the probability content “p” for standard atmosphere) of all doses delivered will fall within the predefined upper and lower specification limits for the 3 dose settings (1 U range, 0.0050-0.0150 ml; 15.5 U range, 0.1473-0.1628 ml; 30 U range, 0.2850-0.3150 ml). Minimum/maximum dose accuracy values were calculated using data collected and a tolerance limit factor. The tolerance limit factor is set by the ISO standard and is based on the confidence level (probability of doses falling within this range), probability content (the proportion of doses), and the number of measurements taken. For this study (with 60 pens included, confidence level of 95% and probability content of 97.5% of doses) the tolerance factor is 2.670. Once applied to the mean and SD measured, the resulting values denote the statistical tolerance interval where there is a 95% confidence level that the interval will contain at least 97.5% of the true population from which this sample is taken.

Results

Dose Accuracy

The half-unit insulin pen met the ISO 11608-1:2012 criteria¹² for dose accuracy at 0.010 ml (1 U), 0.155 ml (15.5 U) and 0.300 ml (30 U) with all 3 types of insulin tested (Table 1). All of the delivered doses were within the predefined upper and lower specification limits or the minimum dial resolution (0.005 ml) of the target dose for insulin glargine (Figures 1A-1C), insulin glulisine (Figures 1D-1F), and biphasic insulin isophane (Figures 1G-1I).

Pen Weight

Pens without the cartridges (n = 60) had a mean weight of 33.4 g (SD = 0.075). The minimum and maximum weights recorded were 33.3 g and 33.6 g, respectively.

Injection Force

The mean injection forces were 6.0 N (SD = 0.8) with an insulin glargine cartridge, 4.3 N (SD = 0.4) with an insulin glulisine cartridge, and 5.1 N (SD = 0.6) with a biphasic insulin isophane cartridge (Figure 2).

Dialing Torque

The insulin pen had a mean dialing torque of 5.09 Ncm (SD = 0.29) when setting a dose and 5.88 Ncm (SD = 0.53) when correcting a dose.

Discussion

JuniorSTAR is a reusable insulin pen with a dosing range between 1 and 30 U with 0.5 U dosing increments. This study demonstrated consistent and accurate dose delivery for all doses tested and for all types of insulin tested. With not a single value of dose delivery outside the specified limits, the ISO criteria 11608-1:2012 for needle-based injection systems for human use was met.¹² Dosing accuracy is an absolute prerequisite of an insulin pen to ensure delivery of the correct medication dose and thereby minimize the risk of complications.¹ Accuracy at a 0.5 U dosing increment is of particular significance for the pediatric population because children and adolescents often require small doses of insulin to reach glycemic goals, and rounding a calculated dose up to the nearest 1 U dose might result in hypoglycemia.^{10,14} The findings of this study suggest that this pen delivers doses accurately, which may promote effective glycemic control.

As measured in this study, the half-unit pens without the cartridges had a consistent mean weight of 33.4 g (SD = 0.075). Since the insulin treatment regimen necessitates the insulin pen to be carried around on a daily basis,

Figure 1. Distribution of 0.010 ml/1 U (A, D, G), 0.155 ml/15.5 U (B, E, H), and 0.300 ml/30 U (C, F, I) doses for insulin glargine (A, B, C), insulin glulisine (D, E, F), and biphasic insulin isophane (G, H, I) delivered using the JuniorSTAR[®] reusable, half-unit insulin pen ($n = 60$). Pens were tested under standard atmospheric conditions (room temperature $23 \pm 5^\circ\text{C}$, relative humidity $50 \pm 25\%$). Dotted line denotes the dose set, and the ISO (ISO 11608-1:2012) specification limits denote the bounds within which there should be a 95% probability that 97.5% of doses fall within for the ISO criteria to be met.

Figure 2. Mean injection force of the JuniorSTAR® reusable, half-unit insulin pen with and without cartridge inserted ($n = 60$). Pens were tested under standard atmospheric conditions (room temperature $23 \pm 5^\circ\text{C}$, relative humidity $50 \pm 25\%$).

a lightweight pen is particularly desirable for use by the pediatric population.

The mean injection force required to dispel 28 U of insulin using JuniorSTAR was between 4.3 and 6.0 N, depending on the type of insulin used. The strength required to use insulin pens in the pediatric population has been evaluated previously by the Department of Trade and Industry (DTI), UK.¹⁵ According to the study by the DTI, the force exerted through a downward-pushing motion using either an index finger or thumb differs based on age group, with the lowest force exerted when using an index finger reported in the 2- to 5-year-old age group (21.82 N).¹⁵ This suggests that children and adolescents will easily be able to achieve the 6.0 N injection force needed to operate the half-unit insulin pen investigated in this study. A low injection force may be particularly important in the pediatric population as reduced injection force also correlates with reduced injection-site pain,⁷ a common barrier to insulin therapy in this age group.¹⁶

Torque is the tendency of a force to rotate an object about an axis. Whereas a force is a push, a torque is a twist. Torque is defined as the product of a lever's distance multiplied by the force vector applied to produce rotation. The torque of an insulin pen is the force required to turn the dose-dispensing ring, which turns in a circle internally. The mean dialing torque of the half-unit pen in this study was consistent for both dialing and correcting a dose, and was between 5 and 6 Ncm. A lower dialing torque signifies the

ease with which a dose can be set and corrected, which is particularly important in a pediatric insulin pen.¹⁷ Although a direct comparison cannot be made due to the variable diameters and shapes of the dial, when the vertical wrist twisting strength of the pediatric population was evaluated using a ridged knob by the UK DTI, subjects were reported to be able to generate between 0.54 and 4.44 Nm (equal to 54-444 Ncm).¹⁵ Therefore, a torque of 5-6 Ncm is expected to allow easy dose dialing and correction in the pediatric population, while retaining dose dialing accuracy, as demonstrated in this study.

The characteristics of the half-unit pen described in this study can be expected to translate into positive user ratings. In a previously reported, noncomparative study, the usability aspects of JuniorSTAR were examined.¹⁸ Participants ($n = 167$) from 5 European countries were analyzed in 2 user groups: nurses working with young people with T1D; and pen users (parents of children with T1D aged 0-12 years; and adolescents with T1D aged 13-18 years). Consistent with the low dialing torque measured in the present study for both dose setting and correction, participants in the overall group of the usability study found it easy to dial and correct a dose (80% and 87%, respectively).¹⁸ Similarly, in the usability study, participants agreed the pen was easy to carry on a daily basis (84% of overall participants) and had an injection force suitable for young people with T1D (87% of overall participants), reflecting the weight and injection force of the pen measured in this present study.¹⁸ Overall,

the half-unit pen was well received by nurses and the parent/young T1D population, and was found to be convenient for everyday use (by 90% of users overall), with 87% of all participants rating the half-unit pen as well suited to the lifestyle of young people with T1D.¹⁸

ADA guidelines state that preschoolers and schoolchildren between the ages of 3 and 7 years need to gain confidence in their ability to participate in diabetes management, but may lack the necessary fine motor control.^{9,19} In older children, many diabetes-related responsibilities can interfere with the adolescent's drive for independence and social acceptance.⁹ Consequently, compliance to diabetes treatment has been reported to be lower in children and adolescents than in adults.²⁰ Thereby, in addition to the benefits of the half-unit pen dosing accuracy for glycemic control, a convenient, robust, discreet, and simple-to-use pen could improve adherence in this vulnerable age group. This may in turn help this young population gain autonomy in managing their diabetes, leading to improved quality of life.^{1,21}

Conclusions

The JuniorSTAR reusable, half-unit pen demonstrated a consistent and accurate dose delivery at all dosage levels tested and for 3 types of insulin manufactured by Sanofi. The pen has also been found to have a low weight, injection force, and dialing torque that are suitable for the young T1D population. The characteristics outlined above may aid attainment of autonomy for self-injection in this population.

Abbreviations

ADA, American Diabetes Association; DTI, Department of Trade and Industry; ISO, International Organization for Standardization; SD, standard deviation; T1D, type 1 diabetes.

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Declaration of Conflicting Interests

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