

ORIGINAL ARTICLE

# A Web-Based Study of the Relationship of Duration of Insulin Pump Infusion Set Use and Fasting Blood Glucose Level in Adults with Type 1 Diabetes

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## Abstract

**Background:** To evaluate the impact of infusion set use duration on glycemic control, we conducted an Internet-based study using the T1D Exchange's online patient community, Glu (myGlu.org).

**Subjects and Methods:** For 14 days, 243 electronically consented adults with type 1 diabetes (T1D) entered online that day's fasting blood glucose (FBG) level, the prior day's total daily insulin (TDI) dose, and whether the infusion set was changed.

**Results:** Mean duration of infusion set use was 3.0 days. Mean FBG level was higher with each successive day of infusion set use, increasing from 126 mg/dL on Day 1 to 133 mg/dL on Day 3 to 147 mg/dL on Day 5 ( $P < 0.001$ ). TDI dose did not vary with increased duration of infusion set use.

**Conclusions:** Internet-based data collection was used to rapidly conduct the study at low cost. The results indicate that FBG levels increase with each additional day of insulin pump infusion set use.

## Introduction

FEW STUDIES HAVE EVALUATED the impact of duration of insulin pump infusion set use on glycemic control or outlined guidelines for when an infusion set should be changed.<sup>1-6</sup> A white paper published from the proceedings of an American Association of Diabetes Educators consensus panel noted the lack of literature regarding subcutaneous insulin infusion devices.<sup>7</sup> To address this gap in evidence, we conducted an Internet-based study using the T1D Exchange's online patient community, Glu (myGlu.org). The study also provided the opportunity to assess the feasibility of using online data collection for longitudinal studies.

## Subjects and Methods

Participants were recruited from the T1D Exchange's online patient community, Glu. E-mails were sent to Glu members who indicated a preference to be contacted about research studies. Additionally, information about the study was provided on Glu, Facebook, and Twitter. Eligibility criteria included age

≥18 years, diagnosis of type 1 diabetes (T1D), and daily use of an insulin pump. Participants signed an institutional review board-approved electronic informed consent form. Participants received no compensation for taking part in the study.

Participants completed a questionnaire on their diabetes history, diabetes management, pump use, and most recent hemoglobin A1c (HbA1c) level. For 14 days, participants received daily e-mail prompts to report the following information using a computer or other device: that day's fasting blood glucose (FBG) level, the prior day's total daily insulin (TDI) dose, and whether the infusion set was changed.

To be included in the analyses, a participant must have completed data entry at least 3 of the 14 days. When infusion set use was more than 5 days, only the first 5 days were analyzed owing to the small number of infusion sets used for more than 5 days.

## Statistical methods

Linear regression models were used to examine the association between (1) typical duration of infusion set wear and

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TABLE 1. INSULIN PUMP USE PRIOR TO STUDY

	Value
Total number of subjects	243
Duration of insulin pump use on a daily basis	
<6 months	12 (5%)
6 months–<1 year	10 (4%)
1 year–<2 years	16 (7%)
2 years–<3 years	18 (7%)
≥3 years	187 (77%)
Duration of use of current pump	
<6 months	38 (16%)
6 months–<1 year	43 (18%)
1 year–<2 years	62 (26%)
2 years–<3 years	41 (17%)
≥3 years	59 (24%)
Brand of insulin pump	
Animas	64 (26%)
Insulet	17 (7%)
Medtronic	147 (60%)
Roche	3 (1%)
Smith's Medical	4 (2%)
Tandem	7 (3%)
Unknown	1 (<1%)
Type of infusion set	
30° Teflon	11 (5%)
90° Teflon	127 (52%)
90° steel	9 (4%)
Unknown	96 (40%)
Typical frequency of infusion set change	
Every other day	12 (5%)
Every 3 days	160 (66%)
Every 4 days	45 (19%)
Every 5 days	12 (5%)
Every 6 days	8 (3%)
Every 7 days	3 (1%)
More than 7 days	3 (1%)
Frequency of earlier than usual infusion set change due to concern about insulin delivery in the last 3 months	
None	35 (14%)
1 time	51 (21%)
2 times	63 (26%)
3 times	38 (16%)
4 times	23 (9%)
≥5 times	33 (15%)

Data are number (%).

annual household income and (2) self-reported HbA1c and typical duration of infusion set wear. Linear mixed models with repeated measures were used to separately examine the association between FBG and TDI dose, with day of infusion set use accounting for the correlation due to multiple measures per participant. To account for possible confounding due to the potential for participants with higher FBG levels to wear infusion sets longer, average duration of infusion set wear was included as an adjustment covariate in the model. The analyses were repeated in the participant subset that completed all 14 daily questionnaires, with results similar to those from the main analysis (data not shown).

Data analyses used SAS software, version 9.3 (2011; SAS Institute Inc., Cary, NC). All *P* values are two-sided.

## Results

Of the 317 participants who completed the electronic consent process, 14 (4%) did not complete the enrollment questionnaire, 45 (14%) failed to enter any daily study data, and 15 (5%) completed <3 days of data collection. A cohort of 243 participants was included in the study analyses. Among the 243 participants, 173 (71%) enrolled on the day the study was announced, 29 (12%) on the second day, eight (3%) on the third day, and the remaining 33 (14%) within 11 days.

Mean age of the 243 participants was 42 ± 14 years (13%, 18–25 years; 36%, 26–40 years; 41%, 41–60 years; and 11%, ≥61 years), median duration of diabetes was 22 years (interquartile range, 12–35 years), 91% were non-Hispanic white, 73% were female, and 29% had an annual household income of ≥\$100,000 (10%, <\$35,000; 25%, \$35,000–<\$75,000; and 19%, \$75,000–<\$100,000; 16% did not provide annual income information). Among study participants, 63% reported using a continuous glucose monitor. Mean HbA1c level was 6.9 ± 1.1%. Typical duration of infusion set use was not related to income; mean typical duration of infusion set use was 3.7, 3.3, 3.5, and 3.5 days for annual income of <\$35,000, \$35,000–<\$75,000, \$75,000–<\$100,000, and ≥\$100,000, respectively (*P* = 0.58). Mean HbA1c level was 7.0% for participants typically changing the infusion set every 2–3 days and 6.7% for those who changed every 4 or more days (*P* = 0.03).

The types of insulin pumps used by the participants are shown in Table 1. Insulin pump use was at least 3 years

TABLE 2. GLYCEMIC CONTROL AND INSULIN AMOUNT ACCORDING TO DAY OF INFUSION SET USE

	Day 1	Day 2	Day 3	Day 4	Day 5
Fasting blood glucose (mg/dL)					
<i>n</i>	236	236	230	163	77
Mean ± SD	125 ± 39	128 ± 44	133 ± 49	140 ± 56	147 ± 68
Median (interquartile range)	119 (100, 146)	116 (99, 149)	125 (97, 158)	132 (94, 171)	128 (99, 174)
% > 180 mg/dL	9%	13%	15%	21%	22%
% > 250 mg/dL	1%	1%	3%	4%	8%
Total daily insulin (units)					
<i>n</i>	236	230	163	77	40
Mean ± SD	40.1 ± 20.5	39.6 ± 19.5	37.9 ± 16.6	36.7 ± 16.4	39.3 ± 15.8
Median (interquartile range)	35.6 (27.0, 45.4)	34.9 (27.0, 45.5)	34.5 (28.0, 45.5)	35.0 (27.0, 43.0)	37.5 (29.5, 46.5)

When infusion set use was more than 5 days, only the first 5 days were analyzed because of the small number of infusion sets used more than 5 days.

TABLE 3. FASTING BLOOD GLUCOSE BY DAY OF INFUSION SET WEAR FOR SUBSETS OF DURATION OF INFUSION SET WEAR

Days of infusion set wear	Fasting blood glucose level (mg/dL)				
	Day 1	Day 2	Day 3	Day 4	Day 5
3 (n = 67)					
Mean ± SD	125 ± 33	133 ± 44	142 ± 53	—	—
Median (interquartile range)	122 (104, 145)	121 (104, 152)	131 (101, 172)	—	—
4 (n = 86)					
Mean ± SD	127 ± 42	127 ± 42	132 ± 44	148 ± 60	—
Median (interquartile range)	116 (100, 142)	115 (100, 148)	123 (95, 161)	142 (99, 180)	—
5 (n = 75)					
Mean ± SD	125 ± 41	125 ± 47	125 ± 49	131 ± 54	147 ± 68
Median (interquartile range)	120 (92, 151)	113 (91, 149)	118 (91, 142)	122 (90, 155)	128 (98, 174)

When infusion set use was more than 5 days, only the first 5 days were analyzed because of the small number of infusion sets used more than 5 days.

TABLE 4. GLYCEMIC CONTROL BY DEMOGRAPHIC AND CLINICAL FACTORS ACCORDING TO DAY OF INFUSION SET USE

Factor	Fasting blood glucose (mg/dL)										P value	
	Day 1		Day 2		Day 3		Day 4		Day 5		Unadjusted <sup>a</sup>	Adjusted <sup>b</sup>
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD		
Gender											0.30	0.64
Female	173	127 ± 39	173	129 ± 45	170	135 ± 52	122	138 ± 56	65	148 ± 69		
Male	63	122 ± 39	63	124 ± 43	60	128 ± 41	41	146 ± 63	12	141 ± 61		
Age (years)											0.07	0.63
18–25	30	146 ± 40	30	139 ± 50	29	136 ± 51	21	140 ± 52	11	133 ± 44		
26–40	83	123 ± 37	83	128 ± 43	81	138 ± 52	62	144 ± 59	36	138 ± 58		
41–60	97	124 ± 40	97	123 ± 44	95	130 ± 49	66	136 ± 61	28	168 ± 84		
≥ 61	26	114 ± 37	26	131 ± 41	25	128 ± 35	14	137 ± 52	2	105 ± 30		
Race/ethnicity											0.33	0.50
White non-Hispanic	216	126 ± 40	216	127 ± 45	212	133 ± 49	150	139 ± 57	68	151 ± 69		
Black non-Hispanic	1	92	1	130	1	70	1	138	1	65		
Hispanic or Latino	8	102 ± 29	8	121 ± 29	7	116 ± 36	5	178 ± 101	3	130 ± 77		
Other race/ethnicity	11	131 ± 35	11	145 ± 43	10	150 ± 57	7	124 ± 33	5	126 ± 45		
Type 1 diabetes duration (years)											0.03	0.22
≤ 9	46	131 ± 48	46	125 ± 43	45	130 ± 47	37	130 ± 54	17	129 ± 39		
10–≤ 20	57	137 ± 37	57	141 ± 48	55	139 ± 52	36	160 ± 74	15	125 ± 64		
21–≤ 31	63	129 ± 38	63	127 ± 45	62	143 ± 55	46	149 ± 46	26	148 ± 53		
> 31	70	110 ± 31	70	119 ± 40	68	122 ± 39	44	122 ± 51	19	181 ± 96		
Annual income											0.74	0.65
< \$35,000	22	136 ± 52	22	145 ± 50	22	129 ± 57	16	145 ± 87	10	147 ± 63		
\$35,000–< \$75,000	63	125 ± 36	63	123 ± 40	62	125 ± 45	43	132 ± 45	17	154 ± 77		
\$75,000–< \$100,000	45	121 ± 37	45	125 ± 48	44	137 ± 50	32	141 ± 53	18	154 ± 70		
≥ \$100,000	68	124 ± 34	68	126 ± 43	66	133 ± 46	43	144 ± 48	17	139 ± 59		
Not provided	38	128 ± 48	38	132 ± 45	36	145 ± 54	29	141 ± 74	15	141 ± 75		
Brand of insulin pump											0.43	0.88
Animas	62	133 ± 42	62	130 ± 39	61	132 ± 47	44	138 ± 56	20	139 ± 52		
Insulet	17	121 ± 34	17	118 ± 37	16	125 ± 52	5	139 ± 54	0	—		
Medtronic	143	124 ± 39	143	129 ± 48	139	135 ± 50	102	139 ± 59	53	154 ± 74		
Roche	2	126 ± 17	2	111 ± 51	2	127 ± 47	2	212 ± 28	1	123		
Smith's Medical	4	96 ± 15	4	106 ± 23	4	98 ± 30	4	126 ± 34	2	96 ± 43		
Tandem	7	126 ± 26	7	121 ± 50	7	151 ± 58	5	159 ± 66	0	—		
Type of insulin <sup>c</sup>											0.87	0.71
Apidra (insulin glulisine)	22	122 ± 35	22	128 ± 50	20	158 ± 73	11	143 ± 55	2	153 ± 91		
Humalog (insulin lispro)	109	126 ± 38	109	133 ± 44	108	136 ± 48	76	139 ± 50	33	152 ± 65		
Novolog (insulin aspart)	104	126 ± 42	104	123 ± 43	101	125 ± 43	75	141 ± 66	41	145 ± 71		

<sup>a</sup>Unadjusted P values from a linear mixed model with repeated measures adjusted for average duration of infusion set wear. Only the adjustment factor, day of infusion set wear, and the indicated factor were included in the model. Age and duration of type 1 diabetes were included as continuous factors.

<sup>b</sup>Adjusted P values from a linear mixed model with repeated measures adjusted for average duration of infusion set wear. In addition to the adjustment factor and day of infusion set wear, all factors in the table were included in model. Age and duration of type 1 diabetes were included as continuous factors.

<sup>c</sup>One participant reported using Humalog R U-500.

in 77% of participants, with 66% of participants usually changing their infusion set every 3 days.

#### Outcome data

Daily data were entered for all 14 days by 213 (71%) of the 243 participants, 10–13 days by eight (3%), 6–9 days by 12 (5%), and 3–5 days by 10 (4%). During the study, the 243 participants reported using a total of 688 infusion sets. Mean duration of infusion set use during the study was  $3.0 \pm 1.0$  days: 1–2 days for 26%, 3 days for 48%, 4 days for 19%, and 5 days for 7%.

Mean FBG increased with each additional day of infusion set wear, increasing from 125 mg/dL on Day 1 to 133 mg/dL on Day 3 to 147 mg/dL on Day 5 ( $P < 0.001$ ) (Table 2). It is interesting that for infusion sets used for 4 days, there was not a substantial increase in the mean FBG until Day 4, and for infusion sets used for 5 days, there was not a substantial increase until Day 5 (Table 3). Other than duration of infusion set use, no other factors were associated with the increase in mean glucose level as seen from Day 1 to Day 5 (Table 4). Mean TDI dose remained relatively constant from Day 1 to Day 5 (from 40 to 39 units/day) ( $P = 0.94$ ).

#### Discussion

Our study used online data collection to address an important clinical question much more rapidly and at lower cost than comparable clinic-based studies. Within 2 days of announcing the study, more than 200 participants had enrolled, and the study was essentially completed within 1 month of initiation. Participants were not compensated, so costs for the study were limited to programming for the Web site's data collection capabilities and data analyses. The study's main finding was that FBG levels increased with each day of infusion set use. It is particularly noteworthy that for those infusion sets used for 4 and 5 days, mean FBG only modestly increased until Day 4 and 5, respectively. Thus patients seem to be able to autotitrate the frequency in which they need to change their infusion sites.

Our findings are consistent with a small prior study conducted in 20 adults with T1D that found that from Day 2 to Day 5 of infusion set use, FBG increased from 120 to 155 mg/dL.<sup>8</sup> In that study, TDI dose increased from  $48.5 \pm 11.8$  units to  $55.3 \pm 17.9$  units, whereas we did not find an increase in TDI dose in our subjects.

In assessing the feasibility of conducting a study using online data collection, potential biases that may be present depending on the characteristics of the participants and the lack of direct monitoring by clinic personnel may require further evaluation. In the case of the current study, even though our participants were better controlled than most adults with T1D in the United States and more likely to be using continuous glucose monitoring,<sup>9</sup> bias with respect to the study participants seems unlikely to have had a major effect on the results because no other factors were found to be associated with the increase in FBG over time. Additionally, because data were entered daily by participants, it seems unlikely that study participants would have falsely entered FBG values. Although FBG data were not verified, a study such as this could have done so if it was required through the uploading of blood glucose meter data at the end of the study.

In conclusion, this study demonstrates the power of using online data collection and a T1D social network to conduct

longitudinal clinical research studies rapidly at low cost. The results of the study indicate that FBG levels increase each day of successive insulin pump infusion set use, which is important for insulin pump users and their healthcare providers to recognize.

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