

Siphon Effects on Continuous Subcutaneous Insulin Infusion Pump Delivery Performance

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Abstract

Background:

The objective was to quantify hydrostatic effects on continuous subcutaneous insulin infusion (CSII) pumps during basal and bolus insulin delivery.

Methods:

We tested CSII pumps from Medtronic Diabetes (MiniMed 512 and 515), Smiths Medical (Deltec Cozmo 1700), and Insulet (OmniPod) using insulin aspart (Novolog, Novo Nordisk). Pumps were filled and primed per manufacturer's instructions. The fluid level change was measured using an inline graduated glass pipette (100 μ l) when the pipette was moved in relation to the pump (80 cm Cosmo and 110 cm Medtronic) and when level. Pumps were compared during 1 and 5 U boluses and basal insulin delivery of 1.0 and 1.5 U/h.

Results:

Pronounced differences were seen during basal delivery in pumps using 80–100 cm tubing. For the 1 U/h rate, differences ranged from 74.5% of the expected delivery when the pumps were below the pipettes and pumping upward to 123.3% when the pumps were above the pipettes and pumping downward. For the 1.5 U/h rate, differences ranged from 86.7% to 117.0% when the pumps were below or above the pipettes, respectively. Compared to pumps with tubing, OmniPod performed with significantly less variation in insulin delivery.

Conclusions:

Changing position of a conventional CSII pump in relation to its tubing results in significant changes in insulin delivery. The siphon effect in the tubing may affect the accuracy of insulin delivery, especially during low basal rates. This effect has been reported when syringe pumps were moved in relation to infusion sites but has not been reported with CSII pumps.

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Abbreviations: (CSII) continuous subcutaneous insulin infusion

Keywords: continuous subcutaneous insulin infusion, insulin administration, insulin delivery, insulin infusion, insulin infusion devices, insulin pump therapy

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Introduction

The lives of people with diabetes have been improved significantly with the use of continuous subcutaneous insulin infusion (CSII) pumps. Studies comparing CSII to multiple daily injections have shown improvements in hemoglobin A1c, blood glucose control, and quality of life.¹⁻³ The landmark study by the Diabetes Control and Complications Trial⁴ demonstrated that tight glucose control decreases the incidence and severity of diabetes-related complications. Unfortunately, with tight glucose control, the possibility of severe hypoglycemia increases; the use of CSII and rapid-acting insulin analogues has improved glucose control without increasing the incidence of severe hypoglycemia. It is now estimated that approximately 375,000 people use insulin pumps to control their diabetes.⁵ The use of pumps is increasing, the market is expanding to include individuals with type 2 diabetes, and the cost of pumps and supplies is often covered by medical insurance, including Medicare and Medicaid after approval. Although the initial cost of obtaining a pump and the supplies may be high, medical complications of diabetes may be reduced long term, thus reducing the overall medical cost while improving quality of life.⁶

For all improvements in glucose control with CSII, problems may occur if patients and health care providers are not aware of, or educated about, potential issues. Unexplained hyperglycemia may occur due to pump tubing occlusion or an infusion site catheter that has become dislodged or was not inserted correctly. In addition, air bubbles may occur in the tubing, which will interrupt insulin delivery. Hyperglycemia that is not detected may lead to diabetic ketoacidosis.⁷ Insulin delivery may be inaccurate due to a failure to purge air from the syringe and to correctly prime the infusion set. Although blockage and kinking of tubing is rare, it can occur. The occlusion alarm on all pumps will sound if delivery is interrupted by a blockage but will not sound if there is a failure at the insertion site.

Another issue that has not been addressed adequately is the siphon effect in CSII tubing; this may affect the accuracy of insulin delivery. Fluctuations in insulin delivery may arise when the pump's height, relative to the cannula, changes during normal use. This has previously been reported when the height of syringes and syringe pumps have moved in relation to intravenous sites in patients⁸⁻¹¹ but has not been reported with CSII use. The objective of this study was to quantify the effect

of pump height in relation to the end of the tubing or insertion site on insulin delivery of CSII pumps during basal and bolus delivery and to evaluate the same effects when the pump is stopped.

Methods

We tested CSII pumps from Medtronic Diabetes (MiniMed 512 and 515), Smiths Medical (Deltac Cozmo 1700), and Insulet Corporation (OmniPod) using a rapid-acting insulin analogue, insulin aspart (Novolog, Novo Nordisk). Three pumps of each model were tested.

Pumps were filled and primed with insulin aspart per manufacturer's instructions. We then measured the change in the fluid level in an inline graduated glass pipette (100 μ l) when the end of the tubing (80 cm Cosmo and 110 cm Medtronic pumps) was moved either up or down to its maximum length in relation to the pump and when it was extended to the maximum length at level (Figure 1). For the OmniPod, the unit was held vertically in a clamp, with the cannula up for "upward" pumping position and the cannula down for the "downward" pumping position. The OmniPod was horizontal for the level pumping position.

For pumps with tubing, we first recorded the changes in a static state, with the pump suspended, and then after bolus doses of 1 and 5 U. Finally, we compared the pumps during basal insulin delivery with rates of 1.0 and 1.5 U/h.

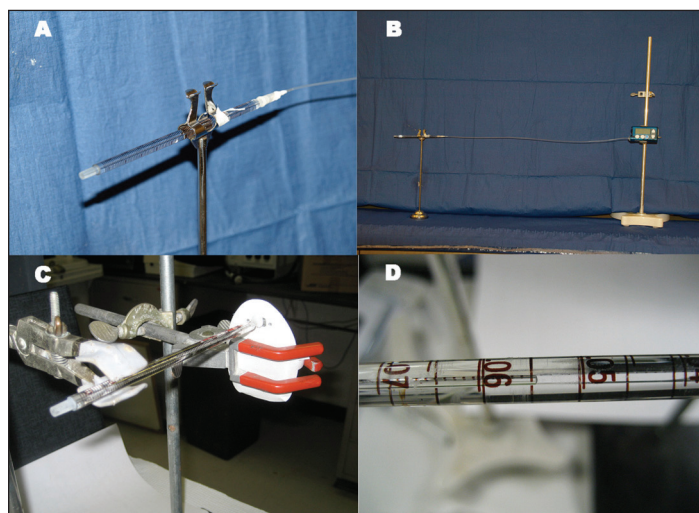


Figure 1. Pump testing setup. A, 100 μ l pipette in stand; B, pump with tubing, level; C, OmniPod in stand; D, pipette close-up.

Pumps were placed in suspend mode immediately after the delivery of each bolus or basal amount. At least three trials were done with each pump in the four delivery modes. All results are reported in units of insulin (1 U = 10 μ l) and in percentage of expected insulin dose. Barometric pressure and temperature were recorded for all runs. An *in silico* simulation was performed using a model based on a modification of the oral glucose meal simulation model of Dalla Man and colleagues.^{12,13} The simulated subject is an 11-year-old child with a body weight of 59 kg and the optimal basal rate is 0.72 U/h.

Statistical Analysis

A sample size was determined to give sufficient power to detect a 0.05–0.10 U difference between pump models. Alpha was set at 0.05. Data were analyzed using Statistical Analysis Software (SAS version 9.1., SAS, Cary, NC). One-way and two-way analysis of variance models were examined using Scheffé's correction for multiple comparisons. In addition, *t* tests were performed to examine differences between actual and expected delivery.

Results

The most pronounced differences in accuracy were seen during basal delivery in the CSII pumps using 80–100 cm tubing. For the 1 U/h rate, differences ranged from 74.5% of the expected delivery when the pumps were below the pipettes and pumping upward to 123.3% when the pumps were above the pipettes and pumping downward. For the 1.5 U/h rate, differences ranged from 86.7% to 117.0% when the pumps were below or above the pipettes, respectively. **Table 1** reports the mean units of insulin delivered and the minimum and maximum after each of the various delivery modes and for each experimental condition. **Table 2** describes how close/far each experimental condition came to providing 100% of its expected delivery. All significant results ($p < .05$) are reported in the notes of **Table 2**. **Figures 2** and **3** show the percentage of expected delivery for 1.0 and 1.5 U/h basal rates, respectively. **Figure 4** displays an *in silico* simulation for inaccurate insulin delivery with the greatest differences. It describes 3 h with the optimal basal and then 8 h with $\pm 25\%$ of the optimal basal. A steady state value of 120 mg/dl is defined as the target glucose and the initial condition for the simulation.

For the static movements with pumps and tubing, moving the pump down resulted in a change in pipette insulin level of -0.2 U, with a range of -0.1 to -0.4 U. Moving the pump up resulted in a change in pipette insulin level of 0.2 U, with a range of 0.5 to 0.0 U.

Table 1.
Mean Units of Insulin Delivered by Mode, Pump Model, and Direction

Delivery mode/ pump	Mean units delivered (min, max)		
	Pumping direction		
	Downward	Level	Upward
1.0 U Basal Delivery for 1 h			
Cosmo	1.11 (1.0, 1.3)	0.96 (0.9, 1.0)	0.75 (0.6, 0.9)
MiniMed 515	1.23 (1.0, 1.4)	0.93 (0.7, 1.2)	0.81 (0.7, 1.0)
MiniMed 512	1.10 (0.7, 1.3)	0.97 (0.6, 1.1)	0.83 (0.5, 1.0)
OmniPod	1.01 (0.9, 1.3)	0.98 (0.8, 1.1)	0.99 (0.7, 1.2)
1.5 U Basal Delivery for 1 h			
Cosmo	1.63 (1.5, 1.8)	1.42 (1.3, 1.6)	1.30 (1.1, 1.4)
MiniMed 515	1.76 (1.6, 1.9)	1.51 (1.4, 1.6)	1.31 (1.1, 1.4)
MiniMed 512	1.63 (1.4, 2.0)	1.54 (1.2, 2.4)	1.33 (0.9, 1.6)
OmniPod	1.52 (1.3, 1.6)	1.44 (1.3, 1.6)	1.54 (1.4, 1.8)
1.0 U Bolus			
Cosmo	1.01 (1.0, 1.1)	0.98 (0.9, 1.1)	0.94 (0.8, 1.0)
MiniMed 515	1.04 (0.8, 1.2)	0.92 (0.6, 1.3)	0.78 (0.5, 0.9)
MiniMed 512	1.01 (0.9, 1.1)	1.01 (0.9, 1.3)	0.84 (0.4, 1.0)
OmniPod	0.94 (0.8, 1.1)	0.99 (0.9, 1.1)	0.98 (0.9, 1.2)
5.0 U Bolus			
Cosmo	5.10 (5.0, 6.0)	4.99 (4.9, 5.1)	4.89 (4.7, 5.1)
MiniMed 515	5.04 (4.9, 5.2)	4.82 (4.5, 5.1)	4.76 (4.5, 5.0)
MiniMed 512	5.13 (5.0, 5.6)	4.97 (4.8, 5.1)	4.98 (4.6, 5.3)
OmniPod	4.96 (4.9, 5.1)	5.03 (4.9, 5.3)	4.97 (4.9, 5.1)

The mean barometric pressure and temperature for all runs was 1012.6 ± 3.2 mbar (29.9 ± 0.1 inHg) and 22.7 ± 0.5 °C (72.8 ± 1.0 °F), respectively.

Discussion

The second century AD Greek physician, Aretus the Cappadocian, is responsible for labeling conditions associated with polyuria as “diabetes,” derived from the Greek for “a passer through, a siphon.” Patients with diabetes “pass water like a siphon.” Siphons have been used for centuries to move liquids from one place to another, and a similar effect was seen in individuals with diabetes. Technically, a siphon is defined as “an instrument, usually in the form of a tube bent to form two legs of unequal length, for conveying liquid over the edge of a vessel and delivering it at a lower level... The action depends upon the influence of gravity (not, as sometimes thought, on the difference in atmospheric pressure—a siphon will work in a vacuum) and upon the cohesive forces that prevent the columns of liquid

in the legs of the siphon from breaking under their own weight."¹⁴ "In other words, the water isn't being pushed over the hump by atmospheric pressure behind it, it's being pulled by the water ahead, as though it were (excuse me, but this is how I conceived of it) a giant stringy booger."¹⁵ Hydrostatic pressure is defined as "the pressure exerted by a fluid at equilibrium at a given point within the fluid, due to the force of gravity."¹⁶ A siphon effect has been reported previously when syringes and syringe pumps have been moved in relation to infusion sites⁸⁻¹¹ but has not yet been reported with CSII devices. Raising and lowering syringes, even

syringes fixed in syringe pumps, will undergo hydrostatic pressure changes, and this will affect fluid delivery.¹⁷⁻²¹ Small boluses can be delivered by simply raising the syringe pump above the insertion site, and the effects are most apparent at low delivery rates for drugs.

Although delivery amounts for the different CSII pumps are tested thoroughly, the usual testing method involves the weight of the insulin delivered. The height of the pump above or below the insertion site and the length and compliance of tubing are not considered when accuracy of delivery is determined. Insulin infusion pumps have

Table 2.
Percentage of Expected Insulin Dose Delivered by Mode, Pump Model, and Direction

Delivery mode/pump	Percentage of expected (min, max)		
	Pumping direction		
	Downward	Level	Upward
1.0 U Basal Delivery for 1 h			
Cosmo ^a	110.8 ^b (100, 130)	95.8 ^b (90, 100)	74.5 ^b (60, 90)
MiniMed 515 ^c	123.3 ^b (100, 140)	93.3 (70, 120)	81.1 ^b (70, 100)
MiniMed 512 ^a	110.0 (70, 130)	96.7 (60, 110)	83.3 ^b (50, 100)
OmniPod	101.3 ^d (90, 130)	98.3 (80, 110)	99.3 ^e (70, 120)
1.5 U Basal Delivery for 1 h			
Cosmo ^c	108.9 ^b (100, 120)	94.4 (87, 107)	86.7 ^b (73, 93)
MiniMed 515 ^a	117.0 ^b (107, 127)	101.0 (93, 107)	87.6 ^b (73, 93)
MiniMed 512 ^f	108.5 ^b (93, 133)	102.8 (80, 160)	88.3 ^b (60, 107)
OmniPod	101.1 ^g (87, 107)	96.0 (87, 107)	102.5 ^d (93, 120)
1.0 U Bolus			
Cosmo ^f	100.8 (100, 110)	98.3 (90, 110)	94.2 ^b (80, 100)
MiniMed 515 ^f	104.4 (80, 120)	92.2 (60, 130)	77.8 ^{b,e} (50, 90)
MiniMed 512 ^h	100.8 (90, 110)	100.8 (90, 130)	84.2 ^b (40, 100)
OmniPod	94.4 ^g (80, 110)	98.8 (90, 110)	98.1 (90, 120)
5.0 U Bolus			
Cosmo ^h	102.0 (100, 120)	99.8 (98, 102)	97.8 ^b (94, 102)
MiniMed 515 ^c	100.8 (98, 104)	96.4 ^{b,e} (90, 102)	95.1 ^{b,i} (90, 100)
MiniMed 512 ^c	102.5 ^b (100, 112)	99.3 (96, 102)	99.5 (92, 106)
OmniPod	99.1 (98, 102)	100.5 (98, 106)	99.3 (98, 102)

^a Up, level, and down are significantly different from each other ($p < .05$).

^b Significantly different than expected ($p < .05$).

^c Down is significantly different from level ($p < .03$); level and up are not different from each other.

^d Significantly different than the other three pumps in this direction ($p < .02$).

^e Significantly different than the other two pumps (not M512) in this direction ($p < .05$).

^f Up is significantly different from down ($p < .03$); neither are different from level.

^g Significantly different than the MM515 (not the other two pumps) in this direction ($p < .05$).

^h Up is significantly different from level ($p < .03$); level and down are not different from each other.

ⁱ Significantly different than the other two pumps (not Cosmo) in this direction ($p < .05$).

an expected range of delivery accuracy of +/-5%. In this experiment, the objective was to quantify the effect of hydrostatic pressure on insulin delivery during bolus dosages, basal rates, and static changes in CSII pumps.

The results demonstrate that raising or lowering a CSII pump to the full extent of its tubing can significantly

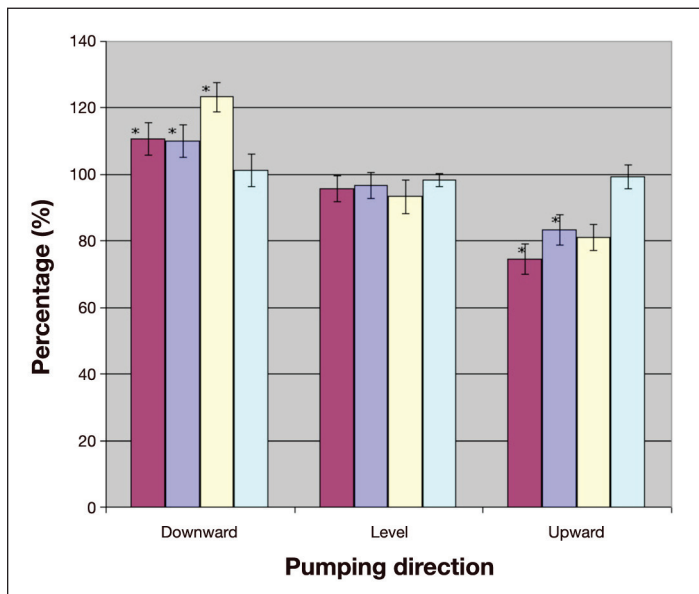


Figure 2. Percentage of expected delivery for 1.0 U/h basal rate. Cosmo, magenta columns; MiniMed 512, blue columns; MiniMed 515, yellow columns; OmniPod, light blue columns. The asterisk represents significant difference from level ($p < .05$).

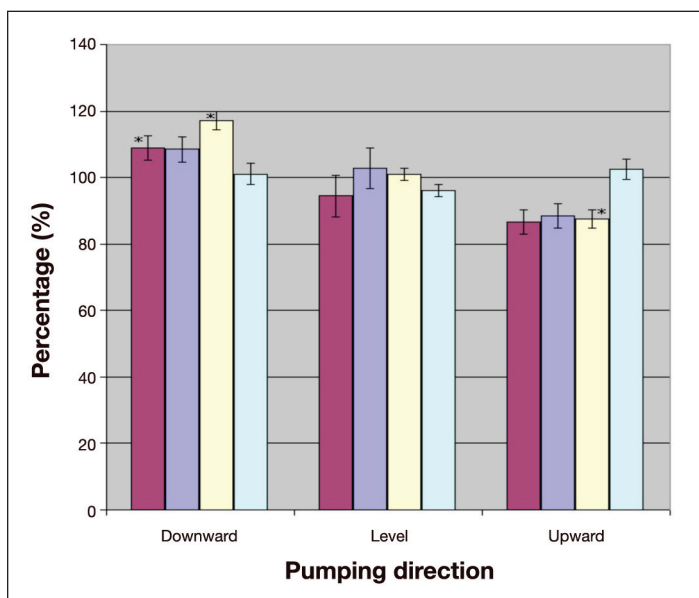


Figure 3. Percentage of expected delivery for 1.5 U/h basal rate. Cosmo, magenta columns; MiniMed 512, blue columns; MiniMed 515, yellow columns; OmniPod, light blue columns. The asterisk represents significant difference from level ($p < .05$).

affect insulin delivery. This effect is pronounced at low basal infusion rates. If the pumps were above the infusion cannula and the pumping direction was downward, then infusion amounts were significantly more than expected. If the pumps were below the infusion cannula and the pumping direction was upward, then the infusion amounts were significantly less than expected. The range of delivery volumes (minimum and maximum) varied for all pumps, but some pumps demonstrated a high variability. For example, the MiniMed 512 pump delivered a mean 1.54 U for a 1.5 U/h basal rate; this is very close to the expected. However, the range showed a minimum of 1.2 U and a maximum of 2.4 U, almost 1 U more than expected. For OmniPod, there is never a height differential created between the reservoir and the site of insulin delivery, and performance was near the expected range of delivery accuracy regardless of pumping direction or orientation.

Many factors, such as temperature and tissue permeability, affect insulin delivery from the depot site to the blood. The siphon effect may be masked by these other factors. Where the pump is usually worn will also affect delivery. Further investigation of the effect of pump height from insertion site can be done by varying the height above and below and then graphing these results. It would also be helpful to test the effects in a person and to clinically validate our observations. As demonstrated in **Figure 3** in our simulated *in silico* worst-case scenarios, the siphon effects on the accuracy of insulin pump delivery may be most important for individuals with low basal rates and especially for children with diabetes when small

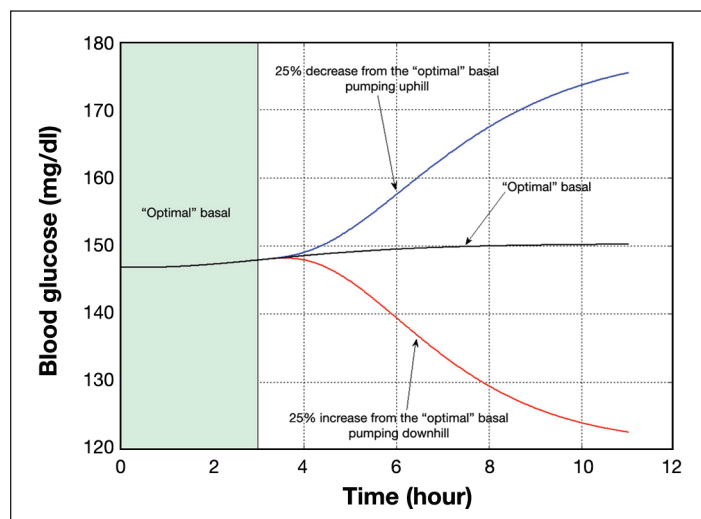


Figure 4. *In silico* basal rate simulation. This simulation describes 3 h with the optimal basal and 8 h with +/-25% of the optimal basal. The target glucose is 150 mg/dl.

differences in insulin amounts will be more significant. Pediatric patients may be more sensitive to varying insulin amounts,²² and this will cause more variability in blood glucose levels. Blood glucose variability has been shown to be a risk factor for the progression of complications of diabetes;²³ thus the importance of reducing glycemic variability for all individuals with diabetes has been gaining recognition. As we enter the era of continuous glucose sensors, communication with insulin pumps, and the inevitable possibility of “closing the loop” for automated delivery of insulin, the accuracy of delivery will become even more important.

In summary, movement of a conventional CSII pump in relation to its tubing results in significant changes or fluctuations in insulin delivery. Such fluctuations arise when the pump’s height, relative to the cannula, changes as a result of normal daily use. The siphon or hydrostatic pressure action significantly affects the accuracy of insulin delivery, especially at basal rate infusions, and this may be most important for the pediatric population, where low basal rates are often used.

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