

## Continuous glucose dynamics monitoring in diabetic patients with peritoneal dialysis

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**Background** : *Glucose dynamics in patients on peritoneal dialysis (PD) is influenced by many factors.*

**Objectives** : *We evaluated the dynamics of interstitial fluid (ISF) glucose in diabetic patients undergoing PD, controlled for caloric food intake, daily activities, and hypoglycemic agents.*

**Methods** : *We studied all type-2 diabetic patients at the PD clinic of King Chulalongkorn Memorial Hospital between 2007 and 2008. They received 1.5% or 4.25% glucose during continuous ambulatory peritoneal dialysis (CAPD 1.5% or 4.25%), or 1.5% glucose continuous cycling peritoneal dialysis (CCPD 1.5%). Continuous glucose monitoring system and finger-stick were used to assess ISF and blood glucose levels for 72 hours, respectively. Sixteen patients (9 CAPD and 7 CCPD) were assessed.*

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**Results** : Median age, diabetes onset, and years on PD were 71, 17, and 1.5 years, respectively. There was strong correlation between ISF and blood glucose level ( $r = 0.937$ ). The mean ISF glucose levels between dialysate and non-dialysate days were not significantly different ( $P = 0.08$ ) in spite of higher total caloric intake on dialysate day ( $P = 0.049$ ). However, in the CAPD 4.25% group, mean ISF glucose and total consumed calories were significantly higher on dialysate than non-dialysate day ( $P = 0.026$  and  $0.031$ , respectively). The difference disappeared after adjustment for food calories. ISF glucose started rising after a 15-minute infusion of dialysate then sustained till 4 hours with a mean increase of 55%.

**Conclusions** : The evidence suggested that high-glucose peritoneal dialysate can increase ISF glucose but the effect is confounded by food caloric intake.

**Keywords** : Blood glucose, diabetes mellitus, extracellular fluid, peritoneal dialysis.

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สมพงษ์ สุวรรณวัลย์กร, สมชาย เอี่ยมม่อง, กฤษณ์ พงศ์พิรุฬห์. ผลวัดของน้ำตาลใน  
ผู้ป่วยเบาหวานที่ล้างไตทางหน้าท้อง วัดโดยใช้ระบบตรวจติดตามน้ำตาลอย่างต่อเนื่อง.  
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- เหตุผลของการทำวิจัย** : ผลวัดของน้ำตาลในผู้ป่วยล้างไตทางหน้าท้องได้รับผลกระทบจากปัจจัยหลายอย่าง
- วัตถุประสงค์** : เพื่อศึกษาผลวัดของน้ำตาลบริเวณช่องว่างระหว่างเซลล์ในผู้ป่วยเบาหวานที่ล้างไตทางหน้าท้อง โดยควบคุมปริมาณอาหารที่รับประทานกิจกรรมประจำวัน และยาลดระดับน้ำตาลในเลือด
- วิธีการทำวิจัย** : ผู้ป่วยเบาหวานที่ล้างไตทางหน้าท้องที่โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย ระหว่างปี พ.ศ. 2550 - 2551 โดยแบ่งเป็น 3 กลุ่ม คือ กลุ่มที่ล้างไตทางหน้าท้องแบบ CAPD ด้วยน้ำยาความเข้มข้นร้อยละ 1.5 และร้อยละ 4.5 และกลุ่มที่ล้างไตทางหน้าท้องแบบ CCPD ด้วยน้ำยาความเข้มข้นร้อยละ 1.5 โดยใช้ระบบติดตามน้ำตาลอย่างต่อเนื่อง และการเจาะน้ำตาลจากปลายนิ้ว เพื่อประเมินน้ำตาลบริเวณช่องว่างระหว่างเซลล์และน้ำตาลในเลือด ตามลำดับ เป็นเวลา 72 ชั่วโมง ในผู้ป่วย 16 คน (แบบ CAPD 9 คน และแบบ CCPD 7 คน)
- ผลการศึกษา** : อายุเฉลี่ย อายุที่เป็นเบาหวาน และจำนวนปีที่ล้างไตทางหน้าท้อง คือ 71, 17, และ 15 ปี ตามลำดับ ระดับน้ำตาลบริเวณช่องว่างระหว่างเซลล์และในเลือดมีความสัมพันธ์กันสูง ( $r = 0.937$ ) ค่าเฉลี่ยของระดับน้ำตาลบริเวณช่องว่างระหว่างเซลล์ในวันที่ล้างไตและวันที่ไม่ได้ล้างไต ไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ( $P = 0.08$ ) แม้ว่าผู้ป่วยได้รับพลังงานสูงในวันที่ล้างไตก็ตาม ( $P = 0.049$ ) อย่างไรก็ตาม กลุ่มที่ล้างไตทางหน้าท้องแบบ CAPD ด้วยน้ำยาความเข้มข้นร้อยละ 4.25 มีค่าเฉลี่ยระดับน้ำตาลบริเวณช่องว่างระหว่างเซลล์และปริมาณพลังงานในวันที่ล้างไต สูงกว่าในวันที่ไม่ได้ล้างไต อย่างมีนัยสำคัญทางสถิติ ( $P = 0.026$  และ  $0.031$  ตามลำดับ) ซึ่งกลับเสียมีนัยสำคัญทางสถิติไป เมื่อควบคุมพลังงานที่ได้จากอาหาร ระดับน้ำตาลบริเวณช่องว่างระหว่างเซลล์เริ่มสูงขึ้นประมาณ 15 นาที หลังจากได้รับน้ำยาล้างไตทางหน้าท้อง และคงอยู่ประมาณ 4 ชั่วโมง คิดเป็นการเพิ่มขึ้นร้อยละ 55 โดยเฉลี่ย

**สรุป** : น้ำยาล้างไตทางหน้าท้องที่มีความเข้มข้นสูง สามารถเพิ่มระดับน้ำตาล บริเวณช่องว่างระหว่างเซลล์ แต่ผลดังกล่าวสามารถถูกรบกวนด้วยพลังงานที่ได้จากอาหาร

**คำสำคัญ** : น้ำตาลในเลือด, เบาหวาน, ช่องว่างระหว่างเซลล์, ของเหลวนอกเซลล์, ล้างไตทางหน้าท้อง.

Diabetes is not uncommon in patients with end-stage renal disease (ESRD) undergoing peritoneal dialysis (PD). As cardiovascular and other vascular complications of diabetes are the major determinants of outcome, good glycemic control is important but difficult to achieve. This is particularly true in patients dialyzed with conventional glucose-containing PD solutions. <sup>(1)</sup>

The continuous effect on blood glucose levels of high-dextrose containing peritoneal dialysate is useful information for maintaining optimal glycemic control, but this has not been well studied. While finger prick blood testing of capillary glucose is feasible and has become part of daily routine, it is not suitable for frequent and/or nighttime assessment. Continuous measurement of glucose in interstitial fluid (ISF) can be carried out through a monitoring system (CGMS) <sup>(2)</sup> with high reliability and accuracy. <sup>(3)</sup> A recent systematic review suggested more effective glycemic control with CGMS in diabetic patients than self-monitoring methods. <sup>(4)</sup> CGMS allowed ISF glucose to be measured at five-minute intervals over a period of days. <sup>(4)</sup>

Past studies of the dynamics of ISF glucose in PD patients has been limited and mostly confounded by caloric food intake, daily activities, and taking of hypoglycemic agents. <sup>(5-8)</sup> The objective of this study was to evaluate the dynamics of ISF glucose in type-2 diabetic patients undergoing PD that is controlled for these factors.

## Methods

All type-2 diabetic patients at the PD clinic of King Chulalongkorn Memorial Hospital between 2007 and 2008 were included in the study regardless of insulin use. The patients received 1.5% glucose

continuous ambulatory peritoneal dialysis (CAPD 1.5%), 4.25% glucose CAPD (CAPD 4.25%), or 1.5% glucose continuous cycling peritoneal dialysis (CCPD 1.5%). Patients who received medications besides insulin that might interfere with plasma glucose such as steroids or oral hypoglycemic agents, were excluded.

The CGMS sensor was inserted into subcutaneous abdominal skin to continuously monitor glucose concentrations of interstitial tissue for 72 hours. Finger-stick blood-glucose measurements were obtained four times per day. To minimize insulin interference, insulin was discontinued in patients who had used insulin less than 20 units per day, whereas those who had used a higher insulin dose, would receive glargine (Lantus<sup>®</sup>) synthetic long acting insulin instead. Glargine was reduced to 70% of prior insulin dose and applied at the same time for the whole study period. No food was allowed the first day of the study. CAPD patients were prescribed 4 X 2L daily PD exchange. Intravenous saline was infused for the first 24 hours to assure adequate hydration. Blood glucose was collected at 0, 5, 15, 30 minutes, 1, 2, 3, 4 hours in CAPD group and 0, 5, 15, 30 minutes, 1 to 12 hours in CCPD group to assess the glucose dynamics after peritoneal dialysate was applied.

Patients were allowed to have controlled caloric meals on the second day with the same PD protocol as at the first day. On the third day, only the controlled caloric meals but not PD were given to the patients. Meal calories were calculated from basal energy expenditure, using the Harris-Benedict equation (age, gender, weight, and height) <sup>(9)</sup>, adjusted for stress factor. <sup>(10)</sup> The calories, type, and time of meals were controlled. Calories from dialysates were also calculated.

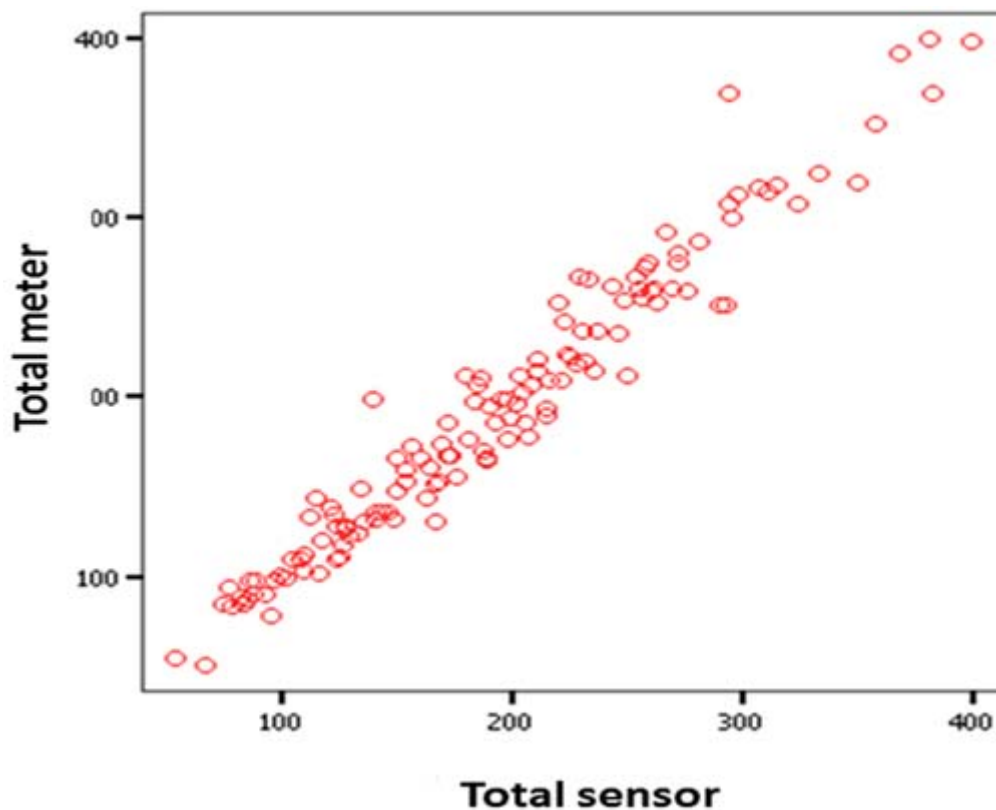
Comparative analysis of ISF glucose, total calories, and food calories between dialysis and non-dialysis days were done using paired *t*-test. As only two patients received CCPD 1.5%, they were dropped from the comparative analysis. Intra-class correlation was used to analyze the correlation between ISF glucose and finger stick blood glucose. Repeated ANOVA was used for analyzing glucose dynamics after PD. Written informed consent was obtained from all participants. This study has been approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB No.148/50).

## Results

Sixteen patients (9 CAPD and 7 CCPD) were assessed. Median age was 71 years (interquartile range [IQR], 55 - 78 years). The patients had been diabetic for 10 - 20 years (median 17 years) and had undergone PD for 0.8 - 2 years (median 1.5 years).

Twelve out of sixteen patients had been using insulin injections with median daily dose of 20 units (IQR, 1.5 - 47.5 units per day). Eleven patients received twice daily premixed insulin and the remaining patients used intermediate acting insulin once a day. The median HbA<sub>1c</sub> was 6.8% (IQR, 6.1- 8.0%).

ISF glucose and finger-stick blood-glucose levels strongly correlated ( $r = 0.937$ ) (Figure 1). There were no significant differences of ISF glucose between dialysate and non-dialysate day in both CAPD 1.5% and CCPD 1.5% groups (test of within subjects effect;  $P = 0.76$  and  $0.08$ ). In CAPD 4.25% group, significant rising of ISF glucose was detected after a 15-minute infusion of dialysate (95% CI, 5.95 to 27.38;  $P = 0.010$ ). The rising of ISF glucose was sustained till 4 hours of dwell (95% CI, 29.6 to 132.0; test of within subjects effect;  $P = 0.003$ ) with a mean increase of 55% (range 32 - 60%).



**Figure 1.** Correlation between interstitial fluid glucose as measured by continuous glucose monitoring (CGMS) (total meter) and finger-stick blood glucose (total sensor).

CGMS data of the second and third days (dialysate and non-dialysate day) were analyzed as 24-hour cycles - from 6 am to 6 am the next day. In CAPD 4.25% group, mean ISF glucose and total calories were significantly higher on dialysate than non-dialysate day (95% CI, 3.86 to 52.02;  $P = 0.026$  and 95% CI, 21.39 to 388.97;  $P = 0.031$ , respectively). The difference disappeared after adjustment for food calories. When only CAPD 1.5% and CCPD 1.5% groups were analyzed, the mean ISF glucose between dialysate and non-dialysate days was not significantly different (95% CI, -2.31 to 35.31;  $P = 0.077$ ), despite higher total calories in dialysate day (95% CI, 1.67 to 547.62;  $P = 0.049$ ).

## Discussion

Previous studies of minute-to-minute effect of high-dextrose peritoneal dialysate on blood glucose levels was done by using CGMS and revealed blood glucose levels above the recommended standards.<sup>(6)</sup> However, the findings were not conclusive because of small sample size and lack of adjustment for potential confounders, especially caloric food intake, daily activities, and hypoglycemic agents.<sup>(5,6)</sup>

With larger sample size and adjustment for potential confounders, ISF glucose measured by CGMS correlated well with finger-stick blood glucose, which was in accordance with previous studies. We did not experience incidents of CGMS catheter disconnection as in previous studies.<sup>(11)</sup>

We also demonstrated how glucose concentration of PD solutions directly affect ISF glucose over time. With high glucose peritoneal dialysate, ISF glucose could rise as early as 15 minutes

after infusion and sustain throughout the 4-hour dwell. These findings were not observed in the groups that utilized 1.5% glucose dialysate.

Our findings may have practical implications in clinical practice. If 4.25% glucose dialysate is used, frequent administration of short acting insulin is necessary in order to achieve acceptable glycemic control. A single daily long-acting insulin injection could not stabilize the baseline glucose level. Alternatively, intra-peritoneal insulin administration or non-glucose containing dialysate should be considered an alternative to high glucose containing dialysate.

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## Conflict of interest statement

The authors have no conflicts of interest to declare. There was no commercial involvement in this project.

### Authors' contributions

SW and TK designed the study, collected and analyzed the data, and drafted the manuscript. KPa helped to analyze the data and drafted the manuscript. SS, NL, KPb, SE helped with study design, data collection, and drafting of the manuscript. All authors have read and approved the final manuscript.

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