Accuracy of Glucose Meters in Measuring Low Blood Glucose Levels

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Abstract

Background : Hypoglycemia is an emergency condition requiring treatment as soon as possible. Therefore, rapid and reliable blood glucose measurements are necessary. There are 2 systems of glucose meters (GMs), the reflectance photometer system (RPS) and the electrochemical biosensor system (BSS). GMs are widely used in monitoring blood glucose (BG) in patients with diabetes. BG values measured by GMs have been confirmed to be accurate especially in measuring normal and high BG levels. However, the data on the accuracy of GMs in measuring low BG levels are limited.

Objective : To compare accuracy and reliability of different systems of GMs in the measurement of low BG values.

Patients and Method : Venous and capillary whole blood specimens were collected from patients who were investigated for pituitary dysfunction. The patients underwent an insulin-induced hypoglycemia test by intravenously administering human regular insulin. The low BG level was defined as having venous plasma glucose (PG) of less than 60 mg/dl (mean ± SD = 36.59 ± 9.19, n = 54). Capillary blood samples were obtained from fingertips. Venous BG (vBG) and capillary BG (cBG) were measured by GMs. Venous PG which considered a reference value was measured by the glucose dehydrogenase method.

Results : The correlation coefficient (r) between vBG measured by GMs-RPS and PG was 0.86 ($p<0.001$), whereas, that between vBG by GMs-BSS and PG was 0.75 ($p<0.001$). Similarly, the r between cBG by GMs-RPS and PG was 0.73 ($p<0.001$), whereas, that between cBG by GMs-BSS and PG was 0.69 ($p<0.001$). The mean difference between vBG by GMs-RPS and PG values was 0.01 ± 4.90 mg/dl, whereas, that between vBG by GMs-BSS and PG values was 10.50 ± 7.07 mg/dl which was significantly greater than the former ($p<0.001$). Moreover, the mean difference between cBG by GMs-RPS and PG values was 14.45 ± 8.76 mg/dl, whereas, that between cBG by GMs-BSS and PG values was 23.87 ± 9.48 mg/dl which was also significantly greater than the former ($p<0.001$). These results demonstrated that vBG measured by GMs-RPS was comparable to PG values. In addition, cBG values by GMs-RPS and GMs-BSS were approximately 14 mg/dl or 38 per cent and 24 mg/dl or 65 per cent greater than PG values, respectively.

Conclusion : In measuring low blood glucose levels, glucose meters using the reflectance photometer system are more accurate than those using the electrochemical biosensor system.

Key word : Glucose Meter, Reflectance Photometer, Electrochemical Biosensor, Low Blood Glucose, Hypoglycemia

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Recently, the Diabetes Control and Complications Trial (DCCT) Research Group has demonstrated that intensive therapy and tight glycemic control decrease complications associated with type I diabetes mellitus, including retinopathy, nephropathy and neuropathy[1]. The American Diabetes Association (ADA) and the National Committee for Clinical Laboratory Standards (NCCLS) recommend the use of self-monitoring of blood glucose (SMBG) to achieve glycemic goals in hospital and home settings[2-4]. Therefore, glucose meters (GMs) are widely used in SMBG in diabetes mellitus. Nevertheless, hypoglycemic episodes occur three-fold following tight glycemic control[1]. To prevent cerebral damage secondary to hypoglycemia, early recognition and treatment should be done as soon as possible[5,6]. Thus, reliable GMs are necessary in detecting low BG levels. To date, there are 2 systems of GMs, the reflectance photometer system (RPS) and the electrochemical biosensor system (BSS). Most studies demonstrated that high and normal BG levels measured by GMs correlate well with those by standard glucose oxidase method[7,8]. There have been few data on the accuracy of GMs in measuring low BG levels[9,10]. In this study, the accuracy and reliability of different systems of GMs in measuring BG values of less than 60 mg/dl were compared with plasma glucose (PG) values by standard glucose dehydrogenase method[11-14].

PATIENTS AND METHOD

Simultaneous venous and capillary blood samples were collected from 54 patients who were investigated for pituitary dysfunction in the Endocrine Clinic at the Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Bangkok, Thailand between April 1997 and January 1998. The patients underwent an insulin-induced hypoglycemia test as part of pituitary function testing by intravenously administering human regular insulin 0.1 u/kg and blood samples were drawn at 0, 20, 30, 60, 90, and 120 min for evaluation of glucose and other endocrine parameters. Fifty-four venous blood samples with low BG levels were obtained from 54 patients for evaluation of BG levels and transferred immediately to tubes containing sodium fluoride (NaF) as anticoagulant and anti-glycolytic agent[15,16]. Samples were measured by the standard glucose dehydrogenase method (Ecoline® 100 Glucose, Diagnostic Merck, Germany) and the remainder were measured immediately by GMs. Simultaneous capillary whole blood samples were obtained from the tip of the fingers with Softclix® Lancet (Boehringer Mannheim) and collected in heparinized capillary blood tubes[15]. The BG in each sample was measured immediately by 3 different brands of GMs using the reflectance photometer system (RPS): Accutrend (Boehringer Mannheim), SureStep (Johnson-Johnson), Glucometer 4 (Bayer) and 3 brands of GMs using the electrochemical biosensor system (BSS): Advantage (Boehringer Mannheim), Precision QID (Medisense), Glucometer Elite (Bayer), according to the manufacturer's instructions. The BG values by GMs were compared with PG measured by the glucose dehydrogenase method. The PG were analyzed within 2 hours after collection. A low BG level was defined as PG of less than 60 mg/dl.

Table 1. Comparison between venous and capillary whole blood glucose measured by meters (RPS & BSS) and plasma glucose by the glucose dehydrogenase method.

	Meters (GMs)	Mean ± SD (mg/dl)	Mean difference of BG measured by GMs minus PG, mean ± SD (mg/dl)	r
Plasma glucose	-	36.59 ± 9.19	-	-
Venous BG	RPS	36.60 ± 9.43	0.01 ± 4.90	0.86‡
(n = 162)*	BSS	47.09 ± 10.42	10.50 ± 7.07†	0.75‡
Capillary BG	RPS	51.04 ± 12.87	14.45 ± 8.76†	0.73‡
(n = 162)*	BSS	60.46 ± 13.08	23.87 ± 9.48†	0.69‡

† p<0.001 significant difference compared with plasma glucose
‡ p<0.001 significant correlation compared with plasma glucose
* 54 samples from 54 patients, each sample was measured by 3 different brands of GMs (RPS and BSS), therefore, each sample gives 3 values of BG in each system
r = correlation coefficient between venous and capillary BG by GMs *vs* PG
GMs-RPS = glucose meters using the reflectance photometer system
GMs-BSS = glucose meters using the electrochemical biosensor system

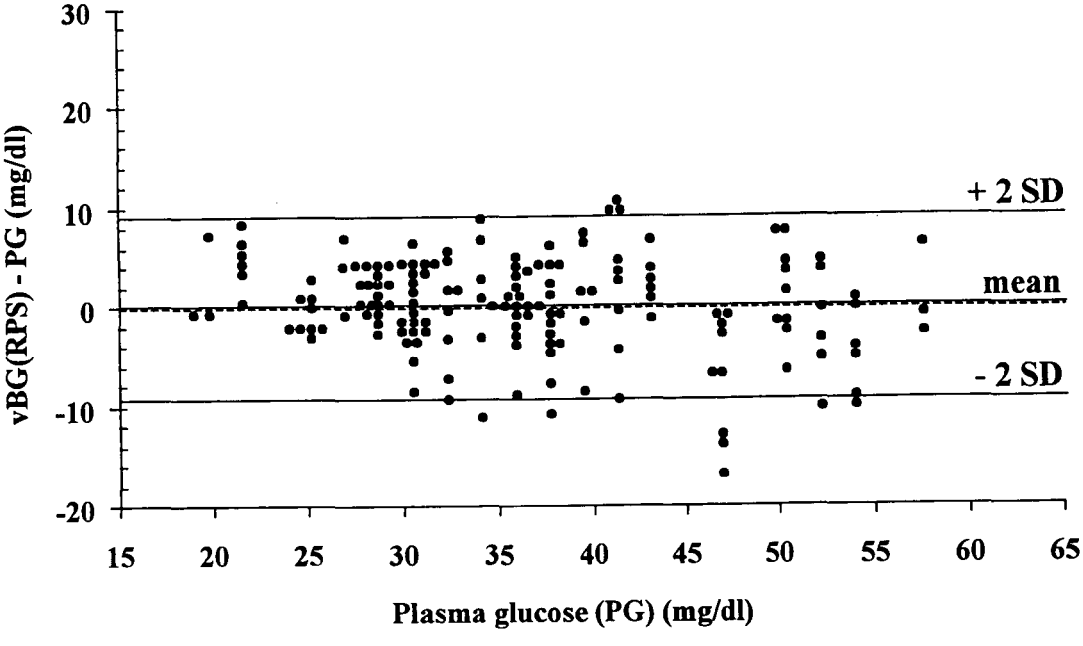

Fig. 1. The difference between venous whole blood glucose (vBG) measured by glucose meters using the reflectance photometer system (RPS) and plasma glucose by the glucose dehydrogenase method in measuring low blood glucose levels (20-60 mg/dl).

Statistical analysis

Blood glucose values (mg/dl) were expressed as mean ± SD. The correlation between venous and capillary BG measured by GMs and PG by the glucose dehydrogenase method was analysed by using the Pearson's correlation. Comparison between both GMs systems was analysed by the method of Bland and Altman[17,18]. A p-value of <0.05 was considered to have significant difference.

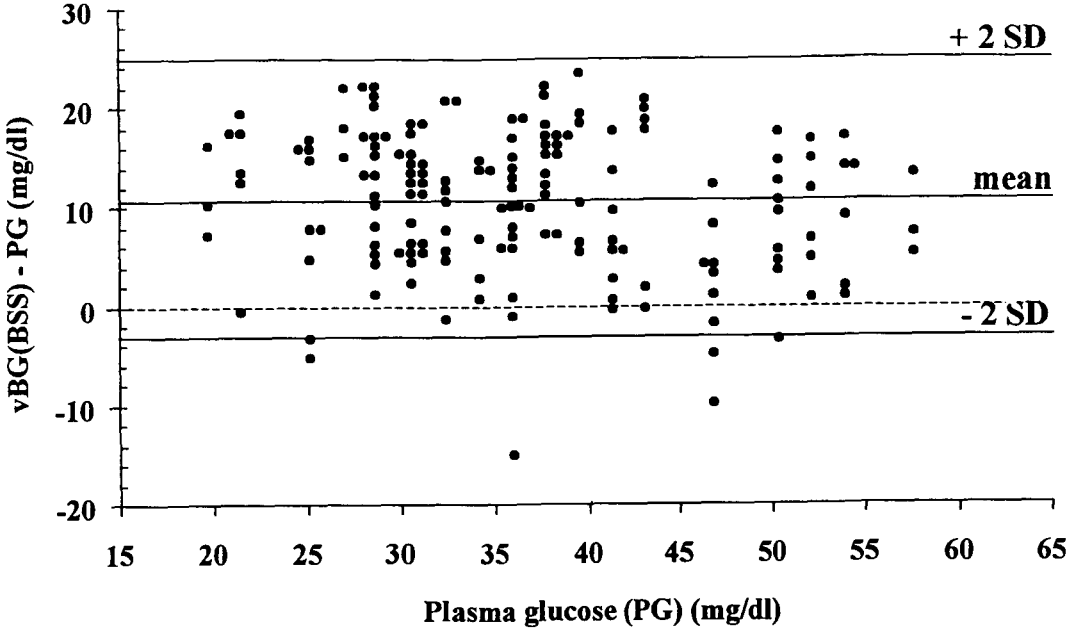

Fig. 2. The difference between venous whole blood glucose (vBG) measured by glucose meters using the electrochemical biosensor system (BSS) and plasma glucose by the glucose dehydrogenase method in measuring low blood glucose levels (20-60 mg/dl).

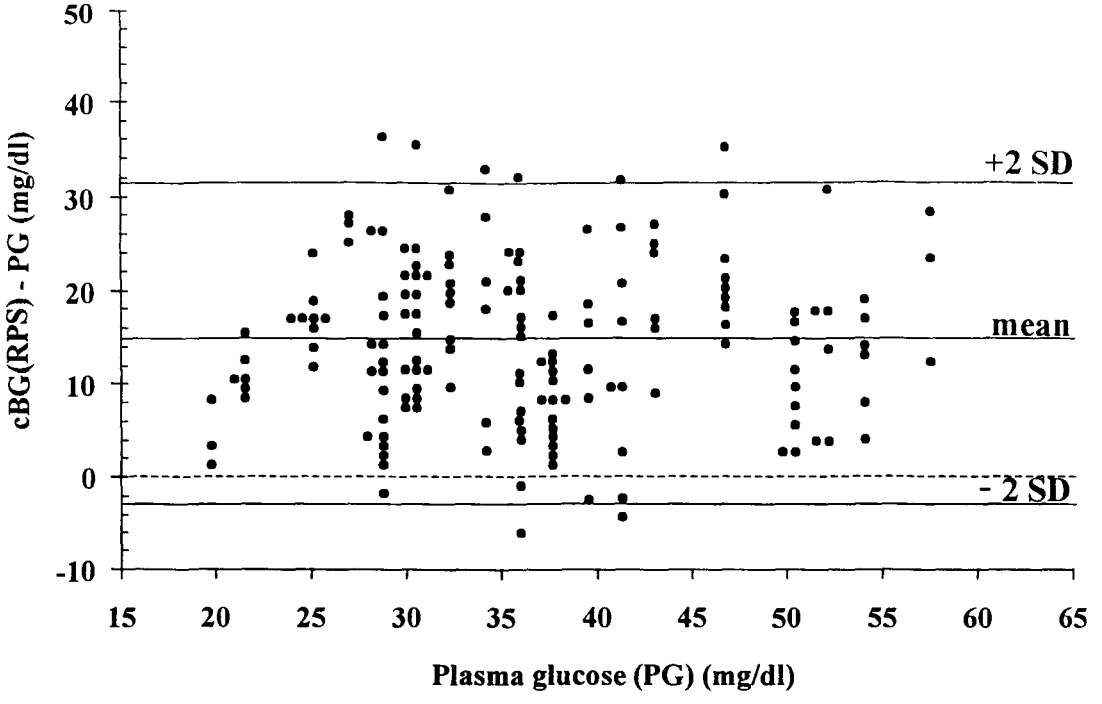

Fig. 3. The difference between capillary whole blood glucose (cBG) measured by glucose meters using the reflectance photometer system (RPS) and plasma glucose by the glucose dehydrogenase method in measuring low blood glucose levels (20-60 mg/dl).

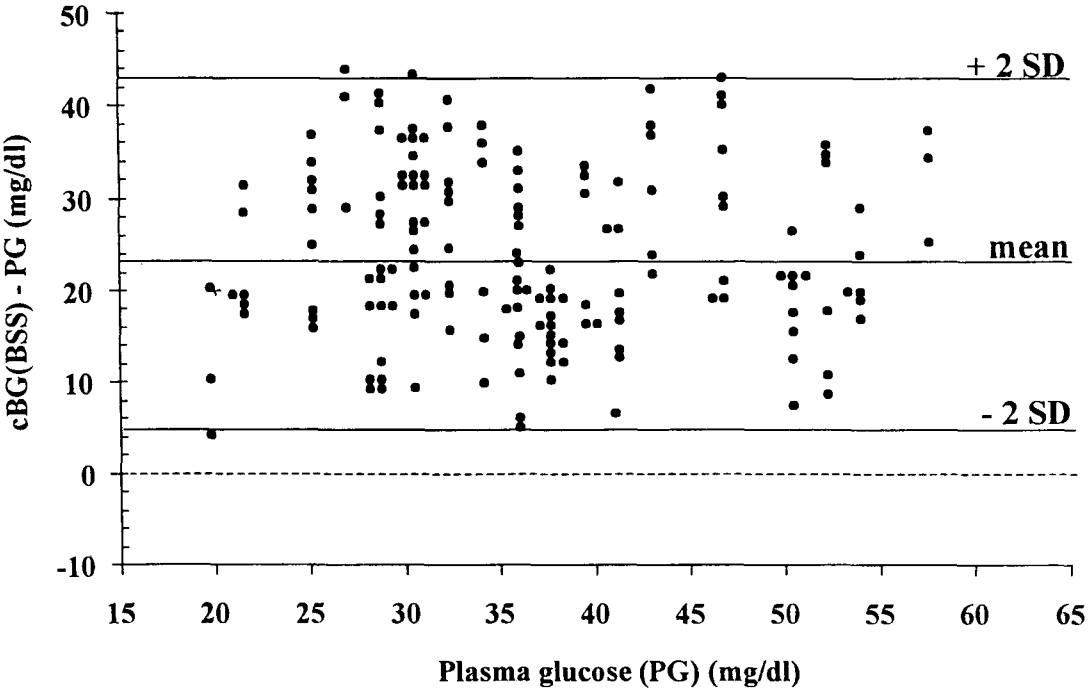

Fig. 4. The difference between capillary whole blood glucose (cBG) measured by glucose meters using the electrochemical biosensor system (BSS) and plasma glucose by the glucose dehydrogenase method in measuring low blood glucose levels (20-60 mg/dl).

RESULTS

The mean PG ± SD was 36.59 ± 9.19 mg/dl. All BG values were within the limit of measurable range of each GMs (20-500 mg/dl). The hematocrits of the patients ranged from 35 per cent to 45 per cent which is within the operative specifications of the GMs used in the present study.

Table 1 and Fig. 1 and 2 illustrate the mean difference (mean ± SD) between venous BG (vBG) by GMs-RPS and by GMs-BSS *vs* PG respectively. The mean vBG ± SD measured by GMs-RPS was 36.60 ± 9.43 mg/dl and by GMs-BSS was 47.09 ± 10.42 mg/dl. The mean difference (mean ± SD) between vBG by GMs-RPS and PG was 0.01 ± 4.90 mg/dl which was not significantly different (p=0.97), and the mean vBG by GMs-BSS was greater than the mean PG by 10.50 ± 7.07 mg/dl which was significantly different (p<0.001). The correlation coefficient (r) between vBG measured by GMs-RPS *vs* PG was 0.86 (p<0.001), whereas, that by GMs-BSS *vs* PG was 0.75 (p<0.001).

Table 1 and Fig. 3 and 4 illustrate the mean difference (mean ± SD) between capillary BG (cBG) by GMs-RPS and by GMs-BSS *vs* PG. The mean cBG ± SD by GMs-RPS was 51.04 ± 12.87 mg/dl and by GMs-BSS was 60.46 ± 13.08 mg/dl. Moreover, the mean cBG ± SD by GMs-RPS was greater than the mean PG by 14.45 ± 8.76 mg/dl which was significantly different (p<0.001) and that by GMs-BSS was greater than the mean PG by 23.87 ± 9.48 mg/dl which was also significantly different (p< 0.001). The correlation coefficient (r) between cBG measured by GMs-RPS *vs* PG was 0.73 (p<0.001) whereas that by GMs-BSS *vs* PG was 0.69 (p<0.001). These results demonstrated that vBG measured by GMs-RPS was comparable to PG values. In addition, cBG values by GMs-RPS and GMs-BSS were approximately 14 mg/dl or 38 per cent and 24 mg/dl or 65 per cent greater than PG values, respectively.

DISCUSSION

In general, evaluation of cBG by GMs is routinely performed at home by the patients themselves. Venous blood is not usually obtained for home monitoring of BG due to inconvenience. In fact, the glucose level in capillary blood is slightly higher than that in venous blood. In addition, venous

whole blood glucose measured immediately should be similar to venous plasma glucose measured in venous blood with NaF. This study clearly showed that, in measuring low BG levels, vBG values by GMs-RPS were almost similar to PG (Table 1). All the values were within 10 per cent interval of reference plasma values which are acceptable according to the ADA consensus statement[19]. In addition, cBG values by GMs-RPS were approximately 14 mg/dl or 38 per cent greater than PG, whereas, cBG values by GMs-BSS were approximately 24 mg/dl or 65 per cent greater than PG values. Therefore, evaluation of low BG levels with cBG by GMs must be interpreted with caution. The results in this study are in agreement with the previous report that cBG values are consistently higher than those of BG[20].

In conclusion, measuring low blood glucose values by reflectance photometer system is more accurate than that by electrochemical biosensor system.

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ความถูกต้องของมาตรวัดกลูโคสในการวัดระดับน้ำตาลในเลือดต่ำ

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ภาวะน้ำตาลในเลือดต่ำจำเป็นต้องให้การรักษาอย่างเร่งด่วน ดังนั้นเครื่องตรวจน้ำตาลในเลือดด้วยตนเอง (glucose meters, GMs) ที่ให้ผลถูกต้อง มีความแม่นยำสูงและได้ผลอย่างรวดเร็วจึงมีความจำเป็นมาก ในปัจจุบัน GMs มี 2 ระบบคือ reflectance photometer (RPS) และ electrochemical biosensor (BSS) การตรวจระดับน้ำตาลในเลือด (blood glucose, BG) ด้วย GMs นิยมใช้กันมากในผู้ป่วยโรคเบาหวานเพื่อตรวจสอบและควบคุมระดับน้ำตาลในเลือด โดยเฉพาะน้ำตาลที่มีค่าปกติหรือสูงซึ่งมีความถูกต้องแม่นยำดี แต่ความถูกต้องของ GMs ในการวัดน้ำตาลที่มีค่าต่ำยังมีการศึกษาค่อนข้างน้อย

วัตถุประสงค์ : เพื่อตรวจสอบความถูกต้องของเครื่อง GMs ในการวัดระดับน้ำตาลในเลือดซึ่งต่ำกว่าปกติ

วิธีการศึกษา : เปรียบเทียบระดับน้ำตาลจากหลอดเลือดดำ (venous BG, vBG) และปลายนิ้ว (capillary BG, cBG) ที่วัดโดย GMs ด้วยวิธี GMs-RPS และ GMs-BSS กับ plasma glucose (PG) ที่ตรวจในห้องปฏิบัติการ โดยทำการตรวจเลือดของผู้ป่วยที่มารับการทดสอบหาความผิดปกติของต่อมใต้สมอง ซึ่งจะได้รับยาฉีดอินซูลินเข้าทางหลอดเลือดดำเพื่อทำให้เกิดภาวะน้ำตาลในเลือดต่ำ โดยเกณฑ์กำหนดของ PG ที่เลือกนำมาศึกษาต้องมีค่าน้อยกว่า 60 มก/ดล ในการศึกษานี้ระดับ PG เฉลี่ย 36.59 $\pm$ 9.19 มก/ดล จากตัวอย่างเลือดจำนวน 54 ตัวอย่าง ตัวอย่างเลือดแต่ละตัวอย่างจะตรวจด้วย GMs และตรวจ PG ในห้องปฏิบัติการเพื่อใช้เป็นมาตรฐานอ้างอิง ซึ่งใช้วิธี glucose dehydrogenase

ผลการศึกษา : ค่าความสัมพันธ์เชิงเส้นตรง Pearson's correlation (r) ระหว่าง vBG กับ PG ที่วัดด้วยเครื่องระบบ GMs-RPS และ GMs-BSS มีค่าเท่ากับ 0.86 และ 0.75 ตามลำดับ ในขณะที่ค่า r ระหว่าง cBG กับ PG ที่วัดด้วยเครื่องระบบ GMs-RPS และ GMs-BSS มีค่าเท่ากับ 0.73 และ 0.69 ตามลำดับ ซึ่งค่า r ทั้งหมดดังกล่าวข้างต้นมีความสัมพันธ์กันไปในทิศทางเดียวกันอย่างมีนัยสำคัญทางสถิติ ($p<0.001$) ส่วนค่าเฉลี่ยของ vBG ที่วัดด้วย GMs-RPS มีค่ามากกว่าค่าเฉลี่ย PG 0.01 $\pm$ 4.90 มก/ดล ซึ่งพบว่าไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p=0.97$) แต่ค่าเฉลี่ยของ vBG ที่วัดด้วย GMs-BSS มีค่ามากกว่าค่าเฉลี่ย PG 10.50 $\pm$ 7.07 มก/ดล ซึ่งพบว่ามีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (<0.001) ส่วนค่าเฉลี่ยของ cBG ที่วัดด้วย GMs-RPS และ GMs-BSS มีค่ามากกว่าค่าเฉลี่ย PG 14.45 $\pm$ 8.76 และ 23.87 $\pm$ 9.48 มก/ดล ตามลำดับ และค่าเฉลี่ยของ cBG เมื่อวัดด้วย GMs-RPS มีค่าน้อยกว่าค่าเฉลี่ย cBG เมื่อวัดด้วย GMs-BSS อย่างมีนัยสำคัญทางสถิติ ($p<0.001$) นอกจากนี้ระดับ cBG ที่วัดด้วย GMs-RPS มีค่าสูงกว่า PG ประมาณ 14 มก/ดล หรือร้อยละ 38 และเมื่อวัดด้วย GMs-BSS มีค่าสูงกว่า PG ประมาณ 24 มก/ดล หรือร้อยละ 65 ตามลำดับ

สรุป : ในภาวะน้ำตาลในเลือดต่ำ เครื่องตรวจวัดน้ำตาลในเลือดซึ่งใช้ระบบ reflectance photometer ให้ค่าถูกต้องกว่าระบบ electrochemical biosensor

คำสำคัญ : เครื่องตรวจน้ำตาลในเลือดด้วยตนเอง, เครื่องตรวจน้ำตาลในเลือดระบบวัดแสงสะท้อนจากแถบสี, เครื่องตรวจน้ำตาลในเลือดระบบ biosensor, ภาวะน้ำตาลในเลือดต่ำ

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