Telemetry Glucose Monitoring Device With Needle-Type Glucose Sensor: A Useful Tool for Blood Glucose Monitoring in Diabetic Individuals

MOTOAKI SHICHIRI, M.D., NOBUYUKI ASAKAWA, M.D., YOSHIMITSU YAMASAKI, M.D., RYUZO KAWAMORI, M.D., AND HIROSHI ABE, M.D.

For continuous monitoring of glucose concentration in ambulant diabetic patients, a telemetry glucose monitoring system with a needle-type glucose sensor has been developed. The system consists of a sensor transmitter (4 × 6 × 2 cm, 50 g) that converts current signals generated in a needle-type glucose sensor to high-frequency audio signals and a receiver that continuously calculates glucose concentrations from the received audio signals. The noise range of a monitoring record with the telemetry system (0.3 ± 0.04%, mean ± SEM) was significantly smaller than that with a wire-connected system, the wearable artificial endocrine pancreas (2.5 ± 0.3%). Postprandial tissue glucose concentration responded well to the plasma glucose concentration, with a time lag of 5 min. Continuous glucose monitoring of five diabetic subjects for 77 ± 22 h revealed that a significant correlation existed between the subcutaneous tissue glucose concentration and the plasma glucose concentration measured simultaneously in each patient. These data indicate the usefulness of the telemetry glucose monitoring system in strict glycemic control of diabetic individuals. DIABETES CARE 1986; 9:298–301.

Self-monitoring of blood glucose[1-3] is a fundamental requirement for long-term glycemic control with intensive insulin therapies. According to the proposed protocol,[3] as many as 40 determinations of blood glucose have been conducted per week. In addition, "spot checks" are necessary to detect asymptomatic hypoglycemias. Therefore, much improvement in glycemic control would be expected when continuous glucose monitoring is realized.

We have developed a needle-type glucose sensor,[4,5] which enables us to monitor subcutaneous tissue glucose concentration without blood withdrawal. In this article, we present a telemetry glucose monitoring system with a needle-type glucose sensor. This device allows the patient to observe glucose concentration during physical activities and to recognize hypoglycemia by alarm sound.

MATERIALS AND METHODS

The device. A telemetry glucose monitoring system consists of a transmitter connected by a needle-type glucose sensor and a receiver (Figure 1). The needle-type glucose sensor is a hydrogen-peroxide electrode converted by immobilized glucose oxidase, which generates a very weak direct current depending on glucose concentration in surrounding fluid. The transmitter converts current signals generated by a glucose sensor to a very-high-frequency (VHF) audio signal. The transmitter, packed with a current-voltage–converting amplifier (ICU7613, Intersil, Inc., Cupertino, CA), a voltage-frequency converter, and a lithium battery, is 4 × 6 × 2 cm and 50 g. It runs for 3 days on a single lithium battery.

The receiver demodulates the audiofrequency signal to a voltage and the glucose concentration calculated from the voltage is continuously displayed in the LED display. Hypoglycemia or hyperglycemia beyond the prefixed threshold is alarmed by sound. The receiver is composed of a VHF oscillator, a frequency modulator, electric filters, a frequency-voltage converter, and an alarm circuit and batteries and is 10 × 12 × 5 cm. The receiver catches the sensor signal within 20 m of the transmitter.

Continuous glucose monitoring in ambulant diabetic patients. After the calibration was made using saline solution with and without glucose (200 mg/dl), a glucose sensor was inserted subcutaneously into the forearm of five diabetic (four insulin dependent, one postpancreatectomized) subjects by means of an 18 to 20-gauge dual cannula without local anesthesia and was fixed in situ with adhesive bandages. In two of the five patients, a needle-type glucose sensor was replaced by a new one after 3 days of continuous monitoring. The

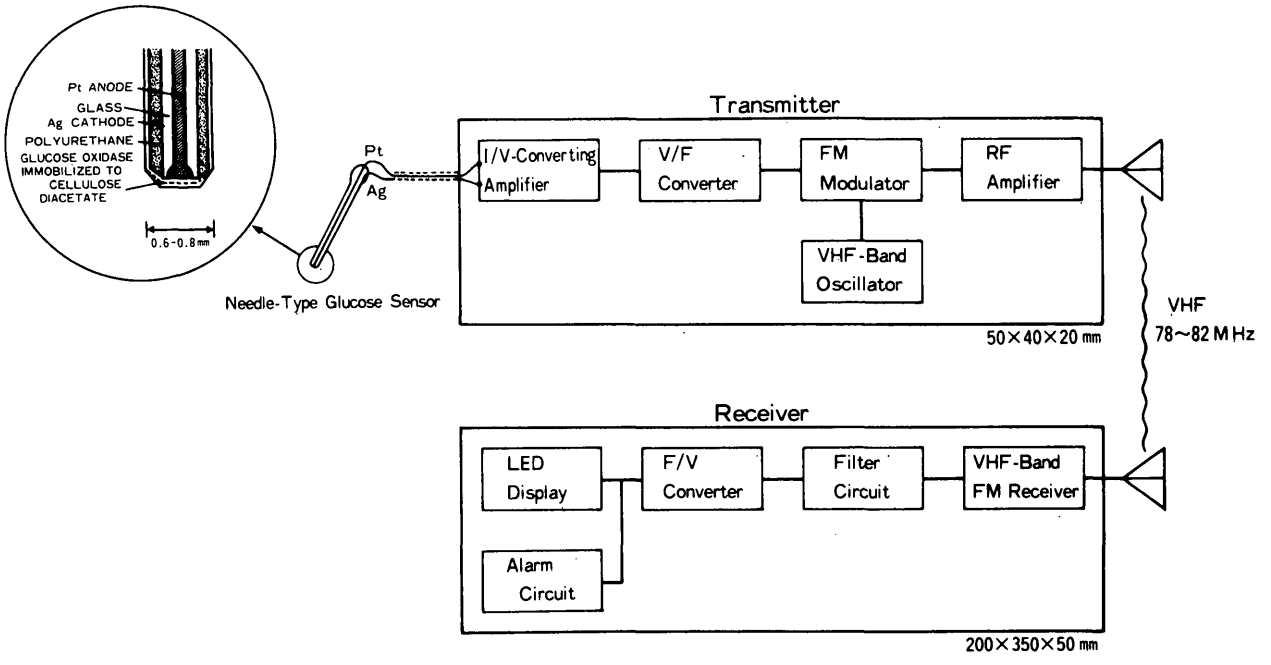

FIG. 1. Block diagram of telemetry glucose monitoring system. Structure of needle-type glucose sensor is also shown in circle.

transmitter was fixed to the forearm or was anchored to a waist belt.

To calculate a noise range of in vivo monitoring, a glucose sensor, inserted into subcutaneous tissue of fasting diabetic patients, was connected to the transmitter of the telemetry system or to the wearable artificial endocrine pancreas,[4-6] and a pen recorder (VP66121A, Matsushita Communication Industrial Co., Ltd., Osaka, Japan) was connected to the receiver of the telemetry system or to the wearable artificial endocrine pancreas. The noise range was expressed as a percentage of the output.

To examine the responsiveness of tissue glucose concentration monitored by the telemetry system, a bedside-type artificial endocrine pancreas[7,8] was connected to the patient. Blood for bedside-type artificial pancreas was withdrawn from an antecubital vein ipsilateral to the needle-type glucose sensor. After insulin injection and 15 min before intake of breakfast, glucose concentration was simultaneously monitored by the two systems until 180 min after breakfast.

RESULTS

The noise range of glucose monitoring with the telemetry system (0.3 ± 0.04%, mean ± SEM) was significantly smaller ($P < .01$) than that with the wearable artificial endocrine pancreas[4-6] (2.5 ± 0.3%). After intake of breakfast, blood glucose concentration of 97 ± 14 mg/dl began to rise at 15 min and reached its peak of 178 ± 16 mg/dl at 70 min.

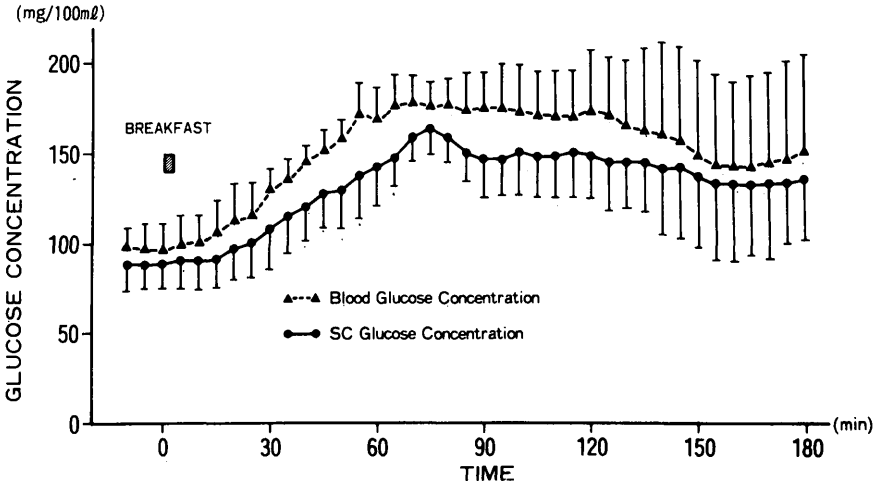

FIG. 2. Postprandial glucose concentrations determined by telemetry glucose monitoring system (●) or by bedside-type glucose monitoring system (▲) in 5 diabetic subjects. Data are shown as mean ± SEM.

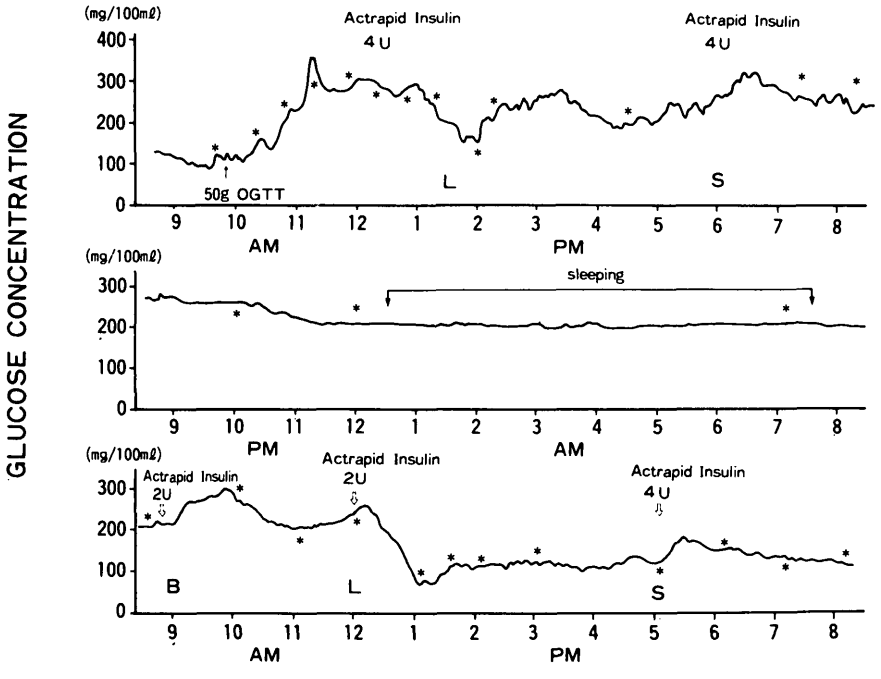

FIG. 3. *Results of 36 h of glucose monitoring by telemetry glucose monitoring system. Patient was pancreatectomized due to pancreatic carcinoma. Thereafter, patient suffered from unexpected hyperglycemias and hypoglycemias despite intensified multiple insulin therapy in Osaka University Hospital. B, L, and S denote breakfast (300 cal), lunch (400 cal), and supper (480 cal), respectively. Asterisks denote plasma glucose concentrations determined by discrete samplings. During glucose monitoring, patient took stool in morning. Continuous monitoring showed that postprandial glycemic rise was variable with each food intake, and small dose of insulin injection caused marked glycemic fall.*

Tissue glucose concentration of 89 ± 17 mg/dl began to rise at 20 min and reached its peak of 165 ± 15 mg/dl at 75 min (Figure 2).

Tissue glucose concentrations were continuously measured on five ambulant diabetic patients with the telemetry system for 36–144 (77 ± 20) h. Figure 3 shows a representative 36-h continuous record on one diabetic patient. Similar continuous monitorings have been completed on the other four subjects. During these monitorings, tissue glucose concentration determined by a telemetry system was highly correlated (r = .865 – .958), with the plasma glucose concentration in the range of 49–388 mg/dl. The tissue glucose concentrations determined by all sensors were 6–22% lower than the plasma glucose concentrations in all patients (Figure 4).

DISCUSSION

In a glucose monitoring device for long-term clinical use, characteristics such as accuracy of measurement, nonvascular access for measurement, long life in bioactivity, and less disturbance in physical activities are essential. In in vitro experiments,[4,5] the needle-type glucose sensor showed a wide range of linearity of output to glucose concentration, independency of output on fluctuation of tissue oxygen tension, and long life of bioactivity. The wearable artificial endocrine pancreas incorporating the needle-type glucose sensor showed glycemic controls on insulin-dependent diabetic individuals by continuous tissue glucose monitoring.[6] We have developed a telemetry glucose monitoring system to augment the clinical usefulness of the glucose sensor.

The telemetry glucose monitoring system is composed of a transmitter and a receiver. As a transmitter, an operation amplifier and a frequency modulator were mounted on a small printed board. Electric charges on body surface or clothes could induce a very weak current on an electric board, which may be detected as a noise in sensing record. The printed board of the transmitter is much smaller than the wearable artificial endocrine pancreas. Therefore, with the aid of the telemetry monitoring system, a noise in glucose monitoring was eliminated.

Simultaneous determinations of tissue glucose concentration and plasma glucose concentration showed high correlation between these measurements in all patients studied, even in hypoglycemic and hyperglycemic ranges. The tissue glucose concentration was 6–22% lower than the plasma glucose concentration in the measured range on all sensors. Simultaneous monitoring of postprandial glycemic change showed that the tissue glucose concentration followed the change in the plasma glucose concentration with a time lag of ~5 min. These data indicate that tissue glucose concentration measured by the telemetry system was closely related to blood glucose concentration.

Continuous glucose monitoring by the telemetry system provides diabetic patients with much more glycemic data than self-monitoring of blood glucose by discrete samplings. Assessment of day-by-day variation of glycemic excursions by the system may improve the glycemic control by intensive insulin therapies. Furthermore, the built-in alarm system notifies the patient of hypoglycemia even while the patient is asleep.

At present, the sensor must be replaced after 3 days of continuous use because of a 20% reduction in the sensor's output. Fixation of protein on the membrane of the sensor and fibrin deposition in the subcutaneous tissue around the sensor insertion recognized by histologic examinations[6] appear

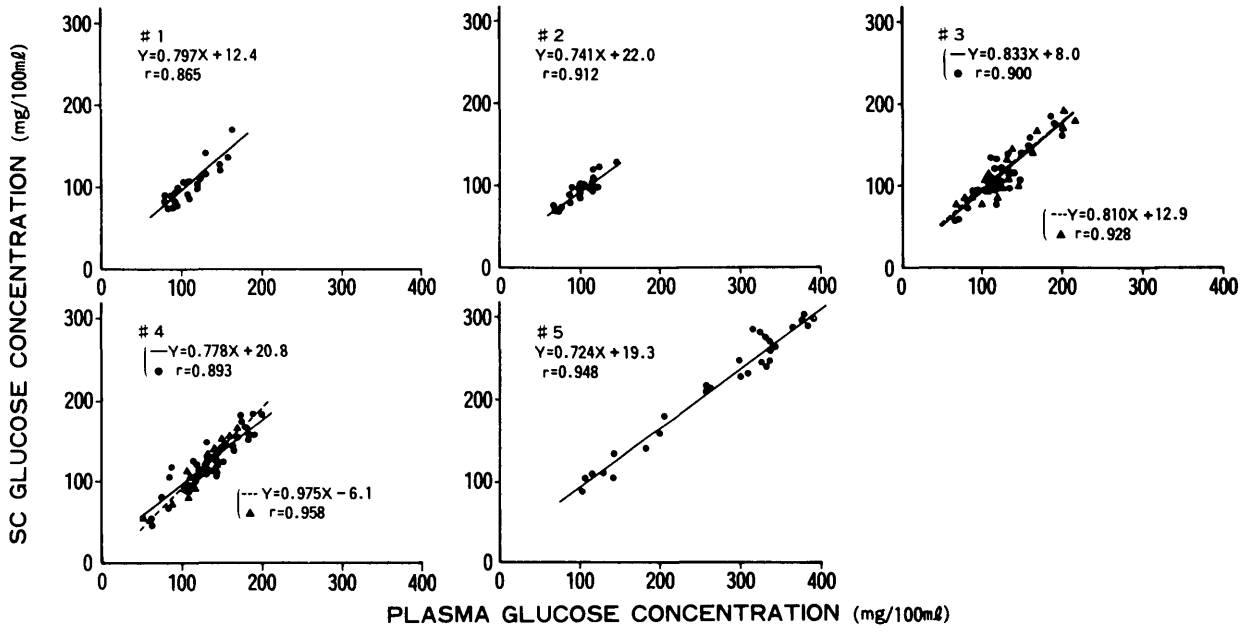

FIG. 4. Relationship between glucose concentrations determined by telemetry glucose monitoring system and plasma glucose concentrations in 5 diabetic subjects. Glucose concentration determined by first sensor is plotted (●), and relation between tissue and plasma glucose concentration is shown (solid line). In 2 patients (nos. 3 and 4), sensor was replaced after 3 days of continuous monitoring; glucose concentration determined by new sensor is plotted (▲). Relation between tissue glucose concentration determined by second sensor and plasma glucose concentration is shown (broken line).

to cause the decrease in bioactivity of the sensor. Suitable membrane design for the sensor, such as selection and combination of hydrophilic and hydrophobic membrane, should extend the bioactivity of the sensor.

We are now developing the wristwatch-type glucose monitor by reducing the size of the telemetry system. This device will enable the transmission of measured glucose concentrations to an implanted system composed of computer, pumps, and insulin reservoir. It is anticipated that the development of such a device will make implantation of an artificial endocrine pancreas system feasible in the near future.

From the First Department of Medicine, Osaka University Medical School, 1-1-50 Fukushima, Fukushima-ku, Osaka, 553, Japan.

Address reprint requests to Motoaki Shichiri, M.D., at the above address.

REFERENCES

[1] Sonkson, P. H., Judd, S. L., and Lowy, C.: Home monitoring of blood glucose. Method for improving diabetic control. Lancet 1978; 1:729–32.

[2] Walford, S., Gale, E. A. M., Allison, S. P., and Tattersall, R. B.: Self-monitoring of blood glucose. Improvement of diabetic control. Lancet 1978; 1:732–35.

[3] Skyler, J. S., Lasky, I. A., Skyler, D. L., Robertson, E. G., and Mintz, D. M.: Home glucose monitoring as an aid in diabetic management. Diabetes Care 1978; 1:150–57.

[4] Shichiri, M., Kawamori, R., Yamasaki, Y., Hakui, N., Nomura, M., and Abe, H.: Wearable-type artificial endocrine pancreas with needle-type glucose sensor. Lancet 1978; 2:1129–31.

[5] Shichiri, M., Kawamori, R., Goriya, Y., Yamasaki, Y., Nomura, M., Hakui, N., and Abe, H.: Glycemic control in pancreatectomized dogs with a wearable artificial endocrine pancreas. Diabetologia 1983; 24:179–84.

[6] Shichiri, M., Kawamori, R., Hakui, N., Yamasaki, Y., and Abe, H.: Essentiality of closed-loop glycemic control in diabetics: day-by-day variations in glycemic response disclosed by a wearable artificial endocrine pancreas. Diabetes 1984; 33:1200–202.

[7] Shichiri, M., Kawamori, R., and Abe, H.: Normalization of the paradoxic secretion of glucagon in diabetics who were controlled by the artificial beta cell. Diabetes 1979; 28:272–75.

[8] Kawamori, R., Shichiri, M., Kikuchi, M., Yamasaki, Y., and Abe, H.: Perfect normalization of excessive glucagon responses to intravenous arginine in human diabetes mellitus with the artificial beta-cell. Diabetes 1980; 29:762–65.