Subcutaneous Peritoneal Access Device for Type I Diabetic Patients Nonresponsive to Subcutaneous Insulin

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SUMMARY

Three type I diabetic patients nonresponsive to subcutaneous insulin were implanted with a subcutaneous peritoneal access device. In these patients, multiple subcutaneous injections had been unable to prevent recurrent hospital admissions for diabetic ketoacidosis. The patients were responsive to intravenous insulin but had limited accessible peripheral veins. Complications of thrombosis and/or septicemia from permanent central venous catheters prevented the long-term use of this route.

The peritoneal access device was implanted subcutaneously adjacent to the umbilicus with its insulin delivery catheter terminating in the peritoneal space. Transcutaneous injection of insulin into the subcutaneous access port resulted in the same quantity of insulin entering the peritoneal space. Using a mixture of regular and protamine zinc insulin in a ration of 1:1 resulted in acute increases in plasma free insulin concentration with meals and a declining background level postprandially. All peritoneal access devices have been functioning well for at least 2 mo and in one of the implanted diabetic subjects, it has been in continuous use for 5 mo with no evidence of peritonitis or resistance to peritoneal insulin. These results suggest that a subcutaneous peritoneal access device may provide an alternative insulin delivery route for patients who are nonresponsive to subcutaneous insulin injections. DIABETES *31*:470–473, May 1982.

For the majority of type I diabetic patients, the subcutaneous tissue is the preferred insulin injection site. However, in a minority of patients, the subcutaneous route of insulin administration does not prevent metabolic decompensation or recurrent hospital admissions for diabetic ketoacidosis.[1] The pathogenesis of this syndrome is complex and may involve both insulin degradation and/or sequestration at the subcutaneous injection site.[1,2] Alternative insulin delivery sites in these patients have been the intravenous and intramuscular routes, but recurrent thrombosis, septicemia, and muscle fibrosis have limited their usefulness.[1,3]

During the past 5 yr, we have been investigating the feasibility of intraperitoneal insulin delivery to control hyperglycemia both in diabetic man and animals.[4] In parallel with these studies, we have been developing a subcutaneously implanted peritoneal access device through which insulin can be safely injected into the peritoneum.[5] Recently, three patients have been referred to us because of repeated failures to prevent diabetic ketoacidosis in spite of large doses of subcutaneous insulin injections. Each of these patients was incapacitated by his or her diabetes, being unable to attend school or work. After establishing that these patients responded to intraperitoneal insulin delivery (via a temporary peritoneal catheter), each patient was implanted with a subcutaneous peritoneal access device. Our results suggest that this device may provide an alternative insulin delivery site in these difficult to manage, subcutaneously nonresponsive diabetic patients.

METHODS

Patient population. The clinical description of the three type I diabetic patients referred to us by their physicians is shown in Table 1. Each physician was a specialist in the care of diabetic patients and was unsuccessful in maintaining these patients in metabolic control. Two of the patients (nos. #1 and #3) had tried the addition of apoprotinin (Trasylol) to their insulin, without success.[1] All patients had limited peripheral access veins and one had been implanted with two subclavian catheters and three intramuscular catheters, all of which had thrombosed or become infected (patient no. 2). All patients were unable to work or attend school because of the multiple hospitalizations required to treat metabolic decompensation. During the previous 6 mo, an

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TABLE 1
Clinical characteristics of the three implanted patients

Patient no. (residence)	Age (yr)	Sex (M or F)	Duration of diabetes (yr)	# of days of hospitalization for metabolic decompensation in previous 6 mo	Management prior to implantation	Previous treatment for subcutaneous insulin nonresponsiveness	Effect of syndrome on lifestyle
1 (St. Paul, MN)	17	F	9	96	Intravenous (insulin pump in hospital)	Trasylol mixed with insulin	Unable to attend school; confined to home or hospital
2 (Dallas, TX)	27	F	10	56	Intravenous (portable insulin pump at home)	2 subclavian venous catheters; 3 intramuscularly implanted catheters	Unable to work; confined to home or hospital
3 (Las Vegas, NV)	15	M	3	112	Intravenous (6 bolus injections of insulin per day at home via an injectable i.v. catheter)	Trasylol mixed with insulin	Unable to attend school; confined to home or hospital

average of 14 days per month per patient was spent in the hospital.

All subcutaneous peritoneal access device implantations were done with the full informed consent of the patients (and their parents, if the patient was under 21 yr of age) and with the approval of the University of New Mexico Human Research Review Committee. The implanted subcutaneous access device met the Food and Drug Administration criteria for a custom medical device.[6]

The subcutaneous peritoneal access. The subcutaneous peritoneal access shown in Figure 1 has three components: (1) an injection port, (2) an 0.5 ml dead space beneath the injection port, and (3) a silicone rubber peritoneal catheter. The injection port is machined from polypropylene, into which is fitted a 1.8-cm-diameter trilayer silicone rubber septum (Hamilton Co., Reno, Nevada). Beneath the septum is a nonexpandable dead space of approximately ½ ml. From this dead space exits a 53-cm silicone rubber catheter, of which 36 cm is coiled beneath the polypropylene shield and 17 cm is external to the shield. The inside volume of this catheter is an additional ½-ml dead space. Eight centimeters distal to the shield, the catheter is encircled by a ½-cm-diameter silicone rubber cuff to permit suturing of the catheter to the linea alba. Nine centimeters distal to the silicone rubber cuff, the peritoneal catheter terminates in a one-way low pressure valve (Ames catheter, Dow Corning, Ann Arbor, Michigan) which prevents obstruction of the catheter by omentum. The entire subcutaneously implanted peritoneal access is coated with medical grade biocompatible silicone rubber (Dow Corning)

The implantation site. The subcutaneous peritoneal access device is implanted above or below the umbilicus through a 5-cm midline incision. The terminal 9 cm of the catheter is placed within the peritoneal space via a 2-mm incision in the linea alba and parietal peritoneum. The silicone rubber cuff is then sutured to the linea alba as the parietal peritoneum is closed. The subcutaneous peritoneal access port is placed lateral (right or left) to the midline

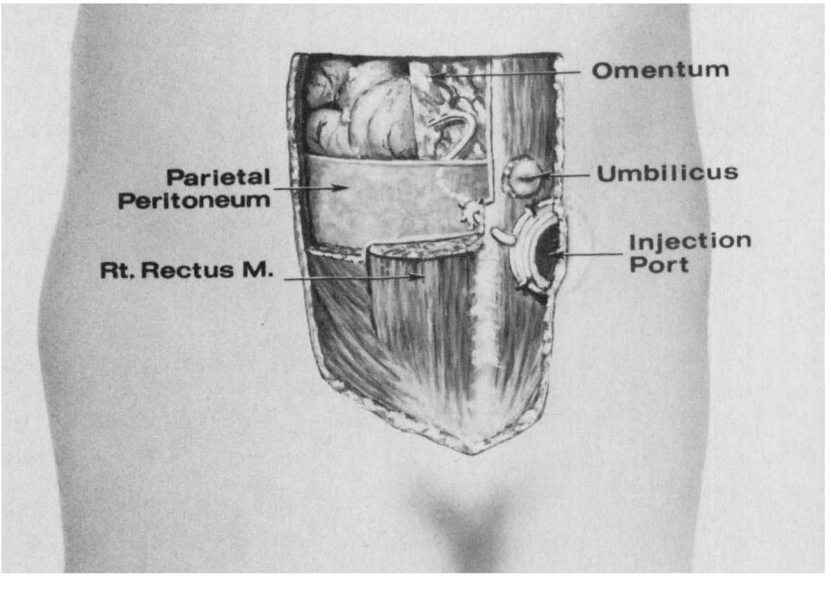


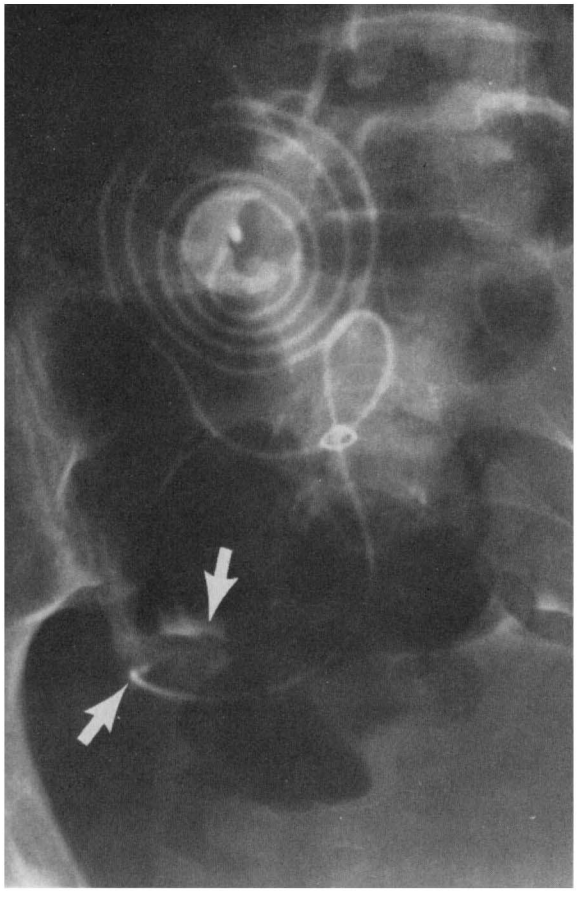
FIGURE 1. Anatomical location of the subcutaneously implanted peritoneal access device. The silicone rubber tubing exiting from the injection port is coiled beneath the injection port before entering the peritoneal cavity (not shown in this diagram, but observable in Figure 2).

incision via a subcutaneous tunnel approximately 1/2 cm below the skin surface. The entire operation is performed under local anesthesia and requires approximately 45 min. Prior to the operation and for an additional 48-h period, the patient is administered broad spectrum antibiotics.[7]

RESULTS

Subcutaneous peritoneal access devices have been implanted in three type I diabetic patients, providing a cumulative experience of 9 mo. No infections, obstructions, or insulin precipitations have been experienced with the implanted devices. Prior to injection of insulin into the implanted subcutaneous peritoneal access port, a radiocontrast study with fluoroscopy was performed to ensure that the device was intact with the appropriate anatomical drainage into the peritoneal cavity (Figure 2). These studies have demonstrated that the peritoneal portion of the catheter is mobile within the peritoneal cavity, thereby not subjecting the same area of peritoneum to continuous insulin exposure. In one patient requiring peritoneoscopy following 2 mo of implantation for right upper quadrant abdominal pain (unrelated to the subcutaneous peritoneal access device), the silicone rubber catheter tip was observed to be free-floating in the peritoneal cavity, without tissue reaction or fatty deposits.

FIGURE 2. A radiocontrast study of an implanted subcutaneous peritoneal access device in diabetic patient #2. The radiocontrast material has partially filled the space between the septum and the shield and has drained down the tubing through the catheter tip. Radiocontrast material can be observed exiting from the catheter tip (arrow) and flowing between two loops of bowel (arrow).



Administration of insulin into the subcutaneous peritoneal access device is easily performed by the patient by injecting the insulin transcutaneously with a 27 1/2-gauge insulin syringe needle through the septum of the subcutaneously palpable port. Confirmation of the correct position of the syringe needle is made by a "specific feel" that the septum and access port give to the injection. Furthermore, when the tip of the needle is in the correct location, the insulin flows without resistance or local sensation into the access device. We use U100 insulin in a ratio of 1:1 of regular to protamine zinc (Eli Lilly and Co., Indianapolis, Indiana). To this mixture is added 25 meq/L of sterile sodium bicarbonate (Abbott Laboratories, Chicago, Illinois) to prevent isoelectric precipitation.[8] Since there is a nonexpandable dead space in the subcutaneous peritoneal access device of 1 ml, once this device is filled with insulin, injection of any volume into the access port results in the same volume of insulin exiting from the device's catheter tip into the peritoneal space.

DISCUSSION

This study demonstrates the successful use of a subcutaneously implanted peritoneal access device for patients who respond poorly to subcutaneous insulin injections. At least 1 wk prior to implantation, a temporary peritoneal catheter was inserted into the abdomen of each patient to document responsiveness to intraperitoneally administered insulin.[9] Following implantation of the device, we recommend that the patients inject insulin at times of meal ingestion every 8 h into the peritoneal access to maintain good metabolic control. The injection of a 1:1 ratio of regular to protamine zinc insulin provides an acute rise in plasma insulin concentration with the associated meals (breakfast, supper, and midnight snack), plus a background dose of insulin throughout the postprandial 8-h period (Figure 3). Although protamine zinc insulin administered subcutaneously may last up to 36 h, when given intraperitoneally, the biologic effectiveness begins to wane at 8 h. When regular and protamine zinc insulin is premixed for up to 2 mo, a loosely dissociated complex occurs which minimally effects the biologic activity of the regular insulin (personal communication, Dr. Richard L. Jackson, Eli Lilly and Company, Indianapolis, Indiana).

The subcutaneous peritoneal access device overcomes the principal drawback of external intraperitoneal insulin delivery, i.e., the risk of peritonitis. By totally implanting the device below the skin, no external bacteria readily gain entrance to the peritoneum. Although injection through the skin into the access port might theoretically introduce bacteria, no infections have been observed in spite of an average of three injections per day throughout 9 mo of experience. The other potential route of bacterial entrance into the peritoneum is via the injection of contaminated insulin. To prevent contaminated insulin from reaching the peritoneum through the device and its peritoneal catheter, a 1 ml dead space is included in its design to self-sterilize insulin.[10]

To date all patients, their families, and their physicians have been pleased with the subcutaneous peritoneal access devices. Throughout the 9 mo of experience, only one of the patients has required re-hospitalization for metabolic control and adjustment of her peritoneal insulin dosage (from two injections per 24 h to three injections per 24 h). Since the access port's septum is only 1.8 cm in diameter,

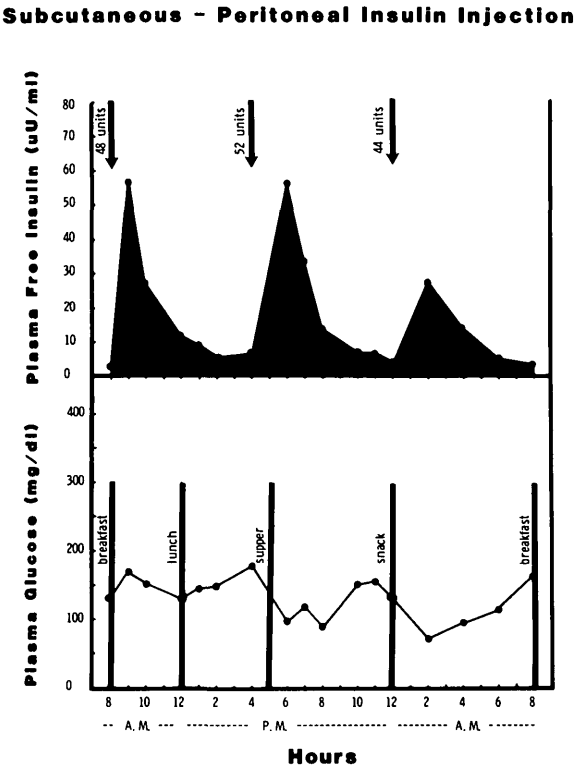


FIGURE 3. Twenty-four-hour insulin and glucose profiles in diabetic patient #3. The insulin was injected transcutaneously into the subcutaneously implanted peritoneal access port every eight hours as indicated, using a mixture of regular to protamine zinc insulin in a ratio of 1:1. The patient was ambulatory and ate a standard 3000-calorie balanced diet (40% carbohydrate, 40% fat, and 20% protein) divided as $^2/_7$, $^1/_7$, $^2/_7$, and $^1/_7$, respectively, starting at breakfast.

the patients must be careful not to repeatedly inject into the septum through the same location in the skin, which might lead to tissue breakdown. To prevent this, the diabetic patient is taught to pull new skin over the access port so that the tenderness does not develop from repeated injections. If the skin does become erythematous, the patient can then use an alternative delivery route (intravenous) for several days to permit skin recovery. Additional experience will be required to define which patient populations will benefit from implantation of a subcutaneous peritoneal access device, and what biologic lifetime may be experienced with the system.

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