

Thrice-weekly Insulin Injection with Nurse's Support for Diabetic Hemodialysis Patients Having Difficulty with Self Injection

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Abstract

Although poor glycemic control is known as an independent predictor of mortality in diabetic hemodialysis patients, it is often difficult for some patients to perform standard self injection insulin therapy. Some practical methods are needed for such patients. We evaluated the usefulness of a new regimen of insulin therapy, namely thrice-weekly insulin injection with nurse's support (TWINS) using insulin NPH or glargine at the end of each hemodialysis sessions in 5 outpatients on hemodialysis with type 2 diabetes mellitus showing HbA1c levels $\geq 8.0\%$ (JDS). HbA1c levels were successfully decreased in all patients from $9.3 \pm 1.1\%$ to $6.9 \pm 0.7\%$ (mean $\pm$ SD) in six months without hypoglycemia symptoms. These preliminary results suggest that this regimen can be one of the practical choices in poor-controlled diabetes patients on regular hemodialysis who have difficulty in self injection of insulin.

Key Words: Diabetes mellitus; Glycemic control; Insulin; Hemodialysis

Introduction

An elevated level of glycated hemoglobin (HbA1c) is an independent predictor of mortality among diabetic patients treated with hemodialysis (DM/HD)^{1,2)}. We previously showed that HbA1c of 8.0% (JDS) or higher was associated with poor survival in an observational cohort of type 2 diabetes patients on maintenance hemodialysis³⁾. Thus, better glycemic control is expected to be beneficial for these patients, although there is no evidence by randomized controlled trials in this specific population.

In the presence of end-stage renal disease, pharmacokinetics of some oral anti-diabetic drugs is altered, and insulin action is also prolonged. Thus, multiple injections of rapid-acting insulin analogue would be one of the choices when we aim strict glycemic control in these patients. In daily practice, however, very few patients are willing to accept multiple self injections, and some

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cases are not able to perform self monitoring of blood glucose (SMBG). Furthermore, intensive glycemic control do not necessarily improve clinical outcome among high-risk patients^{4,5}.

With such background, we invented a practical regimen of thrice-weekly insulin injection with nurse's support (TWINS) at the dialysis unit using insulin NPH or insulin glargine to achieve mild glycemic control. We report here five consecutive patients who were treated with TWINS due to difficulty in performing self injection of insulin.

Methods and Results

We treated five DM/HD outpatients having HbA1c levels of 8.0% (JDS) or higher, who were dialysed in the AM sessions (09:00 to 13:00) three times a week using glucose-containing dialysate (100 mg/dL). Table 1 gives the clinical characteristics the five cases and the changes in HbA1c during the six months of treatment. Cases 1-4 did not want to follow their attending physicians' advise to initiate self injection of insulin, whereas Case 5 could not continue the standard basal-bolus insulin regimen because of severe pain at the right shoulder. Cases 3, 4, and 5 could not perform reliable SMBG.

Table 1. Five hemodialysis cases with diabetes mellitus treated with TWINS

	Case 1	Case 2	Case 3	Case 4	Case 5
Age-Sex	66-M	66-F	69-M	76-M	64-F
Dialysis vintage (years)	1	3	4	7	2
BMI (kg/m ²)	26.8	20.5	20.9	21.4	32.2
Willingness of self injection	no	no	no	no	no
Ability of SMBG	yes	yes	no	no	no
Treatment before TWINS	voglibose	none	none	none	Intensive insulin*
Insulin for TWINS	NPH	NPH	glargine	glargine	glargine
Initial dose (U/shot)	4	4	4	4	10
Dose at 6 months (U/shot)	8	12	8	18	42
HbA1c (%) Before	10.5	8.9	8.0	8.8	10.3
2 months	7.9	7.5	6.0	8.4	7.0
4 months	5.9	7.5	6.5	7.6	7.7
6 months	6.2	7.1	6.9	7.9	6.3
Symptomatic hypoglycemia	none	none	none	none	none

*Case 5 started TWINS because she had given up the standard intensive insulin therapy because of severe pain at the right shoulder. Abbreviations: TWINS; thrice-weekly insulin injection with nurse's support; BMI, body mass index; SMBG; self monitoring of blood glucose; and HbA1c, hemoglobin A1c (JDS).

Before starting TWINS, the lowest glucose level was typically recorded after a dialysis session (or before lunch) in patients who were able to perform SMBG (Fig. 1). To avoid hypoglycemia, we monitored blood glucose level at the end of each dialysis session, and the patients were advised to have insulin injections three times a week after dialysis sessions with assistance by a nurse, and then to take lunch. The initial dose of insulin was 4 to 10 units, and the dose was increased in a stepwise manner at an interval of one week or longer to slowly achieve post-dialysis glucose level between 100 and 150 mg/dL. After starting TWINS, we carefully asked them whether they experienced symptomatic hypoglycemia, but no one did. HbA1c levels were successfully

decreased in all patients from $9.3 \pm 1.1\%$ to $6.9 \pm 0.7\%$ (mean $\pm$ SD, $p=0.043$ by Wilcoxon signed-rank test). They all were satisfied with the treatment.

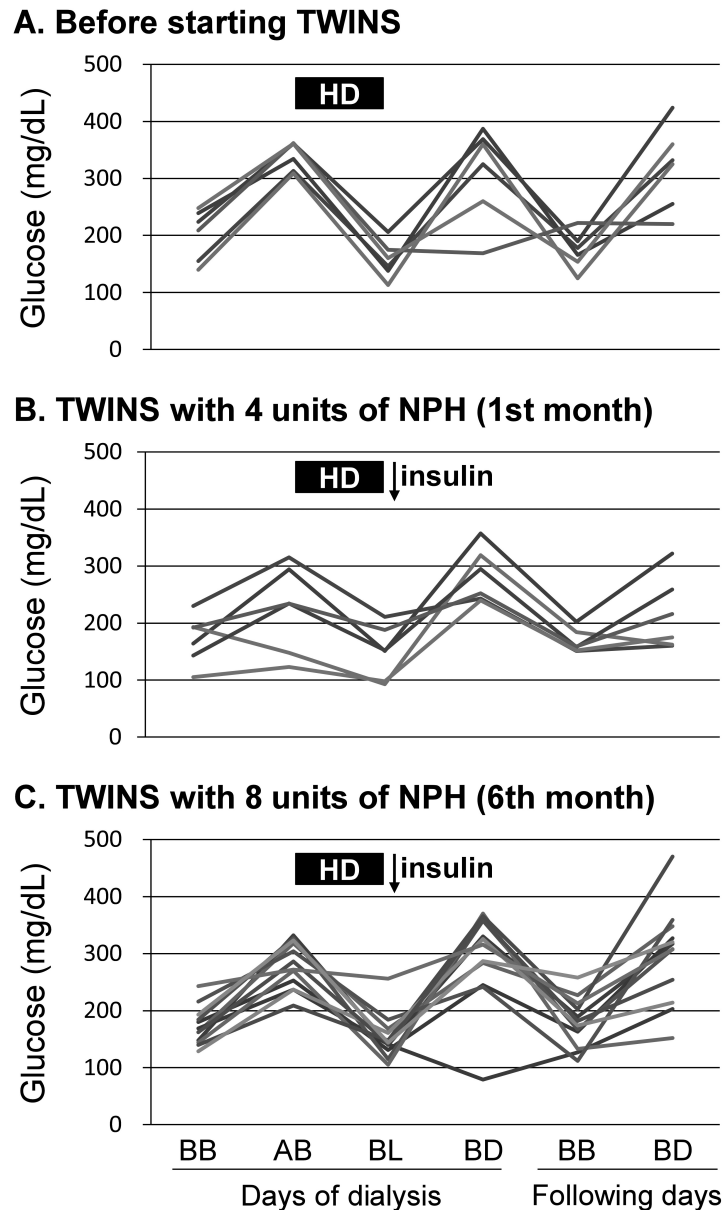


Figure 1. Self monitoring of blood glucose (SMBG) patterns in Case 1 before and after starting thrice-weekly insulin injection with nurse's support (TWINS). Case 1 was able to perform SMBG before breakfast (BB) and before evening dinner (BD) at home, and after breakfast (AB) and before lunch (BL) at the dialysis clinic. The patient received hemodialysis (HD) between AB and BL. SMBG patterns were recorded during the days of hemodialysis and the following days. Panel A illustrates six sets of 2-day SMBG patterns before starting TWINS. Panel B indicates six sets of 2-day SMBG patterns in the first month of TWINS with 4 units of insulin NPH showing the lowest glucose level of 93 mg/dL after hemodialysis (BL). Panel C summarizes 12 sets of 2-day SMBG patterns in the 6th month of TWINS with 8 units of insulin NPH showing the lowest glucose level of 79 mg/dL (BD) in a day of hemodialysis.

Discussion

It is no doubt that intensive insulin therapy with the standard basal-bolus insulin regimen is better than TWINS in achieving tight control of blood glucose. However, we often have diabetic

patients with poor glycemic control who have difficulty in following the standard regimen. Our experience in the five cases indicates that TWINS can be a safe and effective way to improve glycemic control in DM/HD patients who cannot perform multiple insulin injections by themselves.

The achieved levels of blood glucose in our patients were not strict, since the HbA1c is known to often show falsely lower values in dialysis patients because of more rapid turn-over of erythrocytes in anemia and in use of erythropoiesis-stimulating agents⁶⁾. However, recent studies^{4,5)} showed that moderate rather than strict control was associated with better survival in high-risk patients with diabetes mellitus having advanced complications.

Hypoglycemia would be the most important safety issue during treatment with insulin. None of the five patients reported symptomatic hypoglycemia during TWINS. Since they might have had autonomic dysfunction secondary to long-term diabetes mellitus, we cannot completely exclude the possibility of asymptomatic hypoglycemia. Because all the cases in this report were not being hospitalized but outpatients, we could not have close monitoring of their blood glucose levels by nurses. In Case 1 and Case 2 who performed SMBG, we found no evidence for hypoglycemia. Because these cases typically showed the lowest glucose levels before lunch (just after dialysis session), we monitored symptoms and post-dialysis glucose levels at the dialysis unit to avoid hypoglycemia in the five patients being dialyzed in the AM sessions between breakfast and lunch. However, careful observations would be needed, because it is possible that glycemic excursions vary between and within individuals depending upon eating habits, exercise intensity, dialysis prescription, and other factors. In particular, temporal reduction of insulin dose may be appropriate when the patient complains of loss of appetite. Continuous glucose monitoring (CGM), if available, may give more useful information in detecting asymptomatic hypoglycemia and for careful adjustment of insulin dose.

In conclusion, we showed that TWINS may be a safe and effective regimen for hemodialysis outpatients with poor-controlled diabetes who have difficulty in self injection of insulin. Further studies are needed to examine whether or not glycemic control by TWINS improves clinical outcome of such patients.

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