Development and Progression of Retinopathy after Inpatient Management of Diabetes

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Abstract

Objective To examine factors that affect the development of retinopathy after short-term inpatient management of diabetes.

Patients and Methods The subjects were 143 patients with type 2 diabetes who were admitted for inpatient management of diabetes, and did not have retinopathy of the right eye at admission, and had an HbA1c level of ≥ 8.0%. We studied the characteristics of patients who developed retinopathy within one year after discharge.

Results Between the admission date and one year after discharge, twenty-six patients developed retinopathy and the retinopathy subsequently regressed in 5 patients. The 26 patients who developed retinopathy had a significantly longer duration of diabetes (p<0.005), had a higher fasting blood glucose level at admission (p=0.06), and received insulin therapy during the admission at a higher rate (p=0.06) than the 117 patients without retinopathy. The magnitude of the reduction in HbA1c level at 3 months after discharge was smaller in the 13 patients who developed retinopathy within 3 months after discharge than in the 130 patients who did not. Among the 26 patients who developed retinopathy, the HbA1c level at one year after discharge of the 5 patients whose retinopathy regressed was lower than that of the 21 patients whose retinopathy did not regress (p=0.06).

Conclusions A long duration of diabetes, high fasting blood glucose level at admission, and treatment with insulin were associated with the development of retinopathy. Patients with these characteristics should undergo frequent fundus examinations after correction of hyperglycemia. The retinopathy was likely to improve if patients maintained strict glycemic control after discharge.

Key words: diabetic retinopathy, reduction of HbA1c level, development of retinopathy, inpatient, short period

(DOI: 10.2169/internalmedicine.45.1620)

Introduction

Numerous studies have recently reported that strict glycemic control prevents the development of diabetic microvascular diseases. It has also been shown that maintaining good glycemic control for a long period of time inhibits the development and progression of retinopathy (1-5). On the other hand, several reports have shown that rapid correction of poorly-controlled hyperglycemia worsens retinopathy (6-).
It has been reported that the optimal rate of reduction of the HbA1c level in patients with diabetes is less than 3% over a three-month period (11) or less than 3% over a six-month period (5). However, inpatient management that consists of only medical nutrition therapy for several days, often improves poorly-controlled hyperglycemia. Furthermore, improvement of the HbA1c level is a result of treatment and it is rather difficult to provide care for diabetic patients using the HbA1c level as a treatment goal.

As aforementioned, many reports have demonstrated that maintaining good glycemic control for a long period of time can lower the risk of the development and progression of retinopathy (1-5), although other reports have argued that glycemic correction over a short period of time should be avoided to prevent the development of retinopathy (6-11). Thus, it seems necessary to develop a protocol for inpatient management of glycemic control, that is, glycemic correction over a short period of time, in view of retinopathy. To clarify this issue, we investigated the development and progression of retinopathy among diabetic patients who did not have retinopathy at study entry and who showed improvement in glycemic control over a short period of time by inpatient management.

### Patients and Methods

The study subjects were 143 patients with type 2 diabetes who did not have retinopathy of the right eye at admission, whose HbA1c level was 8.0% or higher, and who were followed at our outpatient clinic for one year or longer after discharge, among the patients who were admitted to the Department of Endocrinology and Metabolism, Yokohama City University Graduate School of Medicine, from 1997 through 2002 for glycemic control or diabetes education. During the admission, 19 patients were treated with medical nutrition therapy, 54 patients were treated with oral hypoglycemic agents, and 70 patients were treated with insulin therapy. The length of admission was 21±10 days. Among the 143 patients, 13 patients developed retinopathy between the date of admission and three months after discharge (Group A1) and 130 patients did not develop retinopathy (Group A2). Twenty-six patients developed retinopathy between the date of admission and one year after discharge (Group B1) and 117 patients did not (Group B2). We compared the baseline characteristics and the magnitude of the reduction in the HbA1c level at 3 months after discharge compared with that at admission between Groups A1 and A2, and between Groups B1 and B2. The baseline characteristics that we evaluated were age, sex, duration of diabetes, body mass index, blood pressure, presence of nephropathy, fasting and 2-hour postprandial glucose levels at admission, HbA1c level, total cholesterol level, triglyceride level, fasting and 2-hour postprandial serum C-peptide levels, and urinary C-peptide level. The mode of treatment during the admission was also studied. Among the 26 patients who developed retinopathy between the date of admission and one year after discharge (Group B1) and 117 patients did not (Group B2). We compared the baseline characteristics and the magnitude of the reduction in the HbA1c level at 3 months after discharge compared with that at admission between Groups A1 and A2, and between Groups B1 and B2. The baseline characteristics that we evaluated were age, sex, duration of diabetes, body mass index, blood pressure, presence of nephropathy, fasting and 2-hour postprandial glucose levels at admission, HbA1c level, total cholesterol level, triglyceride level, fasting and 2-hour postprandial serum C-peptide levels, and urinary C-peptide level. The mode of treatment during the admission was also studied. Among the 26 patients who developed retinopathy between the date of admission and one year after discharge (Group B1), the retinopathy regressed in 5 patients prior to the end of the 1-year study period. We compared the HbA1c level at one year after discharge between the 5 patients whose retinopathy subsequently regressed and the 21 patients whose retinopathy did not regress at one year after discharge.

Retinopathy was evaluated by ophthalmologists and internists who were proficient in performing fundus examination.
using the International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales (12) at admission, at discharge, and at 1, 3, 6, and 12 months after discharge.

Glycemic control after initiating treatment in the current admission was assessed by the HbA1c levels at admission, at discharge, and at 1, 3, 6, and 12 months after discharge. The magnitude of the reduction in HbA1c level at 3 months after treatment was calculated by the following equation: \((\text{HbA1c level at admission} - \text{HbA1c level at 3 months after discharge})\%\). Data are presented as mean±standard deviation. Student’s t-test and Fisher’s exact test were used to examine the statistical significance of differences.

This study was approved by the Institutional Review Board of Yokohama City University (#6-7). A detailed explanation of the study was provided to the patients, and informed consent to participate in this study was obtained from each patient.

**Results**

This study included 143 patients with type 2 diabetes who were admitted for glycemic control or diabetes education. The age of the 143 subjects was 55±13 years (range, 24-84 years), and the duration of diabetes was 84±84 months (range, 1-384 months). The clinical characteristics of all 143 subjects, and those of the subjects in Groups A1, A2, B1 and B2 are summarized in Table 1. Within one year after discharge from inpatient management, 26 patients developed retinopathy of the right eye (Group B1). Among the 26 patients, two patients developed retinopathy by the time of discharge, 5 patients developed retinopathy between the discharge date and one month after discharge, 6 patients developed retinopathy between one and 3 months after discharge, 6 patients developed retinopathy between 3 and 6 months after discharge, and 7 patients developed retinopathy between 6 and 12 months after discharge. The retinopathy of the right eye in 5 of the 26 patients subsequently improved during the follow-up period of one year after discharge. Among the three patients who showed improvement of retinopathy upon examination at 6 months after discharge, one patient had developed retinopathy during the admission, one had developed retinopathy between the discharge date and one month after discharge, and one had developed retinopathy between one and 3 months after discharge. Among the two patients who showed improvement of retinopathy upon examination at one year after discharge, one patient had developed retinopathy between the discharge date and one month after discharge, and the other patient had developed retinopathy between 3 and 6 months after discharge (Fig. 1). All 26 patients with retinopathy developed moderate, non-proliferative diabetic retinopathy such as “dot and blot” hemorrhages, and no patient developed severe non-proliferative diabetic retinopathy. The moderate non-
proliferative retinopathy did not progress to proliferative diabetic retinopathy during the follow-up period of one year after discharge in any patient. Group B1, which included the 26 patients who developed retinopathy within one year after discharge, had a significantly longer duration of diabetes and tended to have a higher fasting blood glucose level at admission than Group B2, which included the 117 patients who did not develop retinopathy (duration of diabetes, 123±91 vs. 75±80 months, p<0.005; fasting blood glucose level at admission, 234±95 vs. 203±78 mg/dl, p=0.06). The percentage of patients who received insulin therapy during the admission tended to be higher in Group B1 than in Group B2 (65.4% vs. 45.3%, p=0.06) (Table 1). The magnitude of the reduction in the HbA1c level at 3 months after discharge was smaller in Groups A1 and B1 than in Groups A2 and B2, respectively, although the differences were not statistically significant (Table 1). Among the 26 patients in Group B1 who developed retinopathy, the HbA1c level at one year after discharge in the five patients whose retinopathy regressed tended to be lower than that in the 21 patients whose retinopathy did not regress within one year after discharge (6.1±0.6 vs. 8.0±2.0%, p=0.06) (Fig. 2).

Discussion

In the present study, the HbA1c level in the 143 subjects decreased by an average magnitude of 3.57% at 3 months after discharge compared with that on admission. Among the 143 subjects, 26 (18%) developed retinopathy within one year after discharge. In all 26 patients, the retinopathy involved very mild fundus changes such as “dot and blot” hemorrhage, and it did not progress to severe non-proliferative or proliferative diabetic retinopathy in any patient during the one-year follow-up period. The incidence of retinopathy was highest in the first month after discharge, and gradually decreased thereafter (Fig. 1). In five of the 26 patients who developed retinopathy, the retinopathy subsequently regressed during the follow-up period.

Many epidemiological studies on the incidence of diabetic retinopathy have been published. However, there are considerable differences in the reported incidence of diabetic retinopathy due to differences in patients’ characteristics, diagnostic criteria used, accuracy of diagnosis, calendar period when the study was conducted, geographic region, and so on. Morita (9) reported that 13.5% of patients whose HbA1c level declined by 3% or more over a six-month period developed retinopathy, and 18.6% of patients whose HbA1c level declined by a slower rate developed retinopathy by one year after the treatment. In the current study, 26 patients (18%) developed retinopathy by one year after discharge, although the retinopathy in five patients subsequently improved during the follow-up period: thus, 21 patients (15%) had retinopathy at one year after short-term inpatient treatment. Many reports on factors associated with the development and progression of diabetic retinopathy have also been published. The majority of these studies identified glycemic control and duration of diabetes as significant factors (13). It has been reported that the cumulative incidence of retinopathy at ten years after the onset of diabetes reaches approximately 20 to 60% (14-16). The mean duration of diabetes at study entry among the 26 patients who developed retinopathy was about ten years. It was reported that acute intensive insulin therapy causes a transient worsening of diabetic retinopathy (17). The patients who were treated with insulin during the admission had a propensity to develop retinopathy within one year of discharge at a higher rate (p=0.06) in the present study as well (Table 1).

We also compared the characteristics of patients who did or did not develop retinopathy by three months after discharge (Group A1 and A2), to examine the effect of rapid reduction of the blood glucose level as a result of inpatient management, for retinopathy after 6 months after discharge have influence on blood control after discharge. The magnitude of the reduction in HbA1c level at 3 months after discharge was not particularly large in Group A1, which included patients who developed retinopathy by three months after discharge (Table 1). In many studies (6-11) that reported that rapid correction of hyperglycemia led to progression of retinopathy, the subjects were patients who already had retinopathy, and the suggested reasons for this progression were hypoglycemia or abnormality in coagulation (18-22). The subjects of the current study did not have retinopathy at study entry; our data showed that the rapid reduction of the HbA1c level did not lead to an increased incidence of retinopathy.

Among the 26 patients who developed retinopathy, the retinopathy subsequently improved in five patients within one year after discharge. Glycemic control during the one-year period after discharge tended to be better in these five patients than in the 21 patients whose retinopathy did not improve (Fig. 2). This finding is consistent with the findings of the Diabetes Control and Complication Trial (DCCT) Research Group (1-4), who showed that maintaining strict glycemic control over a long period of time prevents the development and progression of retinopathy. Moreover, hyperglycemia that is corrected in a short period of time would be beneficial for retinopathy if good glycemic control could be maintained thereafter. Shimizu et al (11) followed the changes in the stages of diabetic retinopathy after rapid, drastic correction of hyperglycemia, and found that although a few cases of mild, simple retinopathy (Fukuda Classification A1) progressed, the majority of cases of retinopathy improved after rapid significant correction of glycemia in a short period of time.

The results of the present study suggest that retinopathy develops as a consequence of cumulative poor glycemic control, and that retinopathy occurs at a higher rate in patients treated with insulin than in patients who are not treated with insulin. The rate at which the blood glucose level decreased by the treatment did not significantly differ
between patients who did or did not develop retinopathy after starting inpatient management. Our results also suggest that tightly controlling and maintaining the blood glucose level starting at the time of onset of diabetes would result in better prognosis of retinopathy. Needless to say, internists should take into account the stage of retinopathy when determining the method of glycemic control, and frequent fundus examinations need to be performed after correction of hyperglycemia, especially in patients with a long duration of diabetes or a high fasting glucose level on admission for inpatient management. However, we must avoid persistent hyperglycemia which would lead to progression of retinopathy followed by blindness, and we should not hesitate to reduce the blood glucose level in patients with poor glycemic control for fear of progression of retinopathy due to the rapid correction of hyperglycemia.

We thank the fellows of the Department of Endocrinology and Metabolism, Yokohama City University Graduate School of Medicine, who participated in the care of the patients in this study.

References