

## The Efficacy of Pioglitazone Treatment in Myotonic Dystrophy Type 1 and Type 2 Diabetes Mellitus Patient

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### Introduction

Myotonic Dystrophy Type 1 (DM1) is the most common muscular dystrophy worldwide, with a prevalence of ranged from 1 in 8,300 [1]. The disease is an autosomal dominant neuromuscular disorder and characterized by muscle weakness, dystrophic changes in neuromuscular tissues, frontal baldness, cataracts, cardiac disorder and insulin resistance [2].

The Thiazolidinediones (TZDs) increase insulin sensitivity by acting on adipose, muscle, and liver to increase glucose utilization and decrease glucose production [3]. A few cases of the effect of pioglitazone in diabetic patients with DM1 have been reported. Herein, we describe the efficacy of pioglitazone treatment in DM1 and type 2 diabetes mellitus patient.

### Case Report

A 51-year-old Japanese woman was diagnosed with DM1 at the age of 42-year-old. She noticed recurrent excessive thirst and frequent urination during the previous 3 months and visited our hospital in November 2011. She was admitted to our hospital for further management. Physical examination revealed a blood pressure of 128/87 mmHg, pulse rate of 89/min, body mass index 26.4 kg/m<sup>2</sup> and severe muscle weakness of all four limbs. Laboratory findings showed HbA1c 11.6 %, Fasting Plasma Glucose Level (FPG) 232 mg/dL, the fasting serum insulin level (immunoreactive insulin, IRI) 113 IU/mL, the fasting serum C-peptide level (C-peptide reactivity, CPR) 3.9 ng/mL, 2 hours postprandial blood glucose level 344 mg/dL, 2 hours postprandial CPR 8.4 ng/mL and anti-GAD antibodies were negative. Visceral fat area measured on computed tomography scans was 169.57 cm<sup>2</sup>. She was diagnosed with type 2 diabetes mellitus.

Although diet therapy (1,400 kcal/day) was initiated, the patient's blood glucose level remained high. Accordingly, insulin therapy was administered and the blood glucose level was well controlled with injections of insulin (12 U/day insulin aspart plus 4 U/day insulin detemir; Novo Nordisk). Two weeks after admission, insulin therapy was discontinued and 15 mg/day pioglitazone was administered because it was difficult for her to self-inject insulin. After a week on this treatment, FPG 114 mg/dL, fasting CPR 4.9 ng/mL, 2 hours postprandial blood glucose level 221 mg/dL and 2 hours postprandial CPR 12.0 ng/mL. After discharge from hospital, HbA1c was 7.2 % at a month and 5.7 % at 3 months.

### Discussion

We present here the efficacy of pioglitazone treatment in DM1 and type 2 diabetes mellitus patient. DM1 is an autosomal dominant neuromuscular disorder and characterized by insulin resistance [2]. Insulin resistance is one of the main features characterizing type 2 diabetes mellitus and some studies pointed out that it sometimes is a heritable trait [4]. Further, family history of diabetes increases the risk of coronary heart disease even in non-diabetic subjects [5]. This may be due to an increased prevalence of abdominal fat content in such subjects [6], to elevated systolic blood pressure, higher triglyceride and cholesterol plasma concentration [7], higher plasminogen activator

inhibitor-1 activity [8]. The case-patient didn't have cardiovascular disease, but family history of diabetes account for an increase in cardiovascular risk of individuals [9].

Hyperglycemia in type 2 diabetes mellitus is due to a decrease in insulin action to stimulate glucose uptake in peripheral tissues, muscle, fat and unsuppressed hepatic glucose output. The major phenotypic manifestation of insulin sensitization is increased insulin-stimulated glucose disposal and approximately 80 % of insulin-stimulated glucose disposal occurs in skeletal muscle in humans [10]. Skeletal muscle insulin resistance is among the earliest detectable defects in humans with type 2 diabetes mellitus. Studies using euglycemic, hyperinsulinemic clamps have demonstrated that TZDs increased insulin-mediated peripheral glucose disposal, which occurs predominantly in skeletal muscle [11]. A previous report also supported that TZDs may act directly on muscle and liver cells to increase glucose utilization in vitro studies [12]. There are also reports of the ant diabetic action of TZDs in aP2/DTA mice, whose white and brown fat was virtually eliminated by fat-specific expression of diphtheria toxin A chain [13]. AP2/DTA mice were hyperlipidemic, hyperglycemic, and had hyperinsulinemia indicative of insulin-resistant diabetes. Treatment with TZDs alleviated the hyperglycemia [14]. These data suggest that there is probably important and direct major action of TZDs on skeletal muscle. However, it is reported that TZDs as a risk factor for the development of osteoporosis in postmenopausal women. In our case, we prescribed TZDs because she was in premenopause and didn't have osteoporosis. We should take into consideration side effects when using of TZDs. If side effects of TZDs are not appropriate for DM1 patient, we should use metformin. There is also a report about the usefulness of low dose metformin in the patients with DM1 and type 2 diabetes mellitus [15] and addition of pioglitazone rapidly improves glyceemic control.

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Received August 17, 2015; Accepted September 09, 2015; Published September 16, 2015

Citation: Eguchi T, Miyazaki M, Miyauchi S (2015) The Efficacy of Pioglitazone Treatment in Myotonic Dystrophy Type 1 and Type 2 Diabetes Mellitus Patient. *J Clin Case Rep* 5: 584. doi:10.4172/2165-7920.1000584

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