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Letter to the Editor | Open Access

Effect of Intravitreal Dexamethasone Implant (Ozurdex®) in the Glycemic Control of Patients with Diabetic Macular Edema

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Abstract

Purpose: To evaluate the effect of intravitreal dexamethasone implant (Ozurdex®) in the glycemic control of patients with diabetic macular edema.

Methods: Ten patients with diabetic macular edema received an intravitreal injection (IVI) of dexamethasone implant (DEX implant, Ozurdex®). Glycated haemoglobin (HbA1C) is analyzed before and three months after IVI. The real-time glycemic readings are provided by a new medical device (Dexcom G4® Dexcom, Fr). The primary outcome analysis was the comparison of HbA1C test before and after IVI.

Results: The mean HbA1C level was 7.46 ± 0.70% before IVI and 7.60 ± 1.30% after IVI. No significant difference was found for the percentage of time spent above the target, within the target, and below the target.

Discussion: A bad control of diabetes is identified as a risk factor for both the development and progression of diabetic macular edema. It appears important that IVI of dexamethasone implant have no impact on blood glucose levels in diabetic patients.

Conclusions: To our knowledge, this is the first study that analyzes glycemic control in humans after DEX implant IVI with daily continuous glucose monitoring. In this study, the use of intravitreal steroids in patients with diabetes did not significantly alter glycemic control or increase blood glucose levels.

Keywords: Intravitreal dexamethasone implant; Glycemic control; Hba1c

Introduction

Macular edema is the most common cause of loss of vision in diabetes. Recently, a large phase III clinical trial over 3 years demonstrated that the DEX implant provided robust long-term improvement in visual acuity and macular edema in patients with DME [1]. Dexamethasone implants (DEX implant, Ozurdex®, Allergan Inc., Irvine, CA, USA) that are injected directly into the vitreous have been approved in Europe for the treatment of diabetic macular edema (DME) since September 2014.

The results of the pivotal study are now confirmed by real life studies and support the use of DEX implant in our practice [2].

We know that the oral use of corticosteroids induces elevated glucose levels in patients with diabetes and glucose monitoring is necessary after high-dose intravenous pulse steroids in patients with type 2 diabetes [3]. Several studies have shown that the glycemic profile is disturbed after intra-articular injection of corticosteroids too [4]. Corticosteroids are widely used in ophthalmology too and have been a major therapeutic improvement for patients. Topical steroid administrations do not seem to be associated with a significant risk of adverse systemic effects [5]. Conversely, periocular injections lead to a rapid and nearly total systemic diffusion of the steroid with hyperglycemic effects, as reported in monkeys and humans.

So, the aim of the current study was to evaluate the effect of the intravitreal DEX implant in the glycemic control of patients with diabetic macular edema (DME).

Patients and Methods

Ten patients with type 2 diabetes and DME received an intravitreal injection (IVI) of DEX implant. The mean age of patients was 69.9 ± 8.21 years (range, 54-78 years) (Table 1). Glycated hemoglobin A1c (HbA1C) levels were analyzed before and 3 months after IVI. The real-time glycemic readings, throughout the day and night, over at least 1 week, were provided by a new medical device (Dexcom G4® Dexcom, Fr) that provides data every 5 min and monitors glucose levels continuously. The recording was performed before and 2 months after IVI (at the peak of the corticosteroids implant release).

	Sex	Age	HbA1C initial

Patient 1	femme	62	7,5
Patient 2	femme	78	8,5
Patient 3	homme	71	6,9
Patient 4	homme	54	6,4
Patient 5	femme	63	7,5
Patient 6	homme	76	7,5
Patient 7	homme	78	7,2
Patient 8	homme	77	6,1
Patient 9	homme	75	9,6
Patient 10	femme	71	7,4

Table 1: General characteristics of patients.

The primary outcome analysis was the comparison of the HbA1C test before and after IVI. Other data included mean blood glucose, the percentage of time spent higher than, lower than, and within the glycemic target, and standard deviation over the period.

The medical device can view an overlap of several days of sensor glucose readings or summary glucose statistics for a set number of days, every hour of the day.

We used the Statview 5.0 software (Copyright© 2006) for the statistical analyses. The Wilcoxon test was used to compare data. Statistical evaluation was performed at a significance level of α=0.05.

Results

	Before IVI	After IVI	p
The mean HbA1C level	7.46 ± 0.70%	7.60 ± 1.30%	0.95
The mean of blood glucose levels	154.30 ± 23.82 mg/dl	161 ± 30.42 mg/dl	0,25
The percentage of time spent above the target	27.57%	36.78%	0.16
The percentage of time spent within the target	69.65%	61.49%	0.29
The percentage of time spent below the target	2.78%	1.67%	0.38
The mean highest value of blood glucose	316.8 mg/dl	338.2 mg/dl	0.08
The mean lowest value of blood glucose	55.4 mg/dl	64.2 mg/dl	0.08

Table 2: The results.

The mean HbA1C level was 7.46 ± 0.70% before IVI and 7.60 ± 1.30% after IVI (p=0.95) (Table 2). Blood glucose levels were recorded over an average of 10 ± 3 days. There was no statistical difference for the mean of blood glucose levels before and after IVI: 154.30 ± 23.82 mg/dl before IVI and 161 ± 30.42 mg/dl after IVI (p=0.25).

Glycemic control was then analyzed according to three criteria: percentage of time spent above the target, within the target, and below the target. No significant difference was found for these three criteria. Patients spent 69.65% of the time within the glycemic target before IVI and 61.49% after IVI (p=0.29). Patients spent 27.57% of the time above the glycemic target before IVI and 36.78% after IVI (p=0.16). Patients spent 2.78% of the time below the target before IVI and 1.67% after (p=0.38).

No significant difference was found between extreme values of blood glucose: the mean highest value was 316.8 mg/dl versus 338.2 mg/dl (p=0.08); the mean lowest value was 55.4 mg/dl versus 64.2 mg/dl (p=0.08).

Discussion

Blood glucose is the indirect reflection of systemic absorption of corticosteroids in patients with diabetes [6].

Poor control of diabetes is identified as a risk factor for both the development and progression of DME. The good control of glucose levels is the main goal of endocrinologists in order to reduce vascular complications linked to diabetes. It therefore seems important that IVIs of the DXE implant have no impact on blood glucose levels in patients with diabetes.

The route of administration is important to consider. McCuen et al. previously reported a low systemic rate of DXE after IVI in an experimental rabbit model [7].

Chang-Lin et al. [8] have then compared the plasma DEX concentration according to the route of administration in test animals eyes and human eyes. The sustained-release dexamethasone intravitreal implant in monkeys is associated with a low plasma concentration. This is in contrast with oral and subconjonctival injection that show a high plasma concentration.

Feldman-Billard et al. demonstrated that periocular DEX injections in diabetic patients induce a pronounced hyperglycemic effect, similar

to that observed during an intravenous pulse of methylprednisolone [9].

After retrobulbar injections of triamcinolone acetonide in Humans, blood glucose levels increased in patients with and without type 2 diabetes. Nevertheless a severe hyperglycemia was observed only in patients with type 2 diabetes [10].

Zaka et al. reported that posterior subtenon injections of triamcinolone adds statistically significant quantities to physiologic concentration of corticosteroids in peripherical blood [11].

In this preliminary study, the intravitreal DEX implant injection does not seem to influence the glycemic profile in patients with DME.

A major limitation of our study is the relatively small sample size. To our knowledge, this is the first study that analyzes glycemic control in humans after DEX implant IVI with daily continuous glucose monitoring. These preliminary data are also important for endocrinologists concerned about corticosteroid use in patients with diabetes.

Conclusion

This new continuous glucose monitoring system is indicated for detecting trends and tracking patterns in patients with diabetes. To our knowledge, this is the first study that analyzes glycemic control in humans after DEX implant IVI with daily continuous glucose monitoring. In this study, the use of intravitreal steroids in patients with diabetes did not significantly alter glycemic control or increase blood glucose levels. These preliminary results must be confirmed by further studies with a larger cohort.

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