The Effect of Topical Steroids on Blood Glucose Profile in Diabetic Patients

Irit Bahar*, Shlomo Vinker12 and Igor Kaiserman4
1Department of Ophthalmology, Rabin medical Center, Petah-Tiqva, Israel
2Department of Family Medicine, Clalit Health Services, Central District, Rehovot, Israel
3Department of Family Medicine, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
4Department of Ophthalmology, Barzilai Medical Center, Ashkelon, Israel

Abstract

Purpose: To investigate the effect of topical steroidal eye drops on blood glucose levels and glycemic control among diabetic patients.

Methods: We reviewed the electronic medical records of all the diabetic members in the district of the largest health maintenance organization in Israel (the Central District of Clalit Health Services). All steroidal eye drops prescriptions (n=44,118) filled by diabetic patients in the district between January 1st, 2001 and July 31st, 2006 were documented. We included only those patients that filled at least 3 consecutive prescriptions (n=2697 patients). Of those, 1360 (50.4%) patients had laboratory data for their glycemic control (fasting blood glucose levels and HbA1c) measured around the period of topical steroidal treatment. Main Outcome measures included the relationship of topical steroidal eye drops prescription use on blood glucose levels and Hemoglobin A1C levels among diabetic patients.

Results: The baseline fasting glucose level was 145.8±2.1 (SEM) mg/dl and HbA1c 7.6±0.1%. Fasting blood glucose levels increased up to 157.4±6.3 mg/dl on the 3rd week under topical steroids treatment (p=0.05). HbA1c increased to 8.2±0.3% on the 7th week under topical steroids treatment (p=0.03).

Conclusions: The use of topical steroids by diabetic patients appears to increase blood glucose levels and interfere with glycemic control.

Keywords: Diabetes mellitus; Dexamethasone eye drops; Blood glucose

Introduction

Topical corticosteroids preparations are commonly used in the treatment of ocular inflammation. For anterior segment inflammation, topical steroids treatment is usually preferred over systemic steroids owing to its safety, convenience, and low risk of systemic side effects. Although serum drug levels are apparently low in patients receiving topical corticosteroids [1], there may be a change in levels of plasma cortisol and adrenocorticotropic hormone.[2-6] Fukushima et al. [7,8] showed in two different publications an early effect on serum glucose levels, within hours, after subconjunctival injection of dexamethasone in diabetic and non diabetic rats and an early transient increase in blood glucose levels on the day of surgery in diabetic patients. Our previous study [9] evaluated the effect of dexamethasone eye drops on blood glucose profile following cataract operations and demonstrated that postoperative dexamethasone eye drops have a greater effect on the blood glucose profile of diabetic compared to non diabetic patients.

The aim of the present study is to examine changes in serum glucose concentrations and in haemoglobin A1C (HbA1C) in diabetic patients treated with repeated topical applications of steroidal eye drops.

Methods

All community pharmacies in use by the Clalit Health Services health maintenance organization (HMO) in Israel are computerized and report to a central repository. All prescriptions for ocular topical steroids filled by diabetic members (ICD-9 code: 250.0) of the "central district" of the HMO between January 1st, 2001 and July 31st, 2006, were included (32,454 prescriptions filled by 8995 patients). These included Dexamethasone phosphate 0.1%, Fluorometholone 0.1%, Hydrocortisone acetate 1.5%, Prednisolone acetate 1%.

This HMO dispenses steroidal eye drops with nominal and almost equal co-payment, which ensures that all prescriptions were documented and that drug selection was not influenced by financial aspects. Since there is co-payment we assume that most of the medications that were filled were indeed used by the patients. The collection of data for the study was done anonymously and in conformity with all country laws and the declaration of Helsinki. The study was approved by the Institutional Review Board (Barzilai Medical Center).

To exclude patients receiving steroidal eyedrops treatment for a short period of time, we included only those patients that filled at least 3 consecutive prescriptions at least once every two months. Other exclusion criteria included patients receiving systemic corticosteroids or other drugs that could affect blood glucose (tricyclic antidepressants, diuretics, epinephrine, estrogens, lithium, phenytoin, and salicylates) at the time of the study, a systemic disease known to influence blood glucose levels (i.e. acromegaly, chronic renal failure, cushing syndrome, hyperthyroidism, pancreatic cancer, pancreatitis) at the time of the study, a systemic disease known to influence blood glucose levels (i.e. acromegaly, chronic renal failure, cushing syndrome, hyperthyroidism, pancreatic cancer, pancreatitis) at the time of the study, a systemic disease known to influence blood glucose levels (i.e. acromegaly, chronic renal failure, cushing syndrome, hyperthyroidism, pancreatic cancer, pancreatitis). Cessation of treatment was defined as not receiving the medications for at least 3 months or more. Based on these criteria, we included 2697 diabetic patients using altogether 18,692 ocular topical steroidal prescriptions.

*Corresponding author: Irit Bahar, Department of Ophthalmology, Rabin medical Center, Petah-Tiqva, Israel, Tel: 972-3-9378101; Fax: 972-3-9219084; E-mail: iritbahar@gmail.com

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To evaluate glycemic control, all fasting blood glucose tests and HbA1c laboratory tests performed by diabetics during the study period (2 weeks before till 8 weeks after the beginning of steroid drops treatment) in the district, were documented (225,304 tests).

Of the 8995 diabetic patients followed between January 1st, 2001 and July 31st, 2006, 2697 (30%) were treated with ocular topical steroidal medications (filled at least three prescriptions). Of those, 1360 (50.4%) had laboratory data for their glycemic control (fasting blood glucose levels and HbA1c) measured around the period of topical steroidal treatment (2 weeks before till 8 weeks after the beginning of steroid drops treatment). These 1360 patients were included in this study and considered our study group, 589 males and 771 females with mean age of 67.8±9.1 years. After starting topical steroids, only laboratory data acquired while still being on topical steroids were included.

We investigated the effect of ocular topical steroidal medications on glycemic control among diabetic patients.

Statistical analysis

Student’s t-test was used for continuous variables and chi-square test for proportions (SPSS ver.12 (SPSS Inc. Chicago, IL, USA)). Multiple unpaired t-tests were performed, testing each time point against the baseline time point for both random blood glucose measurement and HbA1c measurement. To account for multiple testing, the p values were corrected according to Bonferroni correction. P-value less than 5% was considered statistically significant.

Results

Before starting topical steroids treatment, the baseline fasting glucose level was 145.8±2.1 (standard error of the mean=SEM) mg/dl and HbA1c 7.6±0.1 %. Figure 1 shows the change in fasting blood glucose levels and HbA1c levels over time while being on topical steroidal treatment. We noted an increase in blood glucose levels, peaking to a mean value of 157.4±6.3 mg/dl on the 3rd week on topical steroids (p=0.05, t-test) and an increase in HbA1c to 8.2 ±0.3% on the 7th week under topical steroids treatment (p=0.03, t-test).

Discussion

We have shown that topical corticosteroid eye drops may induce a significant increase in serum glucose concentration in diabetic patients, and may interfere with their glycemic control.

Maintenance of near-normal glycaemia through intensive diabetes treatment have been proven to delay or prevent microvascular complications. [10,11] The diabetes associations throughout the world have set blood glucose and haemoglobin (Hb) A1c targets to assist care providers and patients with goal setting for diabetes management and control [12,13].

Our study demonstrated the systemic effect of topically administered corticosteroid drops. These drops may be systemically absorbed via several routes, namely the ocular tissues, the nasolacrimal tract or the gastrointestinal tract, when swallowed. [14] Punctal occlusion for a few minutes after the application of the drops might decrease the systemic absorption of the drops. Fukushima et al. [7] demonstrated an increase in blood glucose profile in response to subconjunctival dexamethasone injection in both diabetic and non diabetic groups, in a rat model. Their subsequent study [8] on diabetic patients demonstrated that subconjunctival steroid injection, in the setting of cataract surgery, induced a transient but significant increase in blood glucose on the day of surgery. Although the topically administered steroids may be systemically absorbed, the serum concentration achieved is much less effective compared with sub conjunctival injection.

Feldman-Billard et al. [15] showed recently that periocular steroidal injections in patients with type 2 diabetes induced a marked hyperglycemic effect. Our recent study [9] showed a significant increase in fasting blood glucose levels from 170 ±55.5 mg/dl to 229 ± 76.8 mg/dl in diabetic patients treated with steroid eye drops following...
In conclusion, topical steroids can affect blood glucose levels. Therefore, we recommend that blood glucose levels be monitored in diabetic patients receiving long-term treatment with steroid eye drops.

References


