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

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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 on topical steroids (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). 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.

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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 χ^2 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).

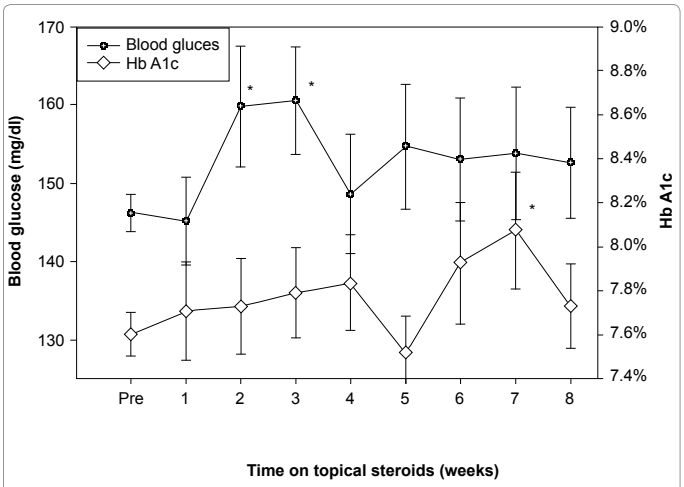

Figure 1: Changes in fasting blood glucose levels and HbA1c levels while being on topical steroidal treatment. One can note an increase in blood glucose levels, peaking to a mean value of 157.4±6.3 mg/dl on the 3rd week on topical steroids (p= 0.05, t-test) and an increase in HbA1c to 8.2 ±0.3% on the 7th week under topical steroids treatment (p= 0.03, t-test). Asterisks signify p<0.05.

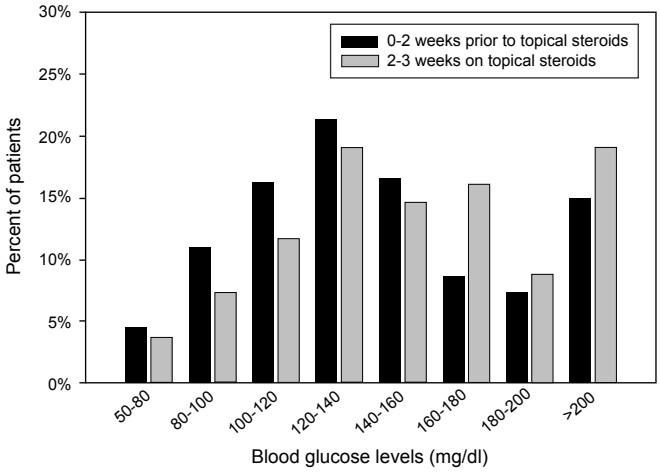

Figure 2: Distribution of blood glucose levels in the study diabetic patients, 0-2 weeks before topical steroidal treatment versus 2-3 weeks after the beginning of treatment. As can be seen, blood glucose levels of >160 mg/dl was documented in 31% of patients before starting the treatment versus 42% on topical steroidal treatment. (p=0.0007).

Figure 2 compares the distribution of blood glucose levels in our patients 0-2 weeks before the topical steroids treatment was initiated versus 2-3 weeks after the beginning of treatment. As can be seen, blood glucose levels of >160 mg/dl was documented in 31% of patients before starting the treatment versus 42% on topical steroidal treatment. (p=0.0007).

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) A_{1c} 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 conjunctial 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 steroidal eye drops following

cataract surgery. (p=0.05) This change was not demonstrated in our two control groups of diabetic patients treated postoperatively with diclofenac drops and non diabetic patients treated with steroidal drops. This finding was the rationale for our present study. Another study, published by Kymionis et al. in 2007 [16], found that intensive application of topical corticosteroids drops for a short

Period of time (7 days) raised the blood glucose levels in patients with controlled diabetes mellitus (p=0.003), which returned to pretreatment levels after discontinuation of the eye drops.

In accordance to these previous studies, our present study found a significant rise in plasma glucose levels and HbA1c, peaking at 3 weeks and 7 weeks, respectively, following topical steroids treatment.

Other causes for hyper glycemia in our study subjects were excluded, namely acromegaly, chronic renal failure, cushing syndrome, hyperthyroidism, pancreatic cancer, pancreatitis, and use of medications known to affect plasma glucose.

HbA1c is produced by glycation of hemoglobin A. Its level reflects the mean blood glucose level over a period of one or two months before the blood sample is taken, and indicates the status of glycemic control. The significant change in HbA1c, demonstrated here, probably reflects a worse glycemic control in the diabetic patient under topical steroid treatment.

Our present study has several limitations. First, its retrospective nature and non randomized design limits the power of our findings. Second, one must view with caution the assumption that filling a prescription for a medication equates with use of the medication as prescribed. Third, it is possible that the condition for which the corticosteroid is required (e.g. uveitis) could itself elevate blood sugar via physical or psychological stress.

Thus, we recommend that a prospective randomized clinical trial be undertaken, on a large series of patients, to further investigate the findings of this study.

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

1. Weijtens O, Schoemaker RC, Romijn FP, Cohen AF, Lentjes EG, et al. (2002) Intraocular penetration and systemic absorption after topical application of dexamethasone disodium phosphate. Ophthalmology 109: 1887-1891.
2. Roters S, Aspacher F, Diestelhorst M (1996) The influence of dexamethasone 0.1% eye drops on plasma cortisol and ACTH concentrations after cataract surgery. Ophthalmologica 210: 211-214.
3. Roberts SM, Lavach JD, Macy DW, Severin GA (1984) Effect of ophthalmic prednisolone acetate on the canine adrenal gland and hepatic function. Am J Vet Res 45: 1711-1714.
4. Krupin T, Mandell AI, Podos SM, Becker B (1976) Topical corticosteroid therapy and pituitary-adrenal function. Arch Ophthalmol 94: 919-920.
5. Eckardt C (1984) Effects of locally administered corticosteroids on mineral metabolism. Klin Monatsbl Augenheilkd 184: 138-140.
6. Meredig WE, Jentzen F, Hartmann F (1980) Systemic side effects of topically applied corticosteroid medication. Klin Monatsbl Augenheilkd 176: 907-910.
7. Fukushima H, Kato S, Hayashi Y, Oshika T (2001) Influence of subconjunctival steroid injection on blood glucose profile in diabetic rats. Eye 15: 326-328.
8. Fukushima H, Kato S, Kaiya T, Yuguchi T, Ohara K, et al. (2001) Effect of subconjunctival steroid injection on intraocular inflammation and blood glucose level after cataract surgery in diabetic patients. J Cataract Refract Surg 27: 1386-1391.
9. Bahar I, Rosenblat I, Erenberg M, Eldar I, Gaton DD, et al. (2007) Effect of dexamethasone eyedrops on blood glucose profile. Curr Eye Res 32: 739-742.
10. Diabetes Control and Complications Trial (1993) The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 329: 977-986.
11. UK Prospective Diabetes Study Group (1998) Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 352: 837-853.
12. American Diabetes Association (1998) Clinical practice recommendations. Diabetes Care 21: S23-S31.
13. Meltzer S, Leiter L, Daneman D, Gerstein HC, Lau D, et al. (1998) Clinical practice guidelines for the management of diabetes mellitus in Canada. Can Diabetes Assoc CMAJ 159: S1-S29.
14. Burch RG, Migeon CJ (1968) Systemic absorption of topical steroids. Arch Ophthalmol 79: 174-176.
15. Feldman-Billard S, Du Pasquier-Fediaevsky L, Heron E (2006) Hyperglycemia after repeated periocular dexamethasone injections in patients with diabetes. Ophthalmology 113: 1720-1723.
16. Kymionis GD, Panagiotoglou T, Tsilimbaris MK (2007) The effect of intense, short-term topical dexamethasone disodium phosphate eyedrops on blood glucose level in diabetic patients. Ophthalmologica 221: 426-429.