RETROBULBAR TRIAMCINOLONE INJECTION AND GLYCEMIC CONTROL

INYECCIÓN RETROBULBAR DE TRIAMCINOLONA Y CONTROL GLUCÉMICO

ASENSIO-SÁNCHEZ VM¹, SOTO A¹, CONDE S¹, JIMÉNEZ-PRADA S², MARTÍNEZ-TELLERÍA MJ¹

ABSTRACT

Objective: To look for alterations of glycemic control as a secondary systemic effect of the retrobulbar injection of triamcinolone acetonide in diabetic and non-diabetic patients.

Materials and methods: We studied 40 patients (25 men and 15 women, 20 with and 20 without diabetes). The injection site in all patients was the retrobulbar space, with one injection of 1ml triamcinolone acetonide (40 mg). Capillary blood glucose was measured at 8 a.m. on the day of treatment as baseline, and on the 7 days following the injection.

Results: The mean capillary blood glucose level was significantly higher at the day 1 post-treatment visit (218.3 ± 70 mg/dl) than at baseline (138.3 ± 21 mg/dl) in the diabetic group (p< 0.001). On day 4 post-treatment, capillary blood glucose remained significantly elevated compared to baseline in the diabetic patients (185.7 ± 67.8 mg/dl) (p= 0.01). Mean capillary blood glucose was significantly higher at the day 1 post-treatment visit (154.2 ± 30.1 mg/dl) than at baseline (119.3 ± 12 mg/dl) in the non-diabetic group (p< 0.001). At the day 4 post-treatment visit, capillary blood glucose remained significantly elevated compared to baseline in the non-diabetic patients (145.5 ± 55.8 mg/dl) (p= 0.01).

RESUMEN

Objetivo: Estudiar las alteraciones en el control glucémico como efecto secundario sistémico de una inyección retrobulbar de acetónido de triamcinolona en pacientes diabéticos y no diabéticos.

Material y método: Se estudiaron 40 pacientes (25 hombres y 15 mujeres, 20 diabéticos y 20 no diabéticos). En cada uno se realizó una inyección retrobulbar con 1 ml de acetónido de triamcinolona (40 mg) y se estudió la glucosa capilar a las 8 de la mañana, en condiciones basales y durante los 7 días post-inyección.

Resultados: La glucosa capilar media fue significativamente mayor en el día 1 post-tratamiento (218,3 ± 70 mg/dl) que la basal (138,3 ± 21 mg/dl) en el grupo diabético (p< 0.001). En el 4° día post-tratamiento, la glucemia capilar permanecía significativamente elevada comparada con la cifra basal (185,7 ± 67,8 mg/dl) (p= 0,01). La glucosa capilar media en el grupo de pacientes no diabéticos fue significativamente mayor en el primer día post-inyección (154,2 ± 30,1 mg/dl) que la glucemia basal (119,3 ± 12 mg/dl) (p< 0,001). Al 4° día de seguimiento, la glucemia capilar permanecía elevada comparada con la basal en el grupo no diabético (145,5 ± 55,8 mg/dl) (p= 0,01).
**INTRODUCTION**

Corticoids are broadly used in ophthalmology for several pathologies which sometimes require prolonged treatment (1,2). In such cases, local administration of the corticoid is preferred because it avoids the side effects inherent to continuous systemic utilization in high dosages (3,4). The local administration of corticoids (peribulbar, retrobulbar) is effective to reach high concentrations of the drug in the posterior pole without apparent secondary systemic effects and is considered by ophthalmologists and internists a safe way to achieve intraocular concentrations. Diabetics, having a more sensitive and rigorous glycemic control (5-8), are a large percentage of patients in an ophthalmology service and account for a broad group of processes affecting the posterior pole and the retro-ocular space, treated with corticoids injections, with repetitive injections in a relevant percentage of cases (1,2). This study aims at analyzing glycemia changes in patients–both diabetic and non-diabetic– after a retrobulbar injection of triamcinolone acetonide.

**SUBJECTS, MATERIAL AND METHODS**

This study was approved by the Ethics, Research and Science Committee of our hospital. The patients were recruited from the retina practice and from the general clinic. Forty patients were studied (20 diabetics and 20 non-diabetics) between 2006 and 2007. Table I illustrates the demographic characteristics of both groups. The inclusion criteria for diabetic patients were:

- Accepting participation in the study, signing and informed consent and commitment to fulfill all the established controls.

- Not having been treated with corticoids 3 months prior to the study.
- Diabetes mellitus type 1 or type 2 treated by endocrine specialist, internist or primary care physician with mean baseline capillary glycemia (fasting) not exceeding 140 mg/dl.
- Authorization for analyzing entire medical records of the patient.
- Patients that continue with the usual out-patient treatment of their diabetes.
- The inclusion criteria for non-diabetic patients were:
  - Accepting participation in the study, signing and informed consent and commitment to fulfill all the established controls.
  - Not having a past or present history of diabetes mellitus.
  - Not having been treated with corticoids 3 months prior to the study.
  - Baseline capillary glycemia not exceeding 120 mg/dl.
  - Authorization for analyzing entire medical records of the patient.

**Key words:** Triamcinolone acetonide, retrobulbar, capillary blood glucose, hyperglycemia, diabetic patients, non-diabetic patients.

**Table I. Demographic characteristics**

<table>
<thead>
<tr>
<th>N°</th>
<th>Diabetics group</th>
<th>Non-diabetics group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>12 (60%) male</td>
<td>13 (65%) male</td>
</tr>
<tr>
<td>Age</td>
<td>52.4 SD 10.3</td>
<td>49.8 SD 12.2</td>
</tr>
</tbody>
</table>

**Definitions**

Baseline capillary glycemia (fasting): is the analysis carried out after 6 hours without having anything to eat.

**Conclusions:** The administration of triamcinolone acetonide by retrobulbar injection was followed by elevations in capillary glycemia in diabetic and non-diabetic patients, but severe hyperglycemia was observed only in the diabetic group (Arch Soc Esp Oftalmol 2009; 84: 599-604).

**Palabras clave:** Acetónido de triamcinolona, retrobulbar, glucemia capilar, hiperglucemia, pacientes diabéticos, pacientes no diabéticos.
Mean baseline capillary glycemia: consists in the mean of several baseline glycemia values. It is very useful because it allows a global assessment to facilitate the implementation of changes closely fitting current conditions.

Clinically controlled patient: a patient with baseline glycemia levels below 140 mg/dl in the diabetic group and 120 mg/dl in the non-diabetic group.

Clinically important difference: baseline glycemia increase above 30 mg/dl.

Table II shows the indication for the retrobulbar injection: 1 ml of triamcinolone acetonide was injected in the retrobulbar region (40 mg, Trigon® depot. Bristol-Myers Squibb, Esplugues, Barcelona, Spain). All the injections were applied by the same person with a 25G, 40 mm needle (Steri-seal®). After the retrobulbar injection the daily activity of the patients was not limited but they were asked to make sure the anti-diabetic treatment was applied correctly. They were asked to return the following day for the first week after the injection (8 a.m. before the insulin injection or the ingestion of oral antidiabetics) for a capillary glycemia. All the capillary controls were made with the same glucometer (Accu-check Sensor®, Roche Diagnostics) with a measurement margin between 10-600 mg, and by the same personnel. The mean pre-injection baseline capillary glycemia was provided by the primary care physicians for the diabetic patients, and for the non-diabetics we took the mean of three consecutive measurements.

The sample size calculations were made considering the number of patients required to detect an increase in 30 mg/dl in glycemia 7 days after the retrobulbar injection. Assuming that the typical deviation of glycemia in patients receiving the usual treatment is of 32.4 mg/dl, with 80% probability of detecting said difference (if it exists) and accepting a Type I error (α) = 0.05, a sample of 18 patients is needed per treatment group. The results obtained were processed with the SPSS statistical program version 12.02 and a value of p < 0.05 was taken as statistical significance level. The comparison of two mean in the samples with independent data was made applying the Mann-Whitney non-parametric test. For the association between 2 categorical variables, the $\chi^2$ test was utilized.

### RESULTS

The patients were divided in two groups based on their diabetes history. The diabetic group with 20 patients and a mean age of 52.4 years (standard deviation –SD–: 10.3) and the group of non-diabetic patients comprising 20 individuals with a mean age of 49.8 years (SD: 12.2). The initial mean baseline capillary glycemia value was of 138.3 ± 21 mg/dl and the non-diabetic group of 119.3 ± 12 mg/dl (p= 0.01) (table III). An increase of glycemia was observed with a significant difference regarding the base values in the two groups 24 hours after the retrobulbar injection. The mean capillary glucose was significantly higher on day 1 post-treatment (218.3 ± 70 mg/dl) than the baseline value (138.3 ± 21 mg/dl) in

### Table II. Indication for retrobulbar injection

<table>
<thead>
<tr>
<th></th>
<th>Diabetics group</th>
<th>Non-diabetics group</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSME</td>
<td>6 (30%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>PsO</td>
<td>8 (40%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>ARMD</td>
<td>5 (25%)</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Traumatism</td>
<td>1 (5%)</td>
<td>5 (25%)</td>
</tr>
</tbody>
</table>

CSME: Clinically significant macular edema; PsO: Orbitary Pseudo-motor; ARMD: age-related macular degeneration.

### Table III. Capillary glycemia curve in diabetic patients (n=20) (mg/dl)

<table>
<thead>
<tr>
<th>Time</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>218.3 ± 70</td>
<td>175.5 ± 41.2</td>
<td>175.3 ± 42.5</td>
<td>185.7 ± 67.8</td>
<td>156.2 ± 53.3</td>
<td>137.5 ± 38.3</td>
<td>130.4 ± 29.9</td>
</tr>
</tbody>
</table>

Baseline glycemia: 138.3 ± 21; Statistical significance p< 0.001.

### Capillary glycemia curve in non-diabetic patients (n=20) (mg/dl)

<table>
<thead>
<tr>
<th>Time</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>154.2 ± 30.1</td>
<td>155.6 ± 23.4</td>
<td>145.4 ± 32.6</td>
<td>145.5 ± 55.8</td>
<td>134.2 ± 45.2</td>
<td>131.5 ± 34.4</td>
<td>123.5 ± 19.4</td>
</tr>
</tbody>
</table>

Baseline glycemia: 119.3 ± 12; Statistical significance p< 0.001.
the diabetic group (p< 0.001). At day 3 post-treatment, capillary glycemia remained significantly higher compared to the base value (185.7 ± 67.8 mg/dl) (p= 0.01). The mean capillary glucose in the non-diabetic group of patients was also higher the first day post-injection (154.2 ± 30.1 mg/dl) than the baseline glycemia (119.3 ± 12 mg/dl) (p< 0.001). On day 4 of the follow-up, capillary glycemia remained high compared to the base value (145.5 ± 55.8 mg/dl) (p= 0.01).

The mean baseline glycemia for the 7 days after the retrobulbar injection was of 168.4 mg/dl ± 49 and 141.4 mg/dl ± 34.4 in the diabetic and non-diabetic groups, respectively (p= 0.01). In the non-diabetic group a better control of glycemia was observed during the follow-up vis-à-vis the baseline data. In both groups a statistically significant difference was found against the baseline glycemia levels (table III). In six diabetic patients (30%) the glycemia values exceeded 200 mg/dl and one (5%) exceeded 500 mg/dl and had to be admitted for treatment. In the diabetic group, the sub-group of patients with a higher glycemic increase were the ones having a previous history of poor diabetic control (p < 0.001).

**DISCUSSION**

Diabetes mellitus is and will continue to be one of the main health problems worldwide due to the increase in the number of diabetics and because it affects multiple systems with biochemical and anatomic consequences. Accordingly, maintaining glycemia within normal levels is the main therapeutic objective (5-8). In this paper we have chosen baseline or fasting glycemia for studying the alteration in its levels because it is taken after 6 hours of fasting and thus shows the genuine metabolic alterations. In addition, it is the type of base level which the patients are unable to control, considering that the other glycemia levels can be adjusted with fast insulin. The eye comprises 0.01% of bodily volume and therefore the best way to achieve optimum concentrations of corticoid in the posterior segment is by applying it at the action spot or nearby (1,2). Systemic corticoids have severe side effects which require careful control, particularly in diabetic patients (3,4). The retrobulbar space has been utilized as a reserve of drugs for direct treatment of intraocular processes as they can be placed in the vicinity of the injury, thus achieving higher local bioavailability than administering it systemically and in comparatively lower dosages. Therefore, it is assumed that the systemic side effects are much smaller. For treating inflammatory processes of the posterior segment and orbit, local treatment is preferred with retrobulbar or sub-tenon injection to avoid the systemic side effects of corticoids. Ophthalmologists are quite satisfied with this option as it increases the treatment safety and allows the use of higher dosages applied at the pathology site, with probably local effects with which the specialist is more familiar.

Triamcinolone acetonide is a long-acting corticoid which is effective in intravitreal or retrobulbar administration (1,2). Its mean line can be of up to 3 months. When studying the adverse effects of triamcinolone, in addition to the side effects derived from the application techniques, the increase of intra-ocular pressure and the formation of cataracts, no reference is made to systemic side effects (9,10). However, in this study a retrobulbar injection of triamcinolone (40 mg) produced very high capillary glycemia values, a side effect which usually goes unnoticed by the ophthalmologist and the internist. In six diabetic patients (30%), glycemic levels exceeded 200 mg/dl and one (5%) had to be admitted to hospital for treatment.

In this study the global analysis of glycemia demonstrated that in both groups the glycemia levels remained over 30 mg/dl (a margin considered to be clinically important), although the non-diabetic group of patients exhibited better control vis-à-vis the diabetic group of patients, with significant differences remaining in the mean glycemia values up to 4 days after the retrobulbar injection. However, in none of the groups it could be considered that the patients were controlled during the follow-up days, with values exceeding 140 mg/dl in the diabetic group and 120 mg/dl in the non-diabetic group, which is not acceptable because the patients were in an out-patient basis, not poly-medicated, free of stress and doing their routine exercises and therefore were controlled before the retrobulbar injection.

The route utilized by triamcinolone to penetrate the vitreous can be trans-scleral diffusion or systemic absorption of the retrobulbar depot. In studies with animals, Bodker et al (11) did not find significant differences of intra-ocular levels of dexametasone between the eye in which a dexametasone retrobulbar injection was made and the opposite eye. Accordingly, they considered that the absorption
was essentially hematogenous. Weijtens O et al (12), after a peribulbar injection of 5 mg dexametasone phosphate, reached serum concentrations of dexametasone similar to those obtained with an oral dose of 7.5 mg, considering that the repetition of this treatment can cause systemic side effects. In dermatological patients treated for localized hair loss, the most effective treatment was intra-muscular triamcinolone, but this treatment also had the most side effects with adrenocortical suppression in 23% against 7% of intravenous pulse corticoid therapy (13). Although the intra-ocular penetration route of retrobulbar triamcinolone cannot be deduced from our study, we cannot exclude the systemic route through the absorption of the retro-ocular depot. In fact, Weijtens O et al (14) verified that the form of the serum curve of dexametasone after a peribulbar injection is similar to the curve after an IV treatment.

It can be concluded that the retrobulbar injection with triamcinolone is a systemic corticoid therapy mode and should not be considered as a simple local treatment, particularly in diabetics and in patients that require repeated treatments. We believe that diabetic patients must be given instructions for managing their diabetes after a retrobulbar injection with corticoids.

REFERENCES


