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THE EARLY EFFECTS OF THE SINGLE LUMBAR EPIDURAL STEROID INJECTION ON FASTING BLOOD GLUCOSE

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ABSTRACT

Background: Epidural steroid injection is one of the safest and most effective ways to treat acute and chronic lumbar back pain syndromes. The aim of this study is to determine the early effects of single lumbar epidural injection on the fasting blood glucose.

Patients and Methods: In this study, thirty-nine patients with chronic back pain and sciatica nerve pain who did not benefit from conventional therapies, such as anti-inflammatory medications and physiotherapy during last 6 months, were investigated. Each patient was given 80 mg triamcinolone acetonide via epidural route. Ten of the selected patients had type II diabetes mellitus and were treated with oral anti-diabetics. The fasting blood glucose were tested at baseline and at each post-treatment day during the first five days after the single epidural steroid injection.

Results: The mean fasting blood glucose levels increased significantly between baseline (106.38± 26.10 mg/dl) and the first two post-treatment day (day 1, 125± 55.52 mg/dl with p= 0.002; day 2, 113.41± 35.19 mg/dl with p= 0.01) but returned to baseline values by the fourth treatment day (day 4, 106.67± 27.96 mg/dl with p= 0.9) in all patients. The mean fasting blood glucose level on the third post-treatment day was also higher than the baseline but the difference was not statistically significant. When patients with and without diabetes mellitus were evaluated as separate groups, the mean fasting blood glucose levels returned to baseline values on the third day of the treatment in non-diabetic patients, whereas on the fourth post-treatment day in diabetic patients.

Conclusion: Epidural steroid injection may increase fasting blood glucose for a longer period in diabetic patients than those without diabetes mellitus. The patients should be informed about the influence of the epidural steroid injection on the blood glucose levels before the treatment procedure, but diabetic patients should also be offered regular blood glucose monitoring in the early period after the treatment.

Key Words: Lumbar epidural steroid injection, low back pain, diabetes mellitus, fasting blood glucose.

Level of Evidence: Retrospective clinical study, Level III.

INTRODUCTION

Nowadays the use of minimally invasive procedures constitutes the basic principle for pain management therapies. Thanks to their anti-inflammatory effects, glucocorticoids have been the drug of choice for various types of pain management therapies. Because of their versatility, glucocorticoids' popularity among clinicians has been increasing. Especially for the treatment of chronic low back pain, epidural administration of glucocorticoids (via interlaminar, transforaminal or caudal) has found wide usage as a minimally invasive intervention, in addition or alternative to other conservative types of treatments, such as oral medication therapy, physiotherapy, weight loss, and exercise [30].

Epidural steroid injections have been used for the treatment of spinal originated acute and chronic low back pain for over 40 years. The first use of the epidural hydrocortisone for the treatment of the low back pain and sciatica nerve pain

was reported by Lievre in 1957 [6]. The first evidence of the presence of inflammation in patients who have radiculopathy has emerged in 1981 [25]. In 1986, Benzon concluded that patients with mechanic low back pain with radiculopathy symptoms may respond to epidural steroid injection therapy [3]. This led to the investigation of the use of epidural steroids in pain management with special focus on the strong anti-inflammatory effects of the corticosteroids. Since then, safety and efficacy of the epidural steroid injection have been established for the treatment of acute and chronic lumbar back pain [4,7,17,24,27,28,31].

The most commonly used corticosteroids for epidural injections are methylprednisolone acetate, triamcinolone acetonide, and dexamethasone acetate [2,5,13,16,21-22]. It has been shown that the fosfolipase activity of the herniation disc is more that of a normal disc (20 to 10.000 times) [26] and the benefits of the epidural steroid injections are due to the anti-inflammatory mechanism, which is secondary to inhibition of fosfolipase A_2 resulting with the blockage of the synthesis of prostaglandins and leukotrienes [1,9,10,15]. Even in pharmacologic doses, both oral or parenteral route type of administration of the corticosteroids have systemic effects (rapid decline in cortisol levels due to suppression of the hypothalamic-pituitary-adrenal axis and decrease in the cortisol levels that may continue for weeks) [19]. Several studies showed that after discontinuation of exogenous steroids, the recovery of HPA axis takes approximately one year [18].

Unfortunately, corticosteroids have adverse effects on the insulin metabolism. The main effect of corticosteroids on the blood glucose is hyperglicemia due to increasing insulin resistance and stimulation of gluconeogenesis in the liver. Several studies suggest that there is a relationship between an excess of cortisol and insulin resistance [32]. Reducing the response of the peripheral tissues to insulin would decrease the glucose uptake and the stimulation of gluconeogenesis in the liver would cause elevation of the blood glucose levels.

While the systemic effects of oral or parenterally administrated glucocorticoids have been studied widely, the effects of local steroid therapy have not been adequately studied. The aim of this study, therefore, is to determine the early effects of a single lumbar injection on the fasting blood glucose.

PATIENTS AND METHODS

For determining the early effects of the single lumbar epidural injection on the fasting blood, we designed our study to include patients who had low back pain and leg pain for at least 6 months. The study included 39 patients (29 women and 10 men) with a mean age 48.56 (age range between 27-70). We excluded any patients who had a history of using local or system steroids in the past 6 months. We also excluded patients who had absolute contraindications (such as local infections) to epidural steroid injections and patients who did not accept to participate in the study. We did not use a control group, since performing the epidural injection with local anesthetic alone would not be an ethical procedure for treating the patients who have low back pain and sciatica.

10 of the 39 patients included in our study suffered from previously diagnosed Type II Diabetes Mellitus. These 10 patients were all using oral anti-diabetics for the treatment of diabetes. These patients continued their usual diet and anti-diabetic therapy during the study. We also adviced all patients to continue their daily physical activities during the study period.

We performed low back pain therapy to all patients in the form of a single lumbar interlaminar epidural steroid injection. During the study, these patients did not use any additional steroids.

All epidural injections were administered through the interlaminar approach to the epidural space. The sitting position is a convenient method for both the patient and the operator in helping determine the midline. In our study, our team performed the interlaminar epidural steroid injections to patients in the sitting position. During the procedure, the loss of resistance technique was preferred, in aseptic conditions as is commonly used by experienced pain physicians. For the injection, we used 80 mg of triamcinolone acetonide and local anesthetics (10mg 0.5 % bupivicaine) diluated to 10 cc with 0.9 % NaCl.

We recorded the patient's baseline fasting blood glucose level before the first epidural steroid injection, and to help determine the early effects of the steroid, we measured the fasting blood glucose values for 5 days after the injection. For evaluating the effects of the epidural steroid injections, we scheduled a post-treatment visit on the tenth day which included a physical examination. We recorded the results of this examination, along with the degree of improvement in pain, improvement in physical activities, and any complications.

In our study, the data were evaluated using mean and standard deviations. "Paired t test" was used for parametric data and " chi-square test" was used for non-parametric data the P values < 0.05 were considered statistically significant.

RESULTS

We first considered all patients, and compared the baseline fasting blood values (106.38 ± 26.10 mg/di) which were recorded before the injection with the first day values (125 ±

55.22). The results showed that there was a large increase (18 %) in the fasting blood glucose values and we found that this increase was statistically significant, with a P value of 0.002. During the following days, especially on 2nd and 3rd days, the increase in the fasting blood glucose persisted (113.41 ± 35.19 and 109.59 ± 44.33 respectively). But, these values were lower than the first day (only 6.60 % and 3.01 % increase in days 2 and 3, respectively). In fact while, the 2nd day values are statistically significantly larger than the baseline, with a P value of 0.01, the 3rd day results showed that an increase that was not statistically-significant (P=0.419) (Figure-1).

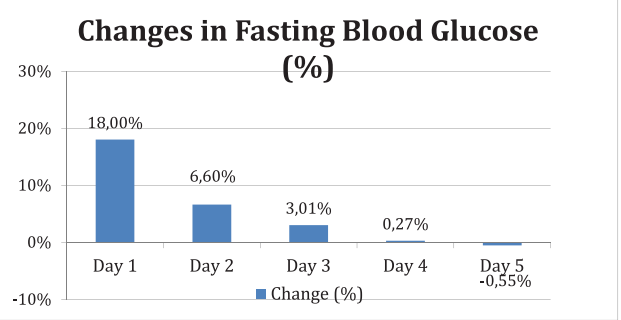

Figure-1. Post-procedure changes in percentage of mean fasting blood glucose according to days after injection

We next considered the non-diabetic and the diabetic patients separately. The results showed that both groups had statistically significant increases (P=0.001 and 0.037, respectively) in fasting blood values on the first day after the injection.

For non-diabetic patients, the fasting blood glucose values showed an increase of 12.70 % (109.24 ± 19.64 mg/dl) on the first day compared with the baseline values recorded before the injection (96.93 ± 7.43 mg/dl). The increase was significant with a P value of 0.001. Second day fasting blood glucose values for this group were 101.37 ± 16.11 with an increase of 4.59 % (P=0.114). In this group, the mean fasting blood glucose values returned close to base values during the last three days of the study.

In the group of diabetic patients, the fasting blood glucose values showed an increase of 23.49 % (165.1 ± 69.11 mg/dl) on the first day compared with the baseline values recorded before the injection (133 ± 39.86 mg/dl). The increase was significant with a P value of 0.037. For these patients, the increase in the blood glucose levels was also statistically significant on the 2nd day (148.2 ± 51.06 mg/dl and P value=0.04). Moreover, unlike the non-diabetic patients, the fasting blood glucose values remained 10.40 % high er also on the 3rd day, but this increase, was not statistically significant (P-value of 0.23). The mean fasting blood glucose values approached the baseline values on the 4th day, also for these diabetic patients.

DISCUSSION

Epidural steroid injection is the preferred treatment method for chronic low back pain. Clinicians prefer this procedure because of its effectiveness and lower rate of side effects: local application of corticosteroid to the epidural area tends to lead to lesser and shorter-time side effects because of its limited systemic distribution. Another advantage of the application of corticosteroid directly to the epidural space is the need to use lower doses of steroids to achieve the desired effects.

General effects of the glucocorticoids include decreasing tissue response to the insulin pathway and inducement of the glucagon pathway. In this study, we investigated the potential effects of single lumbar epidural steroid injection on the average fasting blood glucose in the chronic low back pain and sciatica nerve pain patients. The study results showed that there is a statistically significant change in fasting blood glucose levels for the first and second days after the injection in all patients with or without diabetes mellitus. Previous studies have shown that local injections of the corticosteroids to the intra-articular or epidural area may cause suppression of the hypothalamic-pituitary-adrenal axis [14,29]. A decrease in the cortisol levels is expected via this suppression, but not as much as the systemic routes. The results of our study point to a similar conclusion regarding the local corticosteroids effects on the regulation of the blood glucose. According to the results reported here, this effect is especially significant in the early stages of the treatment.

The application of oral or systemic corticosteroids may impaired the insulin sensitivity in diabetic patients and, for these patients, local glucocorticoids may lead to changes in glucose control. Gottlieb *et al.* reported that, since blood glucose control may change after the application of local glucocorticoids, stricter follow-up is needed for diabetic patients after the treatment [12]. Our study also points to a similar observation: as seen in Figures-2 and 3, after epidural steroid injection, changes in the fasting blood glucose levels are more pronounced in patients with diabetes and the changes last longer than the patients without diabetes mellitus.

In a study done in 2009, Gonzalez [11] has shown that, for diabetic patients, lumbosacral transforaminal and caudal epidural betamethasone injections are associated with statistically significant elevations that lasted for 2 days. Similar results were observed in a 2012 study by Even and colleagues [8] who evaluated the effects of epidural steroid injections on blood glucose levels in patients with diabetes mellitus. Their study reported that increases in blood glucose

levels were seen in approximately 85 % of the patients with diabetes. This increase was transient and blood glucose levels returned back to the baseline within 48 hours after epidural injection. While we also observed similar transient elevations in the blood glucose levels after interlaminar epidural steroid injections on patients with diabetes, blood glucose returned to the baseline levels only approximately four days after the injection.

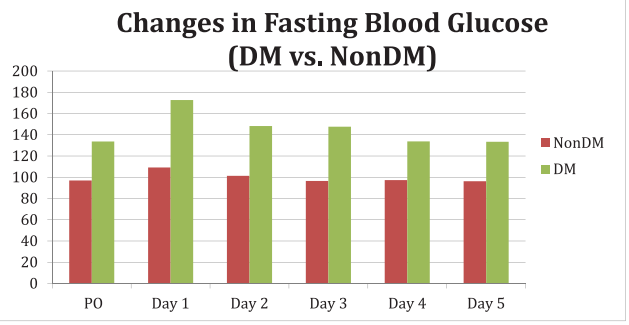

Figure-2. Comparison of the fasting blood glucose in patients with or without diabetes mellitus according to days after injection.

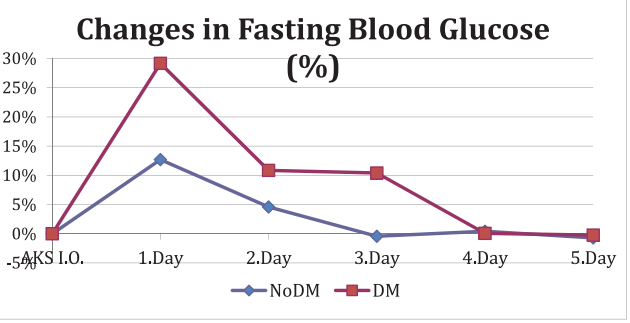

Figure-3. Comparison of the percentage of changes in fasting blood glucose in patients with or without diabetes mellitus according to days after injection.

Moon and colleagues [23] investigated blood glucose and cortisol levels after epidural and shoulder intra-articular glucocorticoid injections in both diabetic and non-diabetic patients. Their study included 29 patients with sciatic or shoulder pain. After glucocorticoid injections, fasting blood glucose and cortisol levels were measured on 1st, 7th, and 21st days and compared with the baseline levels. In all subgroups, fasting blood glucose levels were significantly higher on the first day after the injection. Levels returned to the baseline by the second control on the seventh day. In contrast to Moon's study, to observe how the fasting blood glucose levels vary during the first few days, we measured blood glucose levels every day after the injection; this enabled us to observed that glucose levels returned to the baseline on third day for the non-diabetic patients and fourth day for patients with diabetes.

In a 2007 study, Younes et al. [33] applied local glucocorticoid on 29 patients (epidural injection on 18 patients and intraarticular injection on 11 patients) with or without diabetes mellitus. The results showed a significant postprandial blood glucose elevation for all patients on the first day after the injection. On the seventh day control, high levels of postprandial glucose were seen only on patients with diabetes mellitus. Younes' results differ slightly from the results in our study, where even with diabetic patients blood glucose levels returned to the baseline on the fourth day after the injections. The reason for this difference is likely to be the types and doses of the steroids used in the two studies. In our study, we administered 80 mg triamcinolone acetonide in a single injection, whereas Younes had used 5,625 mg kortivazol per injection and applied three consecutive injections in a row.

Note that in an earlier study with 9 patients, Maillefert and colleagues [20] applied a single epidural injection of 15 mg dexametasone acetate, but they did not observe any change in fasting blood glucose after the epidural steroid injection. In a 2011 study of systemic effects in diabetic patients of single epidural steroid injection, Zufferey [34] administered 80 mg depot methylprednisolone. Also in that study, no effects on the glycemic control were observed. We believe that in these two studies injections failed to produce any effects on the blood glucose control due to the specific pharmacodinamic effects and the different dosing of the preferred drug.

Considering the results of our study and the prior findings, we believe that more comprehensive studies are needed to identify the right medication and dosage, especially for situations in which blood sugar regulation has high priority.

CONCLUSION

Our study has shown that, in all patients, epidural steroid injections may increase fasting blood glucose during the first few days after the procedure. For the patients with the diabetes mellitus, the elevations in the levels of fasting blood glucose may be higher and it may take longer for the glucose levels to return to the baseline levels. Considering these findings, it is important that the patients are informed before the application of epidural steroid injections about the potential impact of the injection on their blood glucose levels. Moreover, diabetic patients should be recommended regular blood glucose monitoring during the first few days after the treatment.

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