Clinical Research in Practice: The Journal of Team Hippocrates

Volume 6 | Issue 2 Article 11

2020

Upper vs. lower extremity: Does the site of steroid injection have a different effect on blood glucose levels in patients with diabetes?

Emilyn Anderi
Wayne State University School of Medicine, gc5844@wayne.edu

Recommended Citation

ANDERI E. Upper vs. lower extremity: Does the site of steroid injection have a different effect on blood glucose levels in patients with diabetes? Clin. Res. Prac. Oct 16 2020;6(2):eP2291. https://doi.org/10.22237/crp/1593562200

Clinical Research in Practice
The Journal of Team Hippocrates
VOL 6 ISS 2 / eP2291 / OCTOBER 16, 2020
https://doi.org/10.22237/crp/1593562200

Upper vs. lower extremity: Does the site of steroid injection have a different effect on blood glucose levels in patients with diabetes?

EMILYN ANDERI, MS, Wayne State University School of Medicine, gc5844@wayne.edu

ABSTRACT A clinical decision report appraising Twu J, Patel N, Wolf JM, Conti Mica M. Impact of variation of corticosteroid dose, injection site, and multiple injections on blood glucose measurement in diabetic patients. *J Hand Surg Am.* 2018;43(8):738-744. https://doi.org/10.1016/j.jhsa.2018.06.005 for a patient with diabetes and osteoarthritis.

Keywords: *diabetic, glucocorticoid injections, osteoarthritis*

Clinical Context

Ryan Carpenter (pseudonym), a 63-year-old Caucasian male with a history of type 2 diabetes mellitus and osteoarthritis (OA) of bilateral knee joints, presented to his family medicine clinic with a complaint of increasing knee pain. When he was first diagnosed with OA, Mr. Carpenter was able to find relief with NSAIDs and physical therapy, however, as time went on this relief became less and less, and his daily activities were becoming severely affected. Upon review of his radiographic findings, severe joint space narrowing and cartilage damage of both knees was visible. Although Mr. Carpenter understood intra-articular steroid was not a long-term therapy, he was only interested in improving his function over the next month with the many activities planned for his daughter's wedding. Due to his increasing pain, the option of a glucocorticoid injection for short-term relief was presented to Mr. Carpenter. Consideration of the effects the glucocorticoid injection would have on his blood glucose took place. Mr. Carpenter stated that he had no issues with his blood glucose when he received a similar type of injection for a frozen shoulder many years ago, but since that time, his diabetes has been more difficult to control, requiring addition of dual oral therapy and low dose long acting insulin at bedtime. He currently has good diabetic control but agreed to monitor his blood glucose more carefully for 2 weeks following the procedure, particularly because the planned social events are often accompanied by "celebratory" foods not in his usual diet.

Clinical Question

Does an intra-articular glucocorticoid injection in a lower extremity have a greater effect on the blood glucose levels compared to an injection of an upper extremity in patients with diabetes mellitus?

EMILYN ANDERI, MS, *is a 4th year medical student at Wayne State University School of Medicine.*

ISSN: 2379-4550
http://digitalcommons.wayne.edu/crp

Clinical Research in Practice
The Journal of Team Hippocrates
VOL 6 ISS 2 / eP2291 / OCTOBER 16, 2020
https://doi.org/10.22237/crp/1593562200

Research Article

Twu J, Patel N, Wolf JM, Conti Mica M. Impact of variation of corticosteroid dose, injection site, and multiple injections on blood glucose measurement in diabetic patients. *J Hand Surg Am.* 2018;43(8):738-744. https://doi.org/10.1016/j.jhsa.2018.06.005.

Related Literature

A review of UpToDate was initially performed to evaluate the current management of patients with moderate to severe OA, as well as the comorbidities that impact the management.[1,2] Currently, the management of OA involves both pharmaceutical and non-pharmaceutical modalities, aimed around reducing inflammation and physical therapy. While intra-articular glucocorticoid injections are not routinely used for patients with knee OA, their use can provide some short-term relief to patients with moderate to severe OA.[1] For patients with diabetes, glucocorticoid injections can produce a transient hyperglycemia, and therefore it is advised that patients monitor their blood glucose for a few days post-injection.[2]

A subsequent search of PubMed was performed using the terms “diabetic” AND “joint injection” AND “blood glucose” returned 33 results. The titles and abstracts were reviewed to find publications relevant to the clinical question. This further refined the results to 15 articles. Of these results, 2 were systematic reviews and 5 were clinical trials. The titles and abstracts of these 21 results were used to determine relevance in relation to the clinical question.

One article discussed the impact of intra-articular betamethasone injections for diabetic patients.[3] However this study focused on the impact on insulin resistance not blood glucose levels and therefore was omitted. Another looked at the impact of methylprednisolone acetate on fructosamine levels, but again was omitted as it did not pertain directly to the clinical question.[4]

A publication by Zufferey et al. studied the effects of epidural steroid injections on blood glucose in patients with diabetes mellitus and found that there was no significant increase in blood glucose levels post-intervention.[5] This paper found conflicting results with one published by Younes et al., but brought up the discussion of how glycemic effects could differ based on the type of steroid used (soluble versus depot type).[6] However, because these papers addressed the use of epidural injections, not intra-articular, they were deemed less relevant to the clinical question.

Two systematic reviews discussed the systemic effects of intra-articular glucocorticoid injections in diabetic patients.[7-8] Both provided insight as to other effects that may need to be considered when a glucocorticoid injection is offered to a diabetic, but were considered too broad in relation to the clinical question.

There are many articles are available discussing the changes in blood glucose after shoulder injections, where the overall consensus is that there is no significant increase in blood glucose levels.[9-11] There was also an article that noted a significant increase in blood glucose after knee injections.[12] While these articles could all be considered relevant to the clinical question, there was one study that directly compared upper versus lower extremity injections and their effects on blood glucose. Utilizing the Twu et al. paper, the comparison of upper versus lower extremity and effect on blood glucose could be directly answered, and therefore was the paper chosen to analyze.[13] Given the above sources discussed, this body of evidence is a Grade-B Strength of Recommendation based on the SORT criteria.

Critical Appraisal

The article by Twu et al. is a prospective cohort study to monitor the effects on blood glucose of 60 patients with diabetes mellitus who were offered a corticosteroid injection for either an upper or lower joint injection. Patients had to have a documented diagnosis of diabetes mellitus, be above the age of 18, able to complete glucose measurements, and not have received any injections in the past 3 months to be included in the study. Once enrolled, patients received standard injections of triamcinolone based on their assigned injection site, and were given a log to record one fasting and one 2-hour postprandial blood glucose measurement for 14 days post-injection. Upon completion of the 14 days, researchers contacted study participants to retrieve measurement data. Based on this study design, this article is considered to have a SORT evidence level of 3.

ISSN: 2379-4550
http://digitalcommons.wayne.edu/crp

Clinical Research in Practice
The Journal of Team Hippocrates
VOL 6 ISS 2 / eP2291 / OCTOBER 16, 2020
https://doi.org/10.22237/crp/1593562200

Table 1 in the article outlines the demographics and baseline characteristics of patients who received different injections. Patients were separated into 3 groups based on the type of injection they were receiving; a single upper extremity injection (n=32), a single lower extremity injection (n=17), or multiple injections (n=11). These patients were approached to join the study based on their diagnosis and treatment offered. Because of this, the study may present with selection bias. As well, the groups were assigned based on documented injection needed, therefore there was no randomization amongst study groups.

It can also be noted that there were some baseline differences between groups. In particular, the average HbA1C varied from 7.65 for patients receiving an upper extremity injection, 7.45 for lower extremity, and 7.6 for multiple injections. Our patient was a 63 year old male receiving a lower extremity injection, with an HbA1C of 7.2. This would indicate that his diabetes was slightly better controlled than then average patient receiving the same injection as him in the study.

Each group received a separate experimental intervention depending on their study group. Since each type of injection requires a specific amount of steroid, patients receiving an upper extremity injection received less steroid than someone requiring a lower extremity injection. This difference in steroid dose could have accounted for some of the differences seen in blood glucose changes post-injection. However, aside from the differences in intervention, all study groups followed the same experimental protocol.

A mixed-model covariant analysis was used to interpret the significance of the changes in fasting and postprandial blood glucose, which accounted for day-to-day measurements, corticosteroid dose, single versus multiple injections, BMI, insulin use, and HbA1C. This allowed for the use of both fixed effects, like how groups differ between a set of treatments, and random effects, such as the variability among study subjects. The entire cohort was analysed together, followed by analysis of each group separately.

The outcome was based on a comparison of days 1-7 compared to days 10-14, with the later days considered “baseline” on the assumption that a change in blood glucose would only occur within the first week. Changes in blood glucose were the highest on day 1—elevated by 35 mg/dl, a clinically meaningless difference. In fact, when reviewing the methodology and the outcomes chosen by the researchers, this article seems to report trivial findings. The usefulness of the evidence is that there was not a bad outcome in any patient, which could be used to reassure Mr. Carpenter.

Clinical Application

Glucocorticoid injections are an effective treatment for a variety of upper and lower extremity joint conditions such as osteoarthritis. However, these steroids have been shown to affect glucose metabolism, and cause abnormal blood glucose measurements in diabetics. This raises the concern of many different glucose-related complications, such as diabetic ketoacidosis, that could arise if diabetics receive an intra-articular injection. The findings by Twu et al. suggest that the location of injection (upper versus lower extremity) does play a role in the differences of post-injection blood glucose measurements for patients with diabetes mellitus. While all patients did see some increase in both fasting and postprandial blood glucose levels up to 72 hours post-injection, this increase was not significant for patients who received upper extremity injections or multiple injections. However, patients who received lower extremity injections were found to have a statistically significant and clinically meaningless increase in fasting blood glucose, with no impact on postprandial blood glucose. The study also found that as HbA1C increased, more significant increases in blood glucose were also seen.

For our patient Mr. Carpenter, this study suggests that he should indeed monitor his blood glucose levels more closely upon receiving a glucocorticoid injection in his knee, as there may be a significant increase in the weeks post-injection. This study could also be used to explain why Mr. Carpenter did not raise any concern when he received a similar injection in his shoulder many years ago. It should be noted that Mr. Carpenter’s demographics did not match up perfectly with the study participants considering he had a lower HbA1C of 7.2, and is Caucasian (90% of study participants were of black ethnicity), and therefore this study cannot truly predict his blood glucose response to glucocorticoid injections. Nonetheless, we thoroughly counselled Mr. Carpenter on the importance of blood glucose control, and that closer monitoring of his blood glucose post-injection was encouraged. In practicality, his dietary consumption is a far greater risk for diabetic control, so we took the opportunity to counsel him on coping strategies to manage calorie intake during the upcoming festivities. Considering how prevalent

ISSN: 2379-4550

Clinical Research in Practice
The Journal of Team Hippocrates
VOL 6 ISS 2 / eP2291 / OCTOBER 16, 2020
https://doi.org/10.22237/crp/1593562200

diabetes is, the information provided by this article does provide opportunity for discussion between physician and patient about the risks and benefits of receiving glucocorticoid intra-articular injections.

New Knowledge Related to Clinical Decision Science

Osteoarthritis and diabetes are common problems in the population. These chronic medical conditions had major impact for our patient, Mr. Carpenter. His OA was no longer controlled, and he needed relief for a specific short-term social activity. Our team proposed corticosteroid injections to provide him with some relief, but it was important for us to consider the impact it may have on his diabetes, which has been well-controlled. The study by Twu et al. showed that it could actually improve his diabetic control if he could be more physically active. Given the prevalence of both diabetes and OA in the population, discussion between the physician and patient in regard to the effect treatment of one disease could have on the other is an important conversation and is the hallmark of Clinical Decision Science.

Should a scenario arise in which a patient with poorly controlled diabetes has uncontrolled OA, the results of the Twu et al. study would have a different meaning and the physician might have a different discussion about the harms and benefits of corticosteroid injections on their particular care. A change of 35 mg/dl in that situation (the size effect documented in this paper) may be more dangerous.

References

1. Deveza LA, Bennell K. Management of moderate to severe knee osteoarthritis. In: Hunter D, Ramirez Curtis M, eds. *UpToDate.* Waltham, MA: UpToDate, Inc. 2019.
2. Louati K, Berenbaum F. Comorbidities that impact management of osteoarthritis. In: Hunter D, Ramirez Curtis M, eds. *UpToDate*. Waltham, MA: UpToDate, Inc. 2019.
3. Habib G, Chernin M, Sakas F, Artul S, Jabbour A, Jabaly-Habib H. The impact of intra-articular depot betamethasone injection on insulin resistance among diabetic patients with osteoarthritis of the knee: a case-control study. *J Clin Rheumatol*. 2018;24(4):193-196. https://doi.org/10.1097/RHU.0000000000000614.
4. Habib G, Sakas F, Artul S, Khazin F, Hakim G, Jabbour A, Jabaly-Habib H. The impact of intra-articular methylprednisolone acetate injection on fructosamine levels in diabetic patients with osteoarthritis of the knee, a case-control study. *Clin Rheumatol*. 2016;35(6):1609-14. https://doi.org/10.1007/s10067-016-3218-9.
5. Zufferey P, Bulliard C, Gremion G, Saugy M, So A. Systemic effects of epidural methylprednisolone injection on glucose tolerance in diabetic patients. *BMC Res Notes*. 2011;4:552. https://doi.org/10.1186/1756-0500-4-552
6. Younes M, Neffati F, Touzi M, Hassen-Zrour S, et al. Systemic effects of epidural and intra-articular glucocorticoid injections in diabetic and non-diabetic patients. Joint Bone Spine. 2007;74(5):472-476. https://doi.org/10.1016/j.jbspin.2006.10.009.
7. Habib GS. Systemic effects of intra-articular corticosteroids. *Clin Rheumatol*. 2009;28(7):749-756. https://doi.org/10.1007/s10067-009-1135-x.
8. Choudhry MN, Malik RA, Charalambous CP. Blood glucose levels following Intra-articular steroid injections in patients with diabetes: a systematic review. *JBJS Rev*. 2016;4(3). https://doi.org/10.2106/JBJS.RVW.O.00029.
9. Moon HJ, Choi KH, Lee SI, et al. Changes in blood glucose and cortisol levels after epidural or shoulder intra-articular glucocorticoid injections in diabetic or nondiabetic patients. *Am J Phys Med Rehabil*. 2014;93(5):372-378. https://doi.org/10.1097/PHM.0000000000000001.
10. Kim YS, Lee HJ, Lee DH, Choi KY. Comparison of high- and low-dose intra-articular triamcinolone acetonide injection for treatment of primary shoulder stiffness: a prospective randomized trial. *J Shoulder Elbow Surg.* 2017;26(2):209-215. https://doi.org/10.1016/j.jse.2016.09.034.
11. Habib GS, Abu-Ahmad R. Lack of effect of corticosteroid injection at the shoulder joint on blood glucose levels in diabetic patients. *Clin Rheumatol.* 2007;26(4)566-568. https://doi.org/10.1007/s10067-006-0353-8.
12. Habib GS, Safia A. The effect of intra-articular injection of betamethasone acetate/betamethasone sodium phosphate on blood glucose levels in controlled diabetic patients with symptomatic osteoarthritis of the knee. *Clin Rheumatol.* 2009;28(1):85-87. https://doi.org/10.1007/s10067-008-1023-9.
13. Twu J, Patel N, Wolf JM, Conti Mica M. Impact of variation of corticosteroid dose, injection site, and multiple injections on blood glucose measurement in diabetic patients. *J Hand Surg Am.* 2018;43(8):738-744. https://doi.org/10.1016/j.jhsa.2018.06.005.

ISSN: 2379-4550
http://digitalcommons.wayne.edu/crp,