Evaluating Short-Term Pain After Steroid Injection

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Abstract

Steroids are injected into joints for various indications. All steroid preparations relieve pain similarly over the long term. Therefore, decisions about which preparation to use are often arbitrary. We evaluated methylprednisolone acetate and a combination of betamethasone dipropionate and betamethasone sodium phosphate for short-term pain and the predictive value of short-term pain.

Eighty-five patients were injected in prospective double-blind randomized fashion. Pain was evaluated by visual analog scale (1 = no pain, 10 = severe pain) at baseline, 3 days, and 3 weeks.

No patient had joint pain immediately after injection. Three days after injection, mean (SD) pain levels were 5.1 (2.9) for methylprednisolone and 5.2 (2.6) for betamethasone (*P* = .97); 3 weeks after injection, they were 4.0 (2.8) and 3.7 (2.5), respectively (P = .57). Short-term pain increased from baseline for both preparations and decreased from 3 days to 3 weeks. Pain at 3 days and 3 weeks was positively correlated.

This study does not support a difference in short-term pain between preparations. The significant correlation between short- and long-term pain may justify early decisions regarding treatment, especially in patients with high levels of initial pain.

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Am J Orthop. 2007;36(1): 128-131.

The various steroid preparations used for injection into and around joints for a variety of indications, including inflammatory arthritis and osteoarthritis, have all been shown to be effective in reducing pain.[1-7] In a well-known clinical phenomenon, pain increases shortly after injection and improves subsequently. The predictive value of this short-term pain for the long-term outcome has not been studied, to the best of our knowledge. In searching the literature, we found mention of only a related phenomenon, crystal synovitis, induced by intra-articular injection of triamcinolone hexacetonide, which has been described but has not received much attention.[7,8]

The purpose of this prospective double-blind study was to compare the short-term effect of 2 types of commonly used injectable steroids—methylprednisolone acetate and a combination of betamethasone dipropionate and betamethasone sodium phosphate—specifically for short-term postinjection pain and its correlation with pain 3 weeks after injection.

Materials and Methods

Eighty-five consecutive patients having shoulder and knee pathology and considered clinically suitable for steroid injection to the joint were recruited for this study. Patients were from a primary care orthopedic clinic and were seen over 6 months. No patient who was approached refused to enroll in the study. Diagnoses included synovitis from osteoarthritis and rotator cuff pathology. Exclusion criteria were history of bleeding diathesis, current anticoagulant treatment, any suspected infection, local or systemic injection of corticosteroid or glucosaminoglycan within the past 3 months, and inaccessibility by phone. All patients consented to participate after the study was fully discussed. Randomization was performed with use of closed envelopes that were seen only by the nurse who prepared the injection; only then was the syringe transferred to the participating doctor.

All patients were examined and injected by 3 experienced orthopedic surgeons. Preparations were injected in a double-blind fashion; neither the surgeon nor the patient was aware of which preparation was injected. Two preparations were used: methylprednisolone acetate 40 mg/mL (Depomedrol) and betamethasone dipropionate 5 mg plus betamethasone sodium phosphate 2 mg/mL (Diprospan). To both preparations, 2 mL of lidocaine 2% were added in the same syringe. The shoulder was injected with 1 mL of either methylprednisolone acetate or the combination

of betamethasone dipropionate and betamethasone sodium phosphate with 2 mL of lidocaine. The knee was injected with 2 mL of either preparation plus 2 mL of lidocaine. With sterile technique, the knees were injected from a lateral suprapatellar approach and the shoulders from a lateral approach. No aspiration was done before injection.

An independent observer gave all patients instructions on how to use the visual analog scale (VAS) and evaluated them immediately after injection, 3 days after injection, and 3 weeks after injection. Pain evaluation was done immediately after injection—validating a common baseline of no pain for all patients with passive and active movement of the joint. We believe this immediate pain relief to be important in establishing correct placement of steroids. Three days after injection, patients were interviewed over the phone to assess short-term pain on the VAS. Three weeks after injection, patients were reassessed for pain. On the VAS, one end of a 100-mm line indicated no pain, and the other end indicated severe pain. Patients were to place an X along the line to indicate present pain intensity.[9] They were also asked specifically about adverse effects. Any complications were noted.

JMP software (version 4.0.4; SAS Institute, Cary, NC) was used to perform statistical analysis. The nonparametric rank-sum Mann-Whitney test was used to compare pain levels. The association between day 3 and week 3 measurements was assessed with the Spearman correlation test. Linear regression was used to calculate the relationship between age and pain level. Significance was set at $P<.05$.

Results

Eighty-five patients (49 women, 36 men) were included in the study. Mean age was 65.6 years (SD, 12.1 years). Fifty-nine shoulders (69.4%) and 26 (30.6%) knees were injected. Forty-six patients received an injection of methylprednisolone (54.1%), and 39 patients received an injection of betamethasone (45.9%). No patient had joint pain immediately after injection. No injection-site pain was reported.

At 3 days, mean pain levels (1 = no pain, 10 = severe pain) were 5.1 (SD, 2.9; median, 5.0) for the entire population, 5.1 (3.1; median, 4.0) for the methylprednisolone subgroup, and 5.2 (2.6; median, 5.0) for the betamethasone subgroup ($P = .85$).

At 3 weeks, pain was reassessed with the VAS. Mean pain levels were 3.8 (SD, 2.6; median, 3.0) for the entire population, 4.0 (2.8; median, 3.0) for the methylprednisolone subgroup, and 3.7 (2.5; median 3.0) for the betamethasone subgroup ($P = .56$).

Pain levels calculated separately for knees and shoulders were not significantly different. At 3 days, mean pain levels were 5.2 (2.8; median, 5.0) for knees and 5.1 (2.9; median, 5.0) for shoulders ($P = .89$); at 3 weeks, they were 3.3 (2.2; median, 2.5) for knees and 4.1 (2.8; median, 3.0) for shoulders ($P = .25$).

A significant and positive correlation was found between pain levels at 3 days and 3 weeks for the entire population (Spearman $r = .57$, $P<.0001$) and similarly for the methylprednisolone ($r = .55$, $P<.0001$) and betamethasone ($r = .61$, $P<.0001$) subgroups (Table).

Table. Positive Correlation Between Pain at 3 Days and at 3 Weeks.

Injected Steroid	Pain (VAS*) 3 days	Pain (VAS) 3 weeks	*P*
Betamethasone	5.2	3.7	<0.0001
Methylprednisolone	5.1	4.0	<0.0001
All	5.1	3.9	<0.0001

*Visual Analog Scale: 1=no pain; 10=severe pain
P≤.05=significant

Effect of High or Low Pain Level. To assess the effect of pain level on the correlation, we divided all patients with pain into a high-level pain subgroup (>5 rating) and a low-level pain subgroup (≤ 5 rating). No significant correlation was found between the entire group and the low-pain subgroup at 3 days or 3 weeks ($r = .14$, $P = .31$), but a significant correlation was found for the high-pain subgroup ($r = .32$, $P = .07$). Further dividing patients according to preparation, we found no significant correlations: low-pain methylprednisolone subgroup ($r = .24$, $P = .22$), high-pain methylprednisolone subgroup ($r = .39$, $P = .10$), low-pain betamethasone subgroup ($r = .07$, $P = .74$), high-pain betamethasone subgroup ($r = .29$, $P = .29$).

For the entire group, the mean difference in pain levels between 3 days and 3 weeks (–1.3) was significant ($P<.002$). For the methylprednisolone subgroup, the mean difference was –1.1 ($P = .08$); for the betamethasone subgroup, the mean difference was –1.5 ($P<.008$).

No significant difference was found between the 2 preparation groups in terms of reduction in pain between 3 days and 3 weeks ($P = .52$).

Effect of Age. Age did not significantly affect short- or long-term pain in the group as a whole. At 3 days, r^2 was .01 ($P = .39$); at 3 weeks, r^2 was .002 ($P = .67$). At 3 days, there was a significant negative correlation between age and short-term pain for the methylprednisolone group ($r^2 = –.13$, $P = .015$); at 3 weeks, this correlation was still negative but not statistically significant ($r^2 = –.07$, $P = .07$). For the betamethasone group, no significant correlation was found, though the trend was toward a positive correlation at 3 days ($r^2 = .09$, $P = .05$) and 3 weeks ($r^2 = .07$, $P = .09$).

Adverse Effects. Reported adverse effects were increased blood sugar values after injection (in 2 patients with diabetes). No other side effect was found.

Discussion

Local steroid injections are used in different joints for a wide variety of indications, including osteoarthritis, rheumatoid arthritis,[1,10] and postarthroscopic surgery.[11,12] In comparisons, all preparations have shown pain relief for various periods after injection.[13-16] Longer-term effects (eg,

improvement in function and influence on joint pathology) have been more difficult to assess.[5,12,17,18]

It is hypothesized that less soluble solutions are more likely to be painful over the short term, as they may take longer to be absorbed. This phenomenon was not previously examined.

The steroid combination of betamethasone dipropionate and betamethasone sodium phosphate is used for local injection into and around joints and tendons. The betamethasone dipropionate component is absorbed slowly; the betamethasone sodium phosphate component is absorbed more quickly.[13] This combination has been shown to be as effective as other injectable steroids for pain relief and functional improvement over the long term[19] but, being more "soluble," has been considered empirically less effective for short-term pain. Methylprednisolone, another potent steroid widely used for injection into and around joints, is absorbed more slowly.[12,20-22]

According to our literature search, only Valtonen[23] compared the treatment efficacy of betamethasone and methylprednisolone for frozen shoulder and supraspinatus tendonitis. Betamethasone was found to be more effective and to have shorter onset. However, failures were excluded from analysis, and the study did not evaluate the relationship of short-term and longer-term pain. A recent laboratory study examined the effect of these 2 medications on rat supraspinatus tendon and found that both had a similar deleterious effect when compared with saline.[24]

In our study, we found an increase in short-term pain from the immediate postinjection level with both medications in all patients. There was a significant pain-level reduction between 3 days and 3 weeks in both preparation groups. At 3 days, mean pain levels were 5.1 (SD, 2.9; median, 5.0) for the entire population, 5.1 (3.1) for the methylprednisolone subgroup, and 5.2 (2.6) for the betamethasone subgroup (P = .97). At 3 weeks, they were 3.8 (SD, 2.6; median, 3.0) for the entire population, 4.0 (2.8) for the methylprednisolone subgroup, and 3.7 (2.5) for the betamethasone subgroup (P = .57). These results are similar to those from previous studies on cortisone injections.[12,18,21,25,26]

We found a significant positive correlation between short-term pain and pain at 3 weeks for both preparations. There was no significant difference between the 2 preparations with respect to short-term pain and pain at 3 weeks—which does not support theories regarding differences between the 2 preparations in relief of short-term pain and pain relief at 3 weeks (intermediate). Although we did not find any significant difference between injectable betamethasone or methylprednisolone, it is difficult to differentiate between the actual increase in pain caused by injection and the amount of the pain contributed by the preceding type and duration of pain. There was no evidence that the 2 preparation types differ in their effects on pain—a finding that should be further evaluated.

For all patients, the short-term pain level was higher than the pain level at 3 weeks—supporting the observation that there is some increased pain in the immediate postinjection period. This "short-term" pain was a good predictor for pain level at 3 weeks, especially in the high-level pain group (pain analog scale, >5). Clinically, this short-term pain may then be used in deciding whether a second injection is warranted or another form of treatment should be used before assessment at 3 to 4 weeks.

In this study, we studied injection to both knees and shoulders. There was no significant difference between injection to the shoulders or knees in terms of short-term pain or pain level at 3 weeks.

Age was found to significantly affect short-term pain only in the betamethasone subgroup. This group's correlation was negative. Thus, older patients had lower short-term pain—a finding that warrants further evaluation.

This study was not designed to evaluate the long-term efficacy of these preparations, and therefore we cannot draw conclusions regarding their long-term efficacy.

Short-term pain was evaluated on the same VAS but by phone interview after 3 days. Theoretically, this type of contact may have influenced the results, though the scale had been shown and explained to the patient at initial evaluation.

We found a significant reduction in pain level between 3 days and 3 weeks after injection of either betamethasone or methylprednisolone. Pain level at 3 days was highly correlated with pain level at 3 weeks mainly in patients with high initial pain. This finding might justify earlier decisions regarding additional treatment in patients with high levels of short-term pain after injection.

Intra-articular injection of steroids carries with it the risk for infection and possible damage to cartilage.[27-29] We inject steroids in arthritic joints as a palliative measure because in our experience pain can be improved for long periods. Often there is no good correlation between pain and extent of cartilage destruction—justification for a trial injection before operative intervention.

Conclusions

From a practical perspective, this study validates our belief that initial relief of postinjection pain is followed by a temporary increase in pain within several days and then a relative decrease in pain after several weeks. Patients should be prepared for these developments. Although the literature has not included descriptions of this sequence of events, we always explain it to our patients. This study also points out that short-term pain level is an important indicator of injection success and that patients can anticipate a further decline in pain over several subsequent weeks.

Authors' Disclosure Statement and Acknowledgments

The authors report no actual or potential conflict of interest in relation to this article.

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