Particulate or Non-Particulate Steroids for Lumbar Transforaminal Injections

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Myth: Particulate steroids are more effective than non-particulate steroids and, therefore, should be preferred for routine use in lumbar transforaminal injections, despite a greater risk profile.

Fact: All particulate corticosteroid preparations have been implicated in rare cases of paraplegia, whereas no definitive evidence exists of paraplegia resulting from injection of non-particulate steroids. Studies directly comparing the effectiveness of particulate and non-particulate steroids largely show no differences between the two, with respect to relief of pain, restoration of function, or rate of spine surgery. There is no evidence-based rationale for routine use of particulate steroids in lumbar transforaminal injections, given the increased risk of paraplegia.

Transforaminal injection of steroids (TFIS) is an effective treatment for lumbar radicular pain [1], but it is associated with a risk of ischemic neurologic injury [2]. The mechanism of injury is believed to be inadvertent intra-arterial injection of particulate corticosteroid resulting in embolic spinal cord ischemia and paraplegia. All particulate corticosteroid preparations (i.e., triamcinolone, betamethasone acetate, and methylprednisolone) have been implicated in published case reports of paraplegia [3-10]. One case of conus medullaris infarction of unclear mechanism has been reported in which particulate steroid was not included in the injectate [11].

Particles in these steroid preparations are either larger than red blood cells (RBC) or form aggregates larger than red blood cells [12]. In a mouse model, several particulate steroids have also been shown to induce aggregates of spiculated RBCs which stop arteriole blood flow [13]. Additionally, other animal studies have also shown CNS infarction after intra-arterial injection of particulate steroids [14]. On the other hand, dexamethasone, with particles smaller than RBCs on microscopic evaluation, has not been associated with any reports of paraplegia, and has not created neurologic complications in animal studies.

In recently published safety guidelines, the Multi-Society Pain Workgroup (MPW) unanimously recommended that only the non-particulate steroid dexamethasone, should be used for therapeutic cervical transforaminal epidural steroid injections [2]. The MPW also recommended that dexamethasone be initially used in lumbar TFIS [2]. Despite the convincing evidence that non-particulate steroids have a stronger safety profile, there is still debate as to whether this is potentially offset by the possible better effectiveness of particulate corticosteroids compared to non-particulate formulations. In this regard, the literature speaks otherwise.

Literature

A poster presentation reported that patients treated with triamcinolone achieved greater reductions in mean pain scores than those treated with dexamethasone [15]. In contrast, a letter declared that improvements in pain were no different when particulate or non-particulate steroids were used [16]. For lack of further detailed information, neither of these reports provides compelling evidence, but they reflect the countervailing views.

The first study published in full, reported that triamcinolone (40mg) achieved greater decreases in mean pain scores than did dexamethasone (7.5 mg), but no significant differences in disability scores were found [17]. A subsequent re-evaluation of the data on pain scores showed no significant difference in success rates between the two groups [18].

A retrospective study of 2,634 patients compared the success rates of TFIS using dexamethasone (10 mg) or triamcinolone (80 mg) or betamethasone (12 mg) [19]. For success defined as at least 50% relief of pain coupled with at least 40% improvement on the Roland Morris Disability Questionnaire, success rates were not significantly different between groups. In a subgroup analysis of patients with symptoms lasting less than 3 months, non-inferiority of dexamethasone was not
demonstrated for achieving >50% pain reduction, but dexamethasone was superior to particulate steroid for achieving >40% improvement in disability.

In a randomized, double-blind, multi-center, prospective study comparing the efficacy of TFIS using 10 mg dexamethasone versus 40 mg triamcinolone for lumbosacral radicular pain due to disc herniation, no significant differences were found for relief of pain, functional improvement, or rates of surgery [20]. However, with respect to numbers of injections used, fewer patients treated with triamcinolone (1/37; 3%) required three injections than those treated with dexamethasone (7/41; 17%), although these proportions are not significantly different.

A double-blind study of 56 patients, randomized to receive either 7.5 mg dexamethasone or 6.0 mg betamethasone found no significant differences between mean pain scores at all follow-up points [21]. At the 6-month follow-up, there was a mean improvement in Oswestry Disability Index at the limit of statistical significance in favor of dexamethasone (p = 0.05, multivariate adjusted p <0.003). The limited categorical data presented were: at 3 months, 59% (95% CI 39% - 76%) of patients achieved at least 50% relief on visual analog scale (VAS) in the dexamethasone group, compared with only 33% (95% CI 17% to 54%) in the betamethasone group. The overlapping confidence intervals preclude concluding that dexamethasone was more often successful, but the important feature is that dexamethasone was not inferior to betamethasone. However, this study could be an unfair test of particulate steroids, for there is evidence that betamethasone is less effective than triamcinolone [22].

A study of patients treated on separate occasions with either 10 mg dexamethasone or 40 mg triamcinolone reported that a significantly greater proportion rated triamcinolone as better or much better than dexamethasone [23], but methodological flaws limit the utility of this study. The injections used were heterogeneous including interlaminar, caudal, and transforaminal routes. The order of administration of agents was not randomized: all patients first received triamcinolone; consequently, the agents were not fairly compared for providing the first period of relief as opposed to reinstating relief. Finally, satisfaction data regarding both the first and second injection were collected by phone call follow-up at the same time, thereby introducing vulnerability to recall bias.

Conclusion

The literature provides no evidence that particulate steroids are more often effective than non-particulate steroids when used for lumbar TFIS. Particulate steroids may [17] or may not [20,21] achieve greater reductions in mean pain scores, but are no more effective [17,20,21] or are less effective [19] than dexamethasone for improving disability. Particulate steroids do not achieve greater success rates for relieving pain, improving disability, or both outcomes combined [18 – 21]. In patients with acute radicular pain, triamcinolone might be slightly more effective than dexamethasone for the relief of pain, but dexamethasone is superior for improving disability [19]. In a minority of patients, the beneficial effects of dexamethasone may not last as long as those of triamcinolone, and need to be reinstated by repeat injection [20].

This evidence supports the guidelines of the MPW that dexamethasone should be the agent of first choice for lumbar TFIS [2]. These guidelines permit the use of triamcinolone, for example when dexamethasone fails to provide relief, but that application has not been evaluated in the literature.

Postscript

A recent publication demonstrated that the combination of dexamethasone 1 ml (both 4mg/ml and 10 mg/ml concentrations) with 1 ml ropivacaine 0.75% results in almost instantaneous formation of crystals large enough to act as emboli [24]. Crystallization was not seen when dexamethasone was mixed with lidocaine or bupivacaine. Given this finding, we recommend against use of ropivacaine as the anesthetic agent when performing lumbar TFIS with dexamethasone.
References