Is there Clinical Improvement Associated with Saline Injection for Discogenic Low Back Pain: Comparison of RCT Outcomes

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Disclosures:

Introduction: Recently, several multicenter clinical trials studying the effect of biologic substances or cell-based injections on lumbar intervertebral disc repair are near completion. These studies all included a placebo injection with saline as a control. These studies were early, randomized, double blinded, and prospective. Their intent was to investigate novel treatment options for intervertebral disc repair. The findings of these studies highlight a possible reduction in pain and disability related to the saline injection. The purpose of this analysis was to evaluate saline related outcomes from multiple intervertebral disc injection studies all conducted at one institution.

Methods: A post hoc comparison was performed using data derived from four similar studies conducted at a single site that were prospective, randomized controlled, and double-blinded. Standard across the studies (A, B, C, D), patients were only included if they had symptomatic disc disease at lumbar levels of L1 to L5/S1, had a positive provocative discography, and failed at least 3 months of nonoperative treatment. Patients (males & females) ranged from 18 to 65 years of age, and were randomized into placebo (saline) or treatment (investigational substance) intervertebral disc injection groups. Self-administered questionnaires including the Visual Analog Scale for back/buttock pain (VAS, 100-mm line, with ‘No Pain’ indicated at the left of the horizontal scale and ‘Most Severe Pain’ at the right end of the scale) and the Oswestry Disability Index (ODI, a likert type scale calculating functional disability) for low back pain, along with surgeon administered physical exam were completed at pre-treatment visit (pretx), and at least at 3, 6, 12 months post injection. Only study B utilized the Roland-Morris Disability Questionnaire instead of the Oswestry Questionnaire. For all studies, side effects and adverse events were systematically collected throughout as per clinical trial standard operating procedures at the site. Statistical analysis included % change variable calculated as: post injection score minus pretx score divided by pretx score per individual patient. Averages of these per patient change scores were calculated for reporting overall improvement. Multiple variable analysis of variance (ANOVA) was applied to specific outcome score measures with a grouping factor for treatment (saline versus investigational treatment) and a repeated factor for outcome score over time (i.e. 12mo vs. pretx) controlling for age, gender, and specific study. Gender and age were evaluated then controlled for in the overall analysis.

Results: Control Variables: Gender and age were controlled in the overall analysis. There was a higher percentage of males enrolled across the four studies (61.5% A, 61.5% B, 60% C, 94% D) with 74% males (37/50) in the combined analysis.

VAS: Males reported slightly less VAS improvement as well as less VAS pain than females preoperatively; This difference was not significant. (Males: 66.8mm VAS pain at pretx, 39.6mm VAS pain at 12 months post treatment, with a 41.5% difference. Females: 81.3mm VAS pain at pretx, 32.4mm VAS pain with a 40.6% difference at 12 months post treatment). Age was only related to VAS at 12 months (p< 0.04, r=-0.31, 9.6% of common variability) Across the studies, by 12 months, there was 58.5% less VAS pain for saline injected patients compared to 36.6% less pain for investigational treatment injected patients (S: 20.4 mm vs I:37.7mm p<0.01, ANOVA controlling for age and gender). Additionally, across the studies there was a statistically significant main effect of decrease in VAS pain for both the investigational treatment or saline injected patients (p<0.004 at 3 months; p<0.007 at 6 months; p<0.0001, 12 months compared to pretx).

Discussion: An intervertebral disc injection regimen of saline may offer patients a chance for some pain resolution and decreased disability, or may merely introduce less substance reaction and injection trauma. Noting the 50% or greater improvement observed for saline injected patients in this study provides a potentially higher threshold and means to define the MCID for injection type treatments. Independent from the underlying reason for the observation herein, future injection studies now have a high baseline improvement threshold. A more thorough understanding of the “Saline Effect” is needed. Future directions include testing for this effect in an independent sample, with more patients, and a longer follow-up period. All are needed to fully differentiate between a placebo effect and a true saline effect. Sham procedures will be included in future clinical injection studies.
Significance: Although the intent was to investigate novel treatment options for intervertebral disc repair, results from these trials have elucidated a possible saline effect. Further research is needed to determine a possible mechanism and to finally establish this saline-associated improvement as a threshold for novel treatments to improve upon.

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References: na

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