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INTERVENTIONAL

Pain reduction after lumbar epidural injections using particulate versus non-particulate steroids: intensity of the baseline pain matters

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Abstract

Objectives To compare pain relief after CT-guided lumbar epidural steroid injections (ESI) using particulate (triamcinolone) and non-particulate (dexamethasone) steroids, and to explore factors affecting the effectiveness of both steroid types.

Methods This retrospective observational study included 806 patients with lumbar radiculopathy and corresponding MRI or CT abnormalities of the lumbar spine, who were matched using the propensity score method, yielding two cohorts of 209 patients each. Pain intensity was evaluated prior to the procedure using a pain numerical rating scale (NRS) with range 0–10. Reevaluation took place 1 day and 4 weeks post-injection. Logistic regression analysis and cubic splines applied to generalized additive models were implemented to assess the differences in pain reduction after ESI in the analyzed patient groups.

Results Four weeks post-injection, the overall chance of ≥ 50% pain reduction was lower in the dexamethasone group than that in the triamcinolone group (odds ratio [OR] = 0.55; $p < 0.012$). In the dexamethasone cohort, the intensity of baseline pain and the presence of a herniated intervertebral disc in the infiltrated segment were both significant and independent predictors of ≥ 50% pain relief. Patients with baseline NRS score ≥ 7 points had markedly less chance of ≥ 50% pain relief than patients with NRS score < 7 (OR = 0.53; $p < 0.032$), whereas disc herniation increased the chances more than twofold (OR = 2.29; $p < 0.044$). There was no significant correlation between the effectiveness of triamcinolone and any analyzed concomitant variables.

Conclusions Triamcinolone was superior for lumbar radiculopathy of severe intensity. For mild to moderate pain, no benefit of using triamcinolone over dexamethasone was found. The effectiveness of dexamethasone was lower for stenotic spinal lesions than for disc herniation.

Key Points

- *Triamcinolone is superior to dexamethasone for epidural treatment of severe lumbar radiculopathy.*
- *For mild to moderate pain, dexamethasone could be equally effective.*
- *Dexamethasone reduces pain caused by disc herniation much better than it does to pain caused by fixed stenotic spinal lesions.*

Keywords Pain · Radiculopathy · Spine · Epidural injections · Steroids

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Abbreviations

CI	Confidence interval
ESI	Epidural steroid injection
FDA	The Food and Drug Administration
IL	Interlaminar
NRS	Numerical rating scale
OR	Odds ratio
PSM	Propensity score matching
SD	Standard deviation
TF	Transforaminal

Introduction

Since the 1990s, the number of epidural steroid injections (ESI) has risen dramatically, and nowadays they constitute a widely used treatment for back and radicular pain [1–4]. Due to slower absorption of microcrystalline suspensions of particulate steroids than solutions of their non-particulate counterparts [5], particulate steroids had been considered more potent formulations and preferentially chosen by interventional pain physicians [6]. With the increasing numbers of procedures performed, a growing body of reports has described neurologic complications after ESI. Between 1997 and 2014, 90 serious neurologic events associated with ESI were submitted to the Food and Drug Administration (FDA) Adverse Event Reporting System. Some of the potential mechanisms of these complications were not related to steroids per se; however, all the cases involving permanent disability or death occurred after injection of a steroid suspension [6].

In April 2014, the FDA published a safety announcement with a warning that injection of corticosteroids into the epidural space of the spine may result in rare but serious neurologic adverse events including "loss of vision, stroke, paralysis, and death," and they also mentioned that "effectiveness and safety of epidural administration of corticosteroids have not been established, and FDA has not approved corticosteroids for this use" [7]. The FDA policy has been subject to substantial criticism [8, 9]. After an intensive investigation in 2015, a collaboration between the FDA Safe Use Initiative, an expert multidisciplinary working group, and representatives of 13 specialty societies issued safety guidelines aimed at reducing the risk of severe neurologic complications arising from ESI. Their recommendations included a statement that in lumbar transforaminal (TF) ESI, a non-particulate steroid should be used for the initial injection; however, they unanimously agreed that a particulate steroid might be considered in this setting, for example, if the initial treatment with a non-particulate steroid had failed. Furthermore, the authors stated that the use of particulate steroids in lumbar interlaminar (IL) injections is acceptable, because there is little risk of intra-arterial injection by this administration route [10]. Finally, a statement from the FDA regarding the risk of serious neurologic events after ESI was issued in December 2015: "Although many experts believe the risk is greatest with suspensions, the available data do not support comparative safety labeling implying that solutions are safer. Such labeling could encourage practitioners to use solutions, even though their relative safety and effectiveness remain an open question" [6]. This cautious approach of the FDA seems to be substantiated by a recently published case report of spinal cord infarction after lumbar TF-ESI using dexamethasone clearly showing that devastating neurologic complications can occur irrespective of the injected steroid type [11].

Safety concerns regarding particulate steroids resulted in a steady increase in utilization of steroid solutions for epidural injections [6], although comparative studies of the efficacy of both steroid preparations have yielded inconsistent results in terms of pain reduction. Superiority of particulate steroids was reported by several studies [12–16], while others found no significant differences between the two steroid types [17–24]. Only one study reported a significantly better reduction in mean pain score after dexamethasone use [21].

Therefore, we set out to compare pain relief after lumbar ESI using both types of steroids and to explore whether their relative effectiveness could differ for specific patient groups in ordinary clinical settings.

Materials and methods

Patient population

This single-center retrospective observational study of prospectively collected data was approved by a local institutional review board. Between March 2005 and December 2014 in the Institute of Medical Radiology of the Solothurn Hospitals (Solothurn, Switzerland), 1140 consecutive lumbar ESI were performed, including 746 using triamcinolone (from March 2005 to May 2009) and 394 using dexamethasone (from January 2010 to December 2014). After reviewing the clinical records, we excluded from further analysis 22 injections without baseline pain score assessment as well as 311 repeated interventions on the same patients and two interventions with simultaneous lumbar facet joint and sacroiliac joint injections. Consequently, the study finally included 806 participants with lumbar radiculopathy and abnormalities on magnetic resonance imaging (MRI) or computed tomography (CT) scans corresponding to nerve root compression or irritation (Fig. 1).

Of 523 subjects who received triamcinolone and 283 who received dexamethasone, 446 were female and 360 were male (mean age, 60.1 ± 16.3 years). The mean baseline pain numerical rating scale (NRS) score was 6.5 ± 2.2. In total, 777 patients received single-level injections, and 29 received two-level injections. The injection route was interlaminar in 490 patients (60.8%), transforaminal in 314 (39%), and combined in 2 (0.2%). All patients were referred to our department by external physicians after failure of conservative treatment.

Procedures

The epidural interventions were performed on an outpatient basis, using three different CT devices: prior to August 2008, a 4-slice CT scanner (GE Lightspeed; GE Healthcare); from September 2008 to February 2013, a 64-slice CT scanner (Toshiba Aquilion 64; Toshiba Medical Systems Europe);

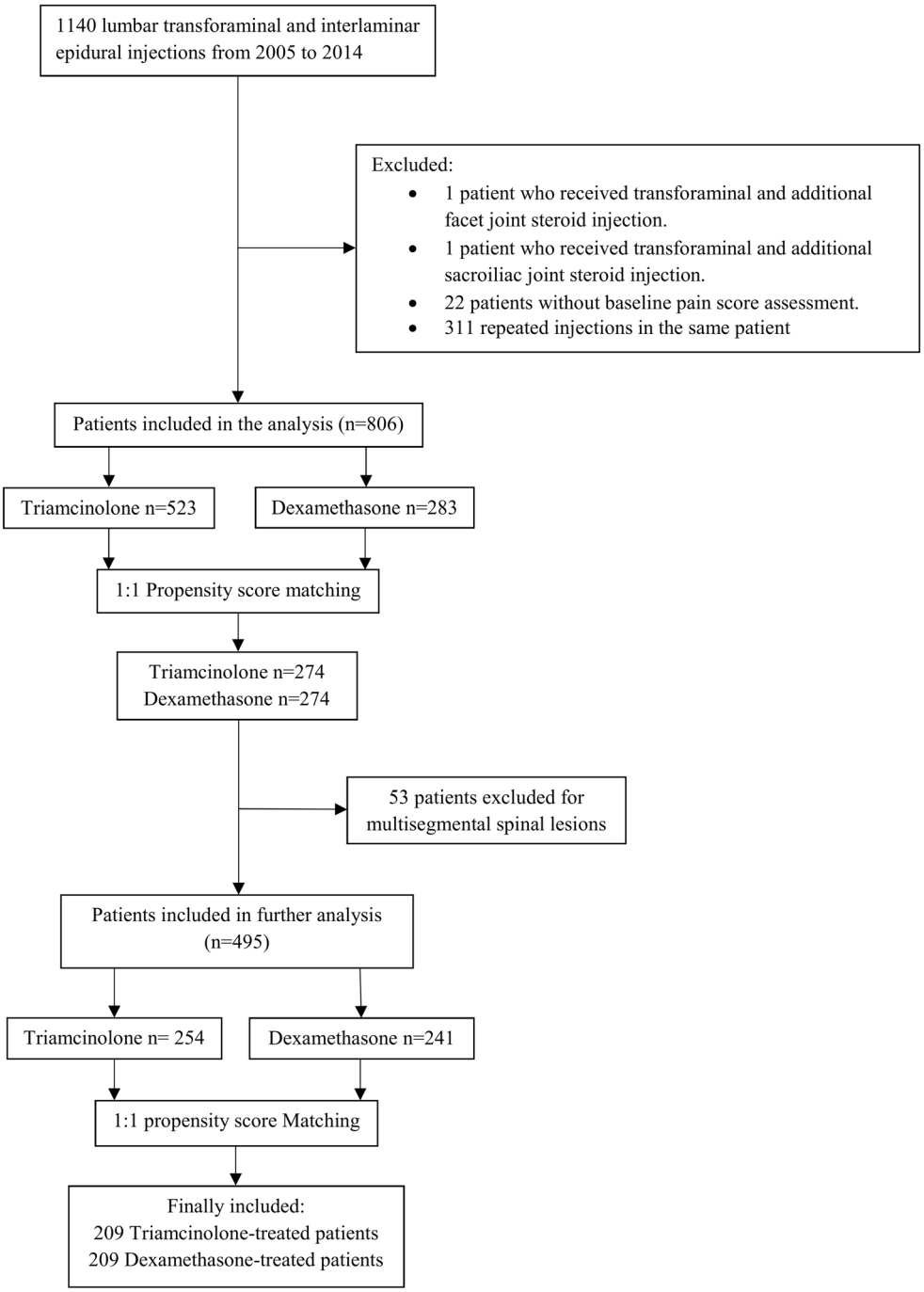

Fig. 1 Flow chart depicting the process of patient selection

and from February 2013, a 128-slice system (Toshiba Aquilion CXL 128; Toshiba Medical Systems Europe). Each patient signed a written informed consent form before implementation of the intervention. The procedures were performed in the prone position on the CT table, using a standardized injection technique, by five interventional radiologists from our department. After obtaining a preliminary scan for planning the intervention and localizing the target area, the needle entry site was marked on the skin, followed by skin disinfection, sterile draping of the puncture area, and local anesthesia with 2% lidocaine hydrochloride. Subsequently, a Spinocan® (22 Ga.) spinal needle was cautiously inserted into the planned region of infiltration. The position of the needle tip was controlled by a CT scan and by careful aspiration. Every injection used a steroid preparation—40 mg (1 mL) of triamcinolone acetonide (Kenacort A 40, Dermapharm) or 4 mg (1 mL) of dexamethasone sodium phosphate (Mephameson Inj Lös 4 mg/mL, Mepha Pharma)—together

with a mixture of 1.5 mL of 0.5% bupivacaine hydrochloride (Carbostesin hyperbar Inj Lös 0.5%, Aspen Pharma), 0.5 mL of 2% lidocaine hydrochloride (Rapidocain 2%, Sintetica), and approximately 0.75 mL of contrast medium (Iopamiro 300, 300 mg of iodine per milliliter, Bracco).

After injection of approximately half of the mixture of bupivacaine, lidocaine, and radiopaque contrast agent, proper epidural distribution of the injectate was verified with a CT scan. Subsequently, the rest of the drug mixture was injected, combined with the corticosteroid preparation. A final CT scan was acquired following removal of the spinal needle.

No serious complications were observed over the entire study period. Only infrequent, minor, post-procedure side effects, such as skin rash, nausea, vomiting, vertigo, and headache, were reported.

Outcome measurement

The patients were asked by a trained radiology technologist immediately prior to the procedure to describe the pain intensity using pain NRS 0–10, where zero corresponds to no pain, and 10 to the worst imaginable pain. The change in pain score was assessed directly after the intervention. Reevaluation of the pain score by a standardized follow-up telephone interview took place 1 day and 4 weeks after the procedure. We categorized pain intensity as mild, moderate, and severe, for NRS pain levels 1–3, 4–6, and 7–10, respectively.

Additionally, we calculated the percentage of subjects achieving at most mild pain 4 weeks post-injection.

Data analysis

Statistical analysis was performed using SAS 9.4 software (SAS Institute Inc.) with the significance level set to 0.05. Propensity score matching (PSM) of the treatment cohorts was applied to minimize confounding effects. The PSM was accomplished in two steps. In the first phase, 806 patients were matched with respect to age, sex, baseline pain score, injection approach, and the number of the infiltrated segments. The nearest neighbor matching method without replacement was applied, with matching ratio 1:1, yielding 274 participants in each treatment group. Subsequently, data concerning imaging abnormalities of the lumbar spine and previous spinal surgery in the infiltrated segments of the matched patients were retrieved from their clinical records. To further reduce potentially confounding effects, 53 individuals in whom spine lesions in lumbar segments other than those infiltrated might have contributed to their pain symptoms were excluded from further analysis.

After performing the Mann-Whitney-Wilcoxon test and Fisher's exact test, statistical differences between the treatment groups in the incidence of foraminal stenosis were revealed. A second PSM was performed with respect to this parameter, yielding treatment cohorts of 209 patients each, without significant differences in any of the analyzed variables (Table 1). Appropriate covariate balance between the treatment groups was confirmed by calculating standardized difference scores of < 0.1 (each).

Subsequently, the main analysis of intergroup differences was performed using logistic regression to examine associations of the steroid type and other concomitant variables with the chances of achieving ≥ 50 pain reduction. The strength of this association was expressed as odds ratios (OR) with 95% confidence intervals (CI). Non-linear correlations of continuous variables (baseline pain intensity and age) with the chances for ≥ 50% pain reduction were also assessed using cubic splines applied to generalized additive models.

Results

One day post-injection, ≥ 50% pain relief was achieved in 58.4% of patients from the triamcinolone group and 56.9% of patients from the dexamethasone group ($p = 0.839$), with mean NRS score reductions of 3.4 and 3.2, respectively (standard deviation (SD) = 2.8 and 2.6, respectively).

Four weeks post-treatment, ≥ 50% pain reduction was observed in 49.2% of triamcinolone-treated patients and in 34.9% of dexamethasone-treated patients ($p = 0.012$). The mean NRS score reductions were 2.6 (±3.2) and 1.9 (±2.7), while the medians and interquartile ranges were 3 (0–5) and 1 (0–3.5) ($p < 0.007$) for the triamcinolone and dexamethasone groups, respectively. The chances for ≥ 50% pain reduction 4 weeks post-treatment were almost twofold lower in the

Table 1 Comparison of dexamethasone- and triamcinolone-treated patients after propensity score matching

	Dexamethasone ($n = 209$)	Triamcinolone ($n = 209$)	$p^{\#}$
Baseline NRS (± SD)	6.6 ± 2.3	6.6 ± 2.2	0.983
Age	60.6 ± 16.3	62.2 ± 16.1	0.311
Sex—female	59.3%	56.5%	0.620
Interlaminar approach	60.3%	59.8%	1.000
Two-level injection	1.4%	1.4%	1.000
Disc herniation	79.0%	77.0%	0.723
Foraminal stenosis	17.2%	17.2%	1.000
Spinal canal stenosis	23.4%	26.3%	0.572
Listhesis	12.0%	12.4%	1.000
Previous spine surgery	4.8%	5.7%	0.827

Data are percentages of patients or mean value ± standard deviation. *NRS*, numerical rating scale for pain. $^{\#}p$ value was provided using the Mann-Whitney-Wilcoxon test and Fisher's exact test for quantitative (baseline NRS score, age) and qualitative variables (other variables), respectively

dexamethasone group compared with the triamcinolone group (OR = 0.55; 95% CI 0.35–0.87; $p < 0.012$) (Table 2).

In the dexamethasone cohort, logistic regression analyses found that increases in baseline pain were associated with decreases in the chances for ≥ 50% pain reduction (OR = 0.86; 95% CI 0.76–0.98; $p < 0.023$; Table 3). Non-linear correlations between the chances for ≥ 50% pain reduction and baseline pain intensity were also tested, revealing significant lowering of chances for ≥ 50% pain reduction with increases in the baseline NRS, and a plateau effect for high pain levels ($p_{nonlin} < 0.005$). The results of this analysis were used to estimate the probability of ≥ 50% pain reduction as a function of the baseline pain score (Fig. 2). This probability was approximately 70% for NRS scores of around 3 points, and steadily decreased through the range of moderate NRS scores. Severe baseline pain (≥ 7 points) was associated with a probability of ≥ 50% pain relief of approximately 30%.

The analysis of qualitative factors showed that in the dexamethasone cohort, the presence of disc herniation in the infiltrated segment was associated with almost 2.5-fold higher chances for ≥ 50% pain relief (OR = 2.46; $p < 0.027$).

Further analysis using forward selection applied to logistic regression revealed that in the dexamethasone cohort, the intensity of baseline pain and the presence of a herniated intervertebral disc in the infiltrated segment were both significant and independent predictors of the chance for ≥ 50% pain relief. Thus, patients with baseline NRS score ≥ 7 points had almost twofold lower chances for ≥ 50% pain relief than patients with NRS score < 7 (OR = 0.53; $p < 0.032$), whereas the presence of disc herniation in the infiltrated segment increased the chances more than twofold (OR = 2.29; $p < 0.044$).

In the triamcinolone-treated patients, no statistically significant linear or non-linear relation was observed between the baseline pain level and the chances for ≥ 50% pain reduction. Furthermore, no statistically significant effects were found for any other of the analyzed concomitant variables (Tables 4 and 5 and Fig. 3).

Four weeks post-injection, ≥ 30% pain relief was achieved in 61.9% and 43.5% of patients from the triamcinolone and dexamethasone groups, respectively ($p < 0.002$). In the dexamethasone cohort, two predictors of ≥ 30% pain relief were found: baseline NRS score and the presence of disc herniation in the infiltrated segment. Thus, the chances of ≥ 30% pain relief were almost twofold lower in patients with baseline NRS score ≥ 7 than in patients with NRS score < 7 (OR = 0.52; $p < 0.022$), and over twofold higher in patients with disc herniation (OR = 2.29; $p < 0.029$).

Four weeks post-injection, the proportions of patients with NRS score ≤ 3 points were 52.3% and 38.7% in the triamcinolone and dexamethasone groups, respectively ($p < 0.015$).

Table 2 Odds of obtaining ≥ 50% pain reduction 4 weeks after treatment in the triamcinolone and dexamethasone groups

	≥ 50% reduction in pain		OR	95% CI	$p^{\#}$
	Yes (%)	No (%)			
Triamcinolone	49.2	50.8	1.00		
Dexamethasone	34.9	65.1	0.55	0.35–0.87	0.012

OR, odds ratio; *95% CI*, 95% confidence interval; $^{\#}p$ value derived from logistic regression analysis

Discussion

Our study found that the overall pain reduction after lumbar ESI was better for triamcinolone than dexamethasone 4 weeks post-injection. However, we observed that the superiority of triamcinolone was dependent on the baseline pain level. With low levels of baseline pain, the proportion of patients achieving ≥ 50% pain reduction was similar for both drugs. In patients with more intense pain, the effectiveness of dexamethasone markedly declined, becoming significantly lower than the effectiveness of triamcinolone for severe pain levels.

Although pain relief of 50% is commonly used as a benchmark of clinical improvement after ESI, there is considerable research indicating that smaller reductions in pain can be clinically relevant [25–32]. Accordingly, we performed a supplemental analysis using a cut-off point of 30%. We found a significantly greater proportion of patients with ≥ 30% pain reduction in the triamcinolone group than in the dexamethasone group, as well as declining effectiveness of dexamethasone for severe pain levels 4 weeks post-injection. These findings, together with the observation of a significantly greater proportion of patients with mild pain levels 4 weeks post-treatment in the triamcinolone group, further corroborate the view that triamcinolone is more effective than dexamethasone in typical clinical practice.

The conclusions of published retrospective comparisons of particulate and non-particulate steroids are disparate. The observational study of 2634 subjects by El-Yahchouchi et al [21] compared the efficacy of dexamethasone, triamcinolone, and betamethasone for lumbar TF-ESI. At a 2-month follow-up, although the proportion of patients with ≥ 50% pain reduction was similar, a slight but significant difference in reduction of the mean NRS score was observed in favor of dexamethasone. Bensler and colleagues, in two retrospective studies [12, 13] that included 531 patients treated with interlaminar lumbar ESI and 494 patients treated with transforaminal lumbar ESI, found that patients receiving triamcinolone had significantly higher NRS change scores than those receiving dexamethasone, at 1 week and 1 month post-treatment. Kim et al [14] conducted a retrospective intra-individual comparison of relative treatment satisfaction in 139 patients who underwent

Table 3 Odds of obtaining ≥ 50% pain reduction 4 weeks after treatment in the dexamethasone group

	≥ 50% reduction in pain		OR	95% CI	$p^{\S}$	$p_{\text{nonlin}}{}^{\&}$
	Yes (%)	No (%)				
Sex						
Male	38.8	61.2	1.00			
Female	32.3	67.7	0.75	0.42–1.34	0.329	
Age	59.2 ± 15.6[#]	61.3 ± 16.6[#]	0.93[$]	0.78–1.10	0.387	0.138
Baseline pain (NRS)	6.1 ± 2.4[#]	6.8 ± 2.2[#]	0.86*	0.76–0.98	*0.023*	*0.005*
Injection approach						
Periradicular	28.9	71.1	1.00			
Interlaminar	38.9	61.1	1.56	0.86–2.84	0.140	
Age distribution						
–50	38.2	61.8	1.00			
51–60	41.3	58.7	1.14	0.51–2.54	0.749	
61–70	38.2	61.8	1.00	0.42–2.42	0.996	
71–80	27.1	72.9	0.60	0.26–1.39	0.234	
81 +	26.9	73.1	0.60	0.21–1.66	0.322	
NRS distribution						
1–3	55.0	45.0	1.00			
4–6	40.5	59.5	0.56	0.20–1.52	0.254	
7–10	27.8	72.2	0.32	0.12–0.84	*0.020*	
Imaging abnormalities						
Disc herniation						
–	20.5	79.5	1.00			
+	38.8	61.2	2.46	1.11–5.47	*0.027*	
Foraminal stenosis						
–	36.4	63.6	1.00			
+	27.8	72.2	0.67	0.30–1.48	0.325	
Spinal canal stenosis						
–	36.3	63.7	1.00			
+	30.6	69.4	0.78	0.39–1.54	0.470	
Listhesis						
–	35.3	64.7	1.00			
+	32.0	68.0	0.86	0.35–2.10	0.744	
Prior spine surgery						
–	35.2	64.8	1.00			
+	30.0	70.0	0.79	0.20–3.15	0.738	

OR, odds ratio; *95% CI*, 95% confidence interval; *NRS*, numerical rating scale for pain; [#] Mean ± SD; [$] OR calculated per 10 years; *OR calculated per 1 point. [§] *p* value derived from logistic regression analysis; [&] *p* value for non-linear effects, derived from generalized additive models. *p* values of 0.05 or lower are indicated in italic font

lumbar ESI using dexamethasone and had previously undergone lumbar ESI using triamcinolone. They reported significant superiority of triamcinolone. A retrospective investigation by Noe and Haynsworth [15] also suggested the superiority of particulate steroids in patients with low back pain. However, this study was limited by a small sample size. A retrospective study by Lee et al [17], in 159 patients, with follow-up within 1 month, reported a non-significant trend toward better effectiveness of triamcinolone than dexamethasone in cervical TF-ESI. Other retrospective studies found no significant differences in the outcomes of particulate and non-particulate steroids in patients with chronic lumbosacral radiculopathy and cervical radiculopathy, respectively [22, 23]. The aforementioned retrospective comparisons were not adjusted for possible confounds caused by imbalances in baseline covariates, which might cause distortion of treatment effect estimates. As opposed to these studies, we ensured that the distribution of known baseline covariates was similar in both treatment groups, and thus reduced the potential for confounding bias.

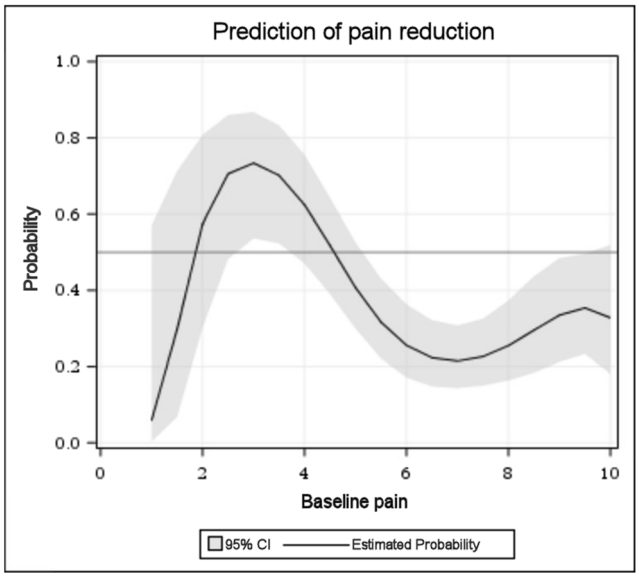

Fig. 2 Probability of ≥ 50% pain reduction 4 weeks post-injection as a function of the baseline pain numerical rating scale score, in the dexamethasone group

The outcomes of previous randomized controlled trials comparing the effectiveness of particulate and non-particulate steroids are inconsistent, as well. The randomized prospective study by Park et al [16], including 106 patients with lumbar radiating pain, showed superiority of triamcinolone over dexamethasone in terms of categorical and mean pain relief 4 weeks post-injection. The double-blind, randomized controlled trial by Kennedy et al [18], examining 78 patients with acute lumbar radicular pain who received TF-ESI, found a trend toward a greater efficacy of triamcinolone than dexamethasone at 2 weeks. However, this trend disappeared at 3-month and 6-month follow-ups. Nonetheless, the dexamethasone group received significantly more injections to achieve the same outcomes, as a possible consequence of its slightly lower efficacy. According to another randomized double-blind study comparing the efficacy of lumbar TF-ESI using dexamethasone and betamethasone in 56 patients, there were no significant differences in mean pain score reduction at the 1-, 3-, and 6-month follow-ups. At 3 months, no significant difference in categorical improvement in pain scores was found, although significance was almost attained in favor of dexamethasone ($p = 0.058$). However, the study was underpowered, with only 46 patients completing 6-month follow-up [24].

Two other randomized trials [19, 20] showed only statistically non-significant trends toward better efficacy of particulate steroids. Additionally, several meeting abstracts suggested better efficacy of particulate steroids [33, 34], and others showed trends toward superior effectiveness [35, 36].

In summary, the majority of previous papers have reported the superiority, or non-significant trends toward superiority, of particulate steroids. Our work illustrated that either an advantage of particulate steroids or non-significant differences in effects of the two types of steroids can be observed, depending on the characteristics of the analyzed patients.

We found that the effectiveness of dexamethasone was substantially higher in patients with a disc herniation in the infiltrated segment than in patients with only fixed stenotic spine lesions (foraminal stenosis or spinal canal stenosis). For triamcinolone, on the other hand, we did not find any significant difference in its effectiveness related to the severity of initial pain, the presence of a herniated intervertebral disc, or any other investigated variable.

Previous investigations comparing the outcomes of ESI in patients with disc herniations and spinal stenosis showed inconsistent results—higher reduction of pain for disc herniation was reported by some authors, while others found non-significant differences between these two patient groups.

The randomized double-blind controlled trial by Tafazal et al [37] demonstrated a trend toward the improved reduction of lumbar radicular pain using methylprednisolone in patients with disc herniation relative to those with spinal stenosis at 3 months post-procedure. Rivest et al [38] showed a significantly better analgesic effect of methylprednisolone for lumbar disc herniation than for spinal stenosis at 2 weeks follow-up. Cyteval et al [39] reported no significant difference in the reduction of lumbar radiculopathy using methylprednisolone between patients with lumbar disc herniation and spinal stenosis at 2 weeks post-injection. An investigation by Ng et al [40] found that methylprednisolone tended to relieve radicular pain better in a lumbar disc herniation group than in a spinal stenosis group ($p = 0.07$). Furthermore, the investigation by Kwon et al [41] on the use of triamcinolone in the performance of cervical interlaminar ESI among patients with neck pain and cervical radiculopathy found significantly better pain reduction for disc herniation than for spinal stenosis at 2 weeks post-injection. On the other hand, the study on cervical transforaminal ESI by Lee et al [17] reported no significant differences on the effectiveness of dexamethasone and triamcinolone in pain reduction according to the causes of radiculopathy—i.e., disc herniation or foraminal stenosis—at the follow-up time within 1 month.

In view of our findings, it is likely that a longer local duration of a steroid's action is needed to produce an adequate analgesic effect on spinal stenosis than is required for disc herniation. Therefore, the difference in the effectiveness of longer acting steroid, triamcinolone, depending on the cause of pain was not observed, while this difference was large enough to be detected for shorter acting dexamethasone. However, further research is needed to corroborate this hypothesis. An important practical implication of our results is that the clinical advantage of triamcinolone over dexamethasone could be significantly more pronounced for fixed stenotic lesions, and less noticeable in the presence of disc herniation.

Table 4 Odds of obtaining ≥ 50% pain reduction 4 weeks after treatment in the triamcinolone group

	≥ 50% reduction in pain		OR	95% CI	$p^{\S}$	$p_{nonlin}{}^{\&}$
	Yes (%)	No (%)				
Sex						
Male	46.3	53.7	1.00			
Female	51.4	48.6	1.06	0.51–2.19	0.874	
Age	62.8 ± 15.0[#]	61.5 ± 15.7[#]	1.10[$]	0.87–1.39	0.427	0.999
Baseline pain (NRS)	6.3 ± 2.1[#]	6.4 ± 2.2[#]	1.07[*]	0.90–1.26	0.448	0.607
Injection approach						
Periradicular	49.1	50.9	1.00			
Interlaminar	49.3	50.7	1.19	0.58–2.45	0.636	
Age distribution						
–50	46.7	53.3	1.00			
51–60	39.1	60.9	0.73	0.24–2.18	0.569	
61–70	62.5	37.5	1.62	0.52–5.08	0.409	
71–80	50.0	50.0	1.11	0.40–3.09	0.840	
81 +	47.1	52.9	1.22	0.36–4.20	0.750	
NRS distribution						
1–3	42.9	57.1	1.00			
4–6	52.3	47.7	2.56	0.75–8.76	0.134	
7–10	48.5	51.5	2.27	0.70–7.33	0.170	
Imaging abnormalities						
Disc herniation						
–	56.5	43.5	1.00			
+	47.6	52.4	0.66	0.25–1.75	0.405	
Foraminal stenosis						
–	48.2	51.8	1.00			
+	55.6	44.4	1.27	0.44–3.65	0.654	
Spinal canal stenosis						
–	51.5	48.5	1.00			
+	40.0	60.0	0.91	0.37–2.22	0.827	
Listhesis						
–	49.1	50.9	1.00			
+	50.0	50.0	1.62	0.48–5.48	0.440	
Prior spine surgery						
–	48.3	51.7	1.00			
+	62.5	37.5	1.92	0.37–9.91	0.438	

OR, odds ratio; *95% CI*, 95% confidence interval; *NRS*, numerical rating scale for pain; [#] Mean ± SD; [$] OR calculated per 10 years; *OR calculated per 1 point; [§] *p* value derived from logistic regression analysis; [&] *p* value for non-linear effects, derived from generalized additive models

Several published studies indicated that the IL injection route could provide a valid alternative to the TF approach. The prospective evaluation by Candido et al [42] reported equivalent reduction in pain scores for IL and TF injections and non-significantly better pain relief at 2 weeks, 1 month, and 6 months post-injection in the IL group. Ghai [43] et al showed equivalent pain relief for IL and TF injection routes in the management of low back pain with lumbosacral radicular pain: 71.9% of patients in the IL group and 63.3% of patients in the TF group achieved ≥ 50% pain relief at 1 month. Manchikanti et al [44], who analyzed data from three randomized controlled trials, showed overall comparable pain reduction and functional improvement between the TF and IL groups; yet, they further found the superiority of the IL approach at 12 months post-injection. The systematic review with meta-analysis by Chang-Chien et al [45] showed slightly better pain improvement after TF-ESI only after 2 weeks of follow-up, with no difference between TF and IL approach after 1- and 6-month follow-ups. Furthermore, the randomized study by Hong et al [46] showed similar improvements in pain

Table 5 Independent predictors for ≥ 50% pain reduction in the dexamethasone and triamcinolone groups

	OR	95% CI	$p^{\#}$
Dexamethasone			
Baseline pain ≥ 7 vs < 7	0.53	0.294–0.945	0.032
DH + vs −	2.29	1.024–5.129	0.044
Triamcinolone			
No predictors			

OR, odds ratio; *95% CI*, 95% confidence interval; *DH*, disc herniation in the infiltrated segment; $^{\#}p$ value derived from multivariable logistic regression

resultant from the TF and IL approaches. Our findings support such results by showing that IL-ESI could yield an analgesic effect equivalent to TF-ESI.

The anti-inflammatory potency of the dexamethasone dose used in our investigation was roughly two times less than that of triamcinolone; however, it may have had only a minimal impact on the outcomes of the comparison. A prospective, randomized, double-blind, dose-response trial by Ahadian et al [47], including patients with disc abnormalities and stenotic spine lesions, showed that there was no difference between the efficacies of 4-mg and 8- or 12-mg lumbar transforaminal epidural injections of dexamethasone. Thus, even with a threefold dose difference, no significant differences in the Visual Analogue Scale scores for radicular pain between dexamethasone-treated patient groups at 4, 8, and 12 weeks post-injection were found. These results indicate that doses greater than 4 mg do not enhance the magnitude or duration of the response. Moreover, in a randomized, double-blind, controlled trial that compared the dosages of triamcinolone in transforaminal epidural injections for lumbar radicular pain due to a herniated disc, Kang et al [48] found that the groups treated with 40 mg and 10 mg triamcinolone did not differ in the degree of participant satisfaction or pain relief. The authors of this study therefore recommended the use of a minimal effective dose of 10 mg triamcinolone to induce sufficient pain relief along with minimal side effects in patients with lumbosacral radiculopathy.

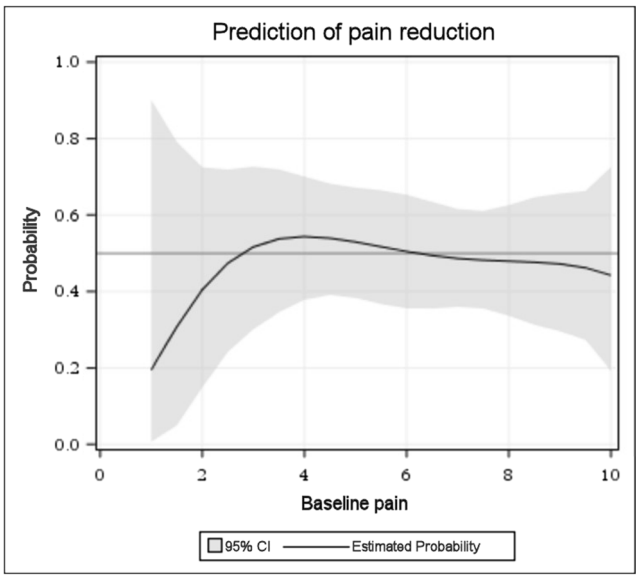

Fig. 3 Probability of ≥ 50% pain reduction 4 weeks post-injection as a function of the baseline pain numerical rating scale score, in the triamcinolone group

The limitations of our study are that it was not a randomized clinical trial with a random treatment allocation, and that it had a relatively short follow-up of 4 weeks. However, we investigated outcomes from real-world clinical practice, and the injection protocol was changed from the use of triamcinolone to dexamethasone after reports of severe complications related to the use of particulate steroids, and not because of any known (or hypothesized) differences between treated patients. Over the study period, there was no change in the policy of the referring physicians regarding patient selection for the procedure. Furthermore, to reduce potential confounding effects, we performed propensity score matching [49] with respect to six baseline variables and consequently achieved similar distribution of these covariates in both study groups. The number of patients lost to telephone follow-up 4 weeks post-injection (83, 19.9%) is another concern, because this data loss could have affected the outcomes of the analysis. Another potential limitation is the lack of information regarding the duration of symptoms or additional oral analgesic medication, although it should be noted that the patients were referred for ESI only after previous ineffective oral therapy. Furthermore, the main analysis of intergroup differences included outcomes of nine patients (five from dexamethasone group and four from triamcinolone group), who received an additional ESI during the 4-week follow-up.

Conclusions

Our work showed that there may be no advantage of using triamcinolone instead of dexamethasone in ESI for mild to moderately intense lumbar radiculopathy, whereas for severe pain (especially that caused by a fixed spinal lesion), the superiority of triamcinolone for pain relief is evident. This finding provides deeper insight into the comparative effectiveness of ESI using particulate versus non-particulate steroids than previously published papers and could improve decision-making before ESI. Moreover, our observations justify further research utilizing sensitivity analyses to explore the outcomes of ESI in specific clinical situations.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Gerhard W. Goerres.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors—Zbigniew Lewandowski—has significant statistical expertise.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap 523 study subjects who received triamcinolone have been previously reported in a doctoral dissertation by Julia Simone Landau at the University of Zurich (2010)—"Short term treatment success and predictive factors of minimally invasive lumbosacral injection therapy" (The original title in German language –" Kurzfristiger Behandlungserfolg und prädiktive Faktoren der minimalinvasiven lumbosakralen Injektionstherapie") and in a poster based on this dissertation—"Short term follow-up in 837 patients undergoing lumbar spine infiltrations" presented at Swiss Congress of Radiology 2010, without subsequent publication in a peer-reviewed journal. Gerhard W. Goerres was the scientific guarantor of this thesis. The main difference between our work and the aforementioned dissertation is that we set out to compare pain relief after lumbar ESI using particulate (triamcinolone) and non-particulate (dexamethasone) steroids, and to explore whether their relative effectiveness could differ for specific patient groups, and the thesis by doctor Landau investigated outcomes and predictive factors for the patients treated only with particulate steroids (triamcinolone).

Methodology
- retrospective
- observational
- performed at one institution

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