Patient Outcomes Following the Use of Methylprednisolone Acetate 40mg Particulate Steroid Versus Dexamethasone 3.3/6.6mg Non-Particulate Steroid in Foraminal Epidural Injections for the Management of Radicular Pain due to Disc Prolapse

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Ethical Approval Not Required

Abstract

Aims: To compare patient outcomes following the use of either methylprednisolone acetate 40mg particulate steroid versus dexamethasone 3.3/6.6mg non-particulate steroid in foraminal epidural injections (TfESIs) for the management of radicular pain due to lumbar disc prolapse

Study Design: Retrospective review of prospective collected data

Methods: Using the Bluespier database, we identified patients who had received a primary TfESI between 11/01/13 and 13/01/19 for the management of radicular pain due to lumbar disc prolapse. Patients were categorised into two groups depending on which steroid they received; dexamethasone (DXM) or methylprednisolone (MPA). Medical records and radiological images were reviewed, and we prospectively collected Patient Reported Outcome Measures (PROMs), which included VAS back, VAS leg and ODI scores. This included scoring for both pre- and post- TfESI. Minimum follow up required was 6 months. These scores were statistically analysed and compared.

Results: 120 patients were identified and included in the study. Of these, 52 patients received DXM and 68 MPA. The age of the patients ranged from 28 to 83 years, (mean 52). There was no statistical difference in gender (p=0.99) or smoking (p=0.929). Prior to the TfESI, there was no statistical significance between the VAS and ODI scores in both drug groups; VAS back (p=0.713), VAS leg (p=0.237) and ODI (0.457). Following the TfESIs, no statistically significant difference was observed between both drug groups in the above scoring systems; VAS back (p=0.814), VAS leg (p=0.908) and ODI (p=0.179). In the DXM group, no statistically significant difference was observed in reduction of VAS back (p=0.842) or VAS leg (p= 0.363) between the 3.3mg and 6.6mg dose, however significant difference in reduction of ODI (p=0.005) in the 3.3mg DXM group over the 6.6mg DXM group. Although more patients in the MPA group went on to receive further injections and/or spinal surgery, no statistically significant difference was noted in outcome between the two cohorts in terms of repeat injections (p=0.459) or surgical intervention (p=0.22). Significantly more patients who received the 6.6mg DXM TfESI required repeat injections than those having received the 3.3mg dose (p=0.039). There were no complications in either group.

Conclusion: The results show that there is no conclusive evidence of the superiority of one drug over the other in the management of radiculopathy following disc prolapse. Both MPA and DXM showed a mean decrease in VAS back, VAS leg and ODI scores. DXM 3.3mg showed greater reduction in VAS leg and ODI scores, and fewer patients required a repeat TfESI following this dose. As there is no statistically significant impact on the patient outcome depending on the drug, and considering the possible risks of particulate steroids in TfESI, the current practice of using non-particulate steroids during TfESIs seems appropriate in radicular pain management.

Introduction

Lower back pain affects approximately one-third of the UK's population, making it a large burden on healthcare resources. [1] A large percentage of these cases present as lumbar radicular pain; a sensation of shooting, sharp pain, commonly presenting in the lower back or legs. [2] The pain arises from compression of spinal nerve roots, secondary to common conditions such as spinal stenosis, scoliosis and disc herniation.

The spine is formed from 33 vertebra, each separated by intervertebral (IV) discs. These fibrocartilaginous discs allow for flexibility, and are composed of the nucleus polposus and the surrounding annulus fibrosus. Disc herniation is a condition where the nucleus polposus protrudes the annulus fibrosis, causing it to become displaces in intervertebral space, most commonly seen at the L4/L5 and L5/S1 level.[4] This can then lead to compression of spinal nerves, resulting in radicular pain. This may be caused by natural spinal degeneration, trauma or some congenital disorders. [5]

Diagnosis of disc herniation is made on the basis of clinical history and examination and radiological imaging (MRI). Possible management may include; analgesia in the form of NSAID's or opioids, physiotherapy, nerve root blocks in the form of transforaminal epidural steroid injections (TfESIs) and surgery. [6]

TfESIs are believed to improve radicular pain by reducing possible inflammation and irritation surrounding the nerve root. [7] They are comprised of a steroid and a small dose of local anaesthetic. In recent years, a series of papers highlighted possible risks associated with the use of particulate steroids in TfESI, including post-procedural paralysis, brainstem infarction and cortical blindness. [8-10] This led to a shift in clinical practice to the use of non-particulate steroids, eg Dexamethosone (DXM) 3.3/6.6mg, in place of particulate steroids, eg Methylprednisolone (MPA) 40mg, in lumbar TfESIs.

Aim

The aim of this study was to assess whether the difference in steroid used in the TfESI, either DXM or MPA, affected patient outcome.

Methodology

Using the Bluespier database, we identified patients who had received a TfESI between 11/01/13 and 13/01/19. Patients who had received a previous TfESI or discectomy were removed from the cohort. Patient notes and imaging via IMPAX were reviewed to determine the cause of their radicular pain and reason for their injection. Patients who received a TfESI due to disc prolapse were kept in the cohort, and those with reason other than this were excluded.

Patients in the cohort received a TfESI injection to the L4/L5 or L5/S1. All injections in this study were performed by the same spinal surgeon. The transforaminal approach was used in all patients included in the study. While the patient lay prone on the operating table, their skin was cleaned by chlorhexidine spray. X-ray imaging was used in anteroposterior (AP) view to visualise vertebral endplates and pedicles. Patients receives a preliminary injection of a local anaesthetic, and then the needle was inserted, with bevel facing medially. For lumbar TfESIs, an oblique x-ray was used to guide the needle to the lateral inferior border of the pedicle and foramen. For an S1 TfESI, an AP view was used to guide

the needle straight through the sacral foramen. 0.5ml of contrast medium (Ultravist) was injected and a further AP x-ray was taken to show the rootogram and medial epidural spill.

A positive patient outcome was defined as the patient receiving symptom relief following the TfESI. This was done by analysing scores obtained from a patient-reported outcome measures (PROMs) questionnaire. [11] Pain was scored using the Visual Analog Scale (VAS), where patient could rate both their back and leg pain, pre- and post- TfESI. On the scales, 0 was 'no pain, and 10 was 'worst pain.' The Oswestry Disability Index (ODI) was used to assess how the patients' pain impacts their daily living. A score of 0 would equate to 'no disability' while a score of 100 represents a severe disability, and being 'bed-bound.' Patient outcome was also measured by asking patients whether they felt the injection "worked, worked and then pain reoccurred, did not work." These values were also compared.

Each patient was asked to fill in the PROMs questionnaire prior to the TfESI, and at their 6 week follow-up appointment following the procedure. These scores were then analysed using IBM SPSS Statistics. Pre- and post- TfESI VAS back, VAS limb and ODI scores were compared in both the DXM and MPA patients. We also compared these results between patients who received 3.3mg and 6.6mg DXM TfESIs. Independent Samples T-test were calculated to assess whether patient outcome was affected by which steroid was used. During analysis, statistical significance was marked at $p<0.05$.

Results

From the Bluespier database, 1046 patients were identified to have had a TfESI between 11/01/13 – 13/01/19. Duplicate names were removed, as well as any patients with a history of previous spinal surgery, or any previous TfESIs. Any patients who received a TfESI for any pathology other than disc prolapse were subsequently removed. Patients with insufficient data were also removed. 120 patients remained in the cohort, with 43% (52/120) having received DXM, and 57% (68/120) having received MPA. Of those having received DXM, 22/52 received the dose of 3.3mg, and 30/52 received the 6.6mg dose. Each was asked to complete the PROMs questionnaires, and full questionnaire response was noted in 85% of patients.

The age of the patients ranged from 28 to 83 years (mean 52). Duration of symptoms ranged from 2 months to 36 months (mean 13.4 months).

Of the 52 patients in the DXM group, 55.8% were male (29/52) and 44.2% were female (23/52). In the MPA group, 54.4% were male (37/68) and 45.6% were female (31/68). There was no statistical significance in gender variation ($p=0.99$).

The number of smokers in each group was analysed, with 34.6% (18/52) of the DXM cohort being current smokers, and 33.8% of the MPA group being current smokers ($p=0.929$).

Figure 1 displays the results of the pre- and post- TfESI questionnaire.

Questionnaire Score	Drug	No. of Patients	Mean	Standard Deviation	Standard Error mean	P value
Pre-ESI VAS back	DXM	49	6.98	2.07	0.87	0.71
	MPA	66	7.14	2.37	0.49	
Post-ESI VAS back	DXM	46	5.07	2.56	0.59	0.81
	MPA	61	5.16	2.64	0.26	
Pre-ESI VAS leg	DXM	49	7.37	2.42	0.86	0.24
	MPA	67	7.84	1.82	0.98	
Post-ESI VAS leg	DXM	46	5.39	3.09	0.74	0.91
	MPA	61	5.33	2.57	0.51	
Pre-ESI ODI	DXM	46	47.22	20.20	3.83	0.46
	MPA	66	49.97	18.50	3.45	
Post-ESI ODI	DXM	48	36.38	22.23	2.60	0.18
	MPA	59	42.07	20.91	2.87	

Figure 1. Comparing PROMs questionnaire scores prior and following a TfESI

As shown in the above table, the VAS back score decreases in both groups, with the DXM group mean score decreasing by 1.94 (27.7%), and the MPA score decreasing by 1.98 (27.6%). There was no significant difference in the reduction of these scores between the two drug groups (p=0.94). Estimated patient effect was rather small (1.96). There was more variability in the DXM group, and confidence intervals (CI) were wide (-1.11 to 1.2)

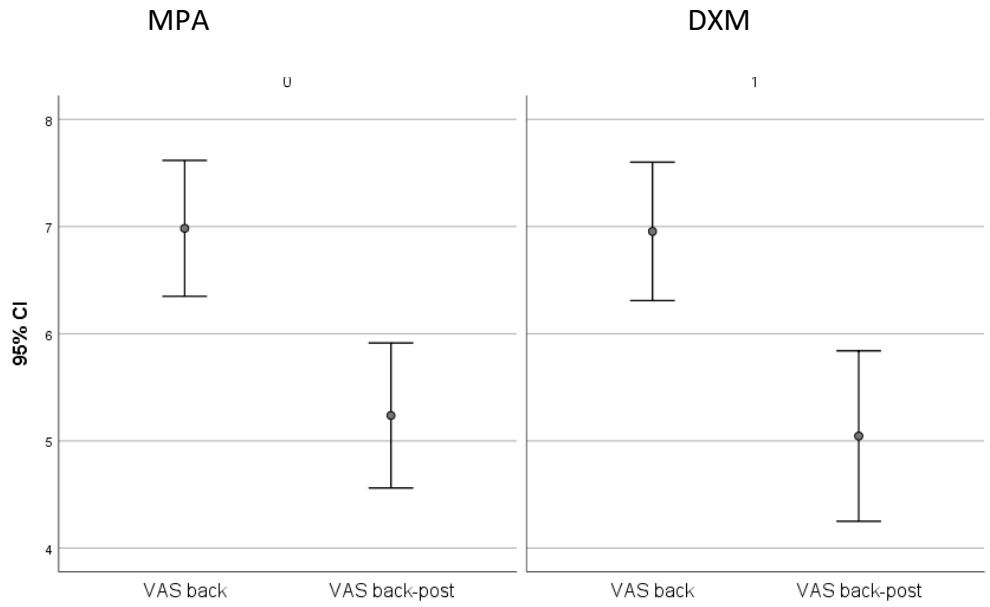

Fig 2. Change in VAS back score pre- and post- TfESI

VAS leg scores also decreased in both groups following a TfESI, with the DXM group showing a mean reduction of 1.98 (26.8%) and the MPA group showing a mean reduction of 2.51 (32%). There was no significant difference in decrease in VAS leg score between the drug groups (p=0.225). Estimated patient effect was small (2.2) CI were wide (-1.12 to 1.32).

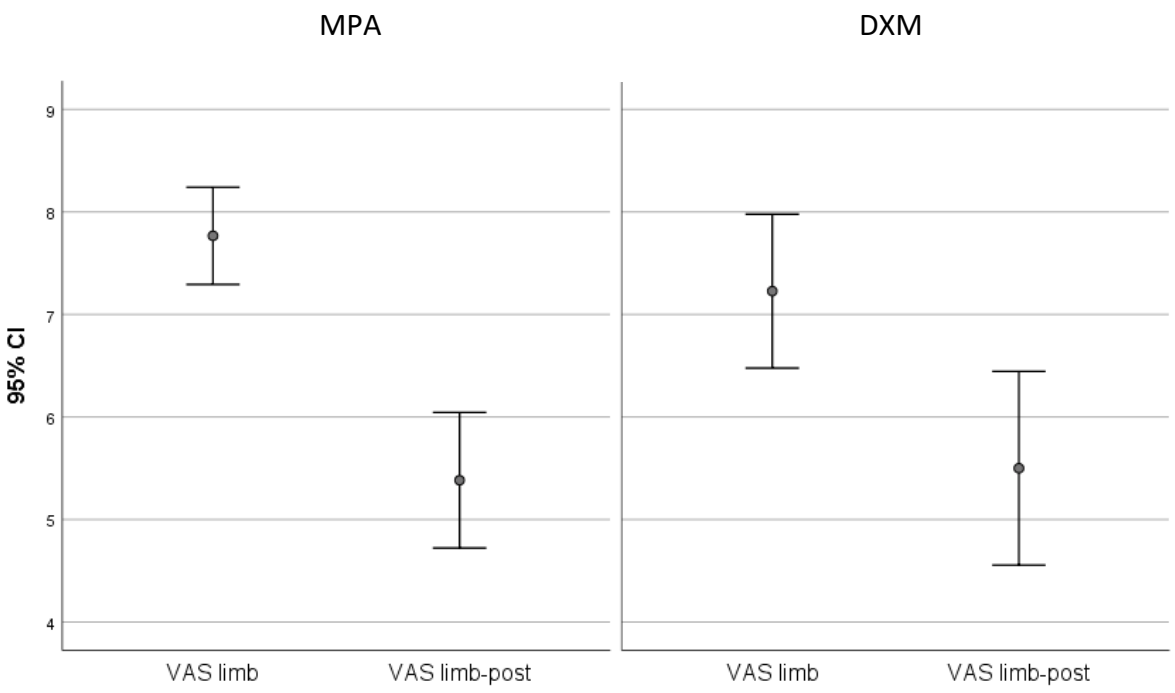

Fig 3. Change in VAS leg score pre- and post- TfESI

When comparing the change in the ODI scores following the procedure, the DXM group showed a mean decrease of 10.84 (23%), while the MPA group showed a mean decrease of 7.9 (15.81%). There was no significant difference between the two drug groups when comparing the change in ODI score (p=0.441), and confidence intervals were wide (-5.9 to 13.6).

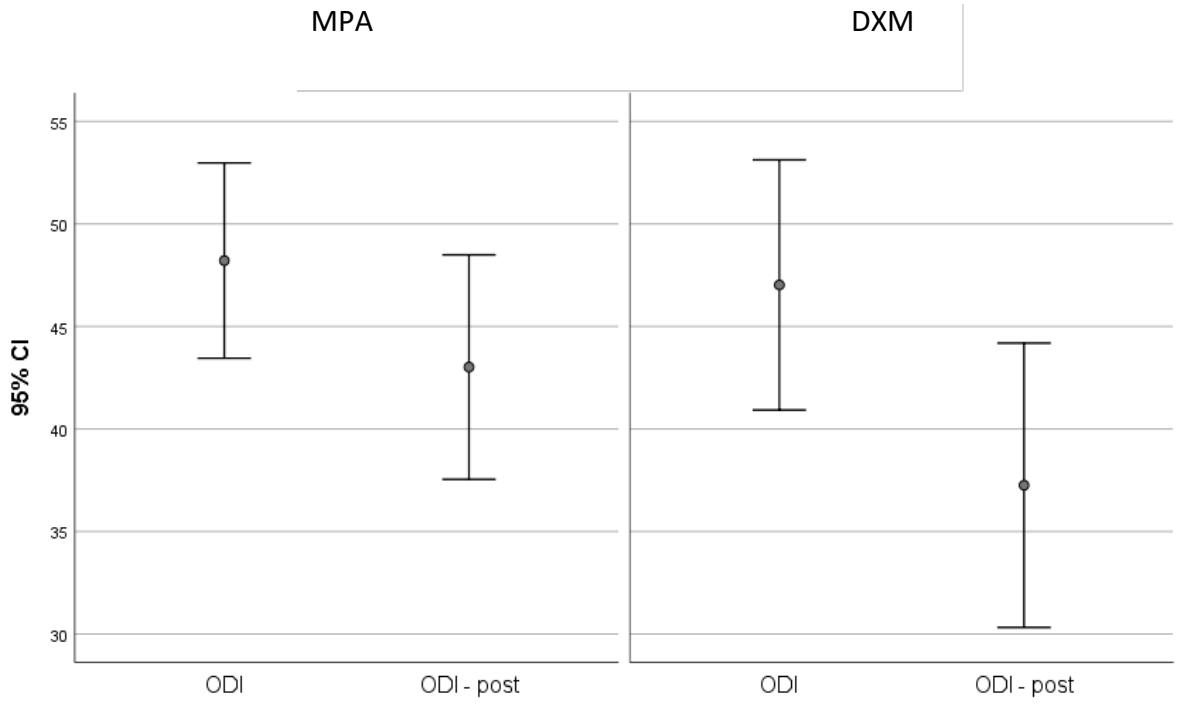

Fig 4. Change in ODI score pre- and post- TfESI

We then later compared these scores between DXM 3.3mg and DXM 6.6mg. The below table summarises the results. VAS back scores reduced by 1.79 in the 3.3mg group, and 2.05 in the 6.6mg group (p=0.842). The confidence interval was wide (-2.24 to 1.83). VAS leg scores reduced by 2.45 in the 3.3mg group, and 1.51 in the 6.6mg group (p=0.363), with a broad confidence interval (-1.12 to 3.06). ODI scores were also reduced in both, with the 3.3mg dose displaying a reduction of 22.4, and the 6.6mg dose showing a reduction of 9.15. The difference in reduction in ODI scores was significant between the two groups (p=0.005), and confidence interval was wide (-2.4 to 6.6). These scores and confidence intervals can be observed in Fig.5 and Fig. 6.

	VAS Back Pre	VAS Back post	VAS leg pre	VAS leg post	ODI pre	ODI post
DXM 3.3	7.05 (0.033)	5.26 (0.038)	8.25 (0.021)	5.53 (0.045)	56.4 (0.262)	34 (0.348)
DXM 6.6	6.93 (0.021)	4.88 (0.028)	6.76 (0.032)	5.30 (0.034)	43.15 (0.210)	34 (0.228)
All DXM	6.98 (0.018)	5.07 (0.022)	7.37 (0.021)	5.39 (0.027)	47.22 (0.176)	36.38 (0.194)
MPA	7.14 (0.018)	5.16 (0.020)	7.84 (0.013)	5.33 (0.019)	49.96 (0.141)	42.07 (0.160)

Figure. 5 showing comparison of means in all scores

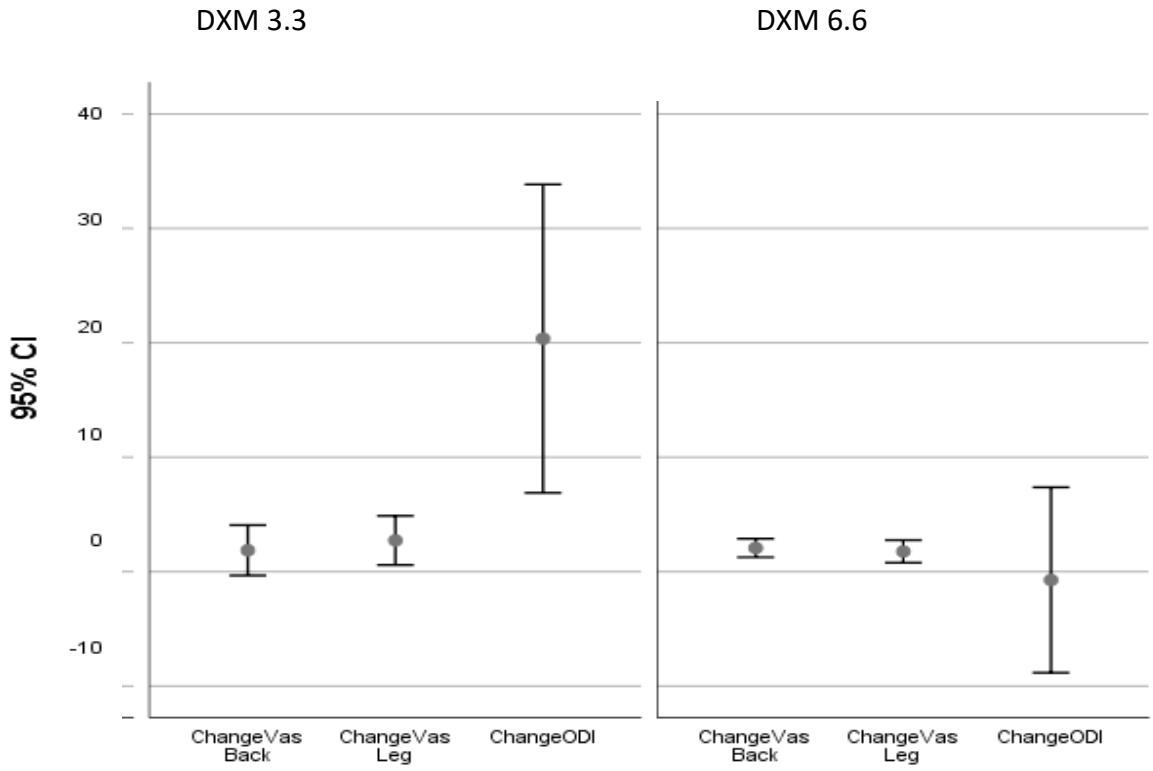

Figure 6. Graph showing confidence intervals in comparisons between DXM 3.3 and 6.6

Patients also graded their outcome as “worked”, “worked but pain reoccurred” and “did not work”, and 97.5% (117/120) engaged in this exercise. The graded outcomes can be seen in Figure 5. Within the DXM group, 22% (11/49) felt the injection did not work, 43% (21/49) felt the injection worked for a while, and then pain reoccurred, and 35% (17/49) felt the TfESI worked well. Within the MPA TfESI group, 31% (21/68) felt the injection did not work at all, 38% (26/68) felt the TfESI worked but pain reoccurred, and 31% (21/68) felt the injection worked well. There was no significant difference in what patients determined their outcome to be between the two different TfESI drugs, as can be seen in Figure 7.

Outcome	Drug		P value
	DXM	MPA	
Did Not Work	22.4%	31%	0.236
Worked But Pain Reoccurred	43%	38%	0.438
Worked	35%	31%	0.834

Figure 7. Table demonstrating patient outcome following TfESI

Within the DXM group, of those who felt it did not work 54.5% (6/11) received the 3.3mg dose, and 45.5% (5/11) received the 6.6mg dose (p=0.365). With those who felt the TfESI did work but pain reoccurred, 19.05% (4/21) received the 3.3mg dose and 80.95% (17/21) received the 6.6mg dose (p=0.02). Of those who felt the injection worked, 58.8% (10/17) were of the 3.3mg group, and 48.1% (7/17) were of the 6.6mg group (p=0.096).

Of those who underwent a DXM TfESI, 28.8% (15/52) had a repeat nerve root block injection within one year and 35.2% of those who received an MPA TfESI also received a repeat TfESI within a year. There was no significant difference in repeat treatment within a year between the two drug groups (p=0.459).

Within a year since the initial TfESI, 28.8% (15/52) of the DXM group and 39.7% (27/68) of the MPA group underwent surgery, for example discectomy. No significant difference was noted between the two groups (p=0.22).

However, when comparing drug dosage within the DXM group, 20% (3/15) of those who required a repeat injection received 3.3mg, where 80% (12/15) of those having required a repeat injection received 6.6mg (p=0.039) (CI 95%= -0.51 to -0.01). Of the DXM patients requiring an operation, 53.3% (8/15) had received a primary TfESI of 3.3mg, and 46.7% (7/15) had received a 6.6mg primary TfESI (p=0.315), with a anrrow confidence interval (-0.13 to 0.39).

Discussion

Multiple studies have previously highlighted the efficacy of the use of both dexamethasone and methylprednisolone in the management of radicular pain. [12-14] While risks associated with particulate steroid use in TfESIs changed practice, the aim of this study was to

determine whether there was any difference in patient outcome depending on the type of steroid, DXM or MPA, in the primary TfESI.

The PROMs questionnaire was then used to analyse patient VAS and ODI scores prior to and following the TfESI. By comparing the VAS back scores, we could see that there was no significant difference in the reduction in score between both groups (p=0.94), and this was also seen in VAS leg scores (p=0.225). ODI score reduction was also observed in both groups following the TfESI, but the amount of reduction was not statistically significant based on the drug received (p=0.441). This shows that patient outcome was independent of the type of steroid received in the primary TfESI. The wide confidence intervals observed in Fig. 2, Fig. 3 and Fig. 4 highlights that both drugs offer a meaningful benefit, and the fact that the confidence intervals overlap also underlines the fact that there is no statistically significant difference in patient outcome depending on whether they receive MPA or DXM. However, there is a trend in each of these figures that a greater reduction in each of these scores can be observed in the DXM group.

When comparing these scores based on drug dosage within the DXM group, although VAS back scores reduced 0.26 more in the 6.6mg group (p=0.842), VAS leg scores were reduced more (0.94) by the 3.3mg dose (p=0.363), and ODI scores were also reduced much more (13.25) by the 3.3mg dose rather than the 6.6mg dose (p=0.005). This suggests that DXM 3.3mg is better at reducing pain and improving mobility than the 6.6mg dose. However, it is worth noting the smaller population in the 3.3mg group than the 6.6mg cohort, and therefore further studies with a larger population base would be required to be confident that this was the case.

Although both MPA and DXA show a mean decrease in all scoring systems used in this study, it should be noted that 10.8% (13/120) of the population of this study experienced increased back or leg pain; 9.6% (5/52) in the DXM group and 11.8% (8/68) in the MPA group. These results could highlight adverse effects in patients or be anomalies. This may also highlight the psychological nature of lower back pain, in that other studies have highlighted that certain psychological factors may impact on patient outcome more than the procedure itself. [15,16] No other complications following the procedure were found in any patients included in this study.

When comparing patient outcome in terms of a repeat TfESI or a spinal operation, there was no significant difference between the drug groups. There was also no statistical difference between drug groups when comparing patient decided outcome, as seen in Fig. 7. However, fewer patients required an operation following a DXM TfESI. This suggests that DXM makes the pain more bearable than MPA and is therefore the preferred steroid if the aim was to avoid surgical intervention.

There was no difference between the dosage groups in those who felt the TfESI did not work or worked, however significantly more patients in the 6.6mg group felt the TfESI worked but then pain reoccurred. (p=0.02). Within the DXM group, a much greater proportion of patients who received the 6.6mg dose required a repeat TfESI than in the 3.3mg group (p=0.039). However, there was no significant difference in the number of patients receiving an operation within a year of the primary TfESI depending on the drug dosage.

Further studies echo the results stated above, in that no difference in pain reduction could be observed between the types of steroid used. [17] This information combined with the potential risks associated with the use of a particulate steroid suggest that DXM is the best choice for primary TfESIs. Some studies suggested that the impact in patient outcome

between these steroids could only be observed in patients who received repeat TfESIs, and MPA could be more beneficial in repeat use, or in greater doses of DXM. [18]

Drug dosage in dexamethasone has been studied previously to ascertain whether an optimal dose of this steroid could be discovered, previously being cited as a dose of less than 4mg.[19] This would echo the results of this study, which shows that a dose of DXM 3.3mg reduces both VAS leg and ODI scores more than in a 6.6mg dose. However, other studies argue that different doses of steroid should be considered for individual patients, and for different regions of the spine, with 10mg being cited as optimal for lumbar TfESIs. [20] Other studies argue that it is not the type of steroid that impacts patient outcome, but rather the volume of steroid used in the injection, with higher volume resulting in greater pain relief. [21]

Despite this, it is known that TfESIs are an effective method of pain relief in disc herniation due to their anti-inflammatory effects. A pattern can be seen in the literature which echoes that which is found in this study, in that TfESIs, both MPA and DXM, are effective analgesia in short term, but commonly, pain will re-occur within a matter of weeks. [22,23] This commonly results in the pattern of repeat injections, which has been shown to statistically improve patient outcome and have a greater effect on pain reduction. [24] As seen in this study, where less than half of all participants required surgical intervention, other studies also suggest that TfESIs reduce the need for spinal surgeries such as discectomies, which is both time and cost effective. [25]

Conclusion

The results show that there is no conclusive evidence of the superiority of one drug over the other in the management of radiculopathy following disc herniation. Both MPA and DXM showed a mean decrease in VAS back, VAS leg and ODI scores. No difference was observed in reducing need for repeat injection or the need for surgical intervention in either group. A TfESI of DXM 3.3mg showed greater reduction in both VAS leg and ODI, and fewer patients who received this dose required a repeat TfESI. As there is no statistically significant impact on the patient outcome depending on the drug, and considering the possible risks of particulate steroids in TfESI, the current practice of using non-particulate steroids during TfESIs seems appropriate in radicular pain management.

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