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Comparative Efficacy of Methylprednisolone Acetate and Dexamethasone Disodium Phosphate in Lumbosacral Transforaminal Epidural Steroid Injections

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Abstract

Objective: Transforaminal epidural steroid injection (TFESI) is an effective treatment for lumbosacral radicular pain. But in view of accidental intravascular injections and consequent neurological injuries, the safety profile of particulate steroids has been questioned. Dexamethasone (DEXA), being non-particulate, is presumed to be a safe replacement for earlier particulate agents. However, the efficacy of DEXA is still doubtful as compared to particulate steroids. The present study aims to determine the comparative efficacy of DEXA and methylprednisolone (MP) in terms of pain relief and improvement of disability.

Methods: Seventy-six patients were sorted into two groups (MP and DEXA) to receive lumbar TFESI. A protocol of one-time single- or two-level TFESI with equipotent doses of MP or DEXA was followed. Numeric Rating Scale (NRS) and Roland-Morris Disability Questionnaire (RMDQ) scores were collected pre-treatment and at different times for a duration of 6 months at follow-up appointments.

Results: Overall, the extent of pain relief (determined from NRS) and quality of life (determined from RMDQ) were significantly better ($p<0.01$) in patients belonging to MP group following TFESI. NRS was 2.8±1.2, 3.3±1, 5.1±1.6 and 3.9±1.4, 4.5±1.3, 6.2±1.1 respectively in MP and DEXA group at 1 month, 3 months and 6months of follow-up, whereas RMDQ was 7.9±2.8, 7.4±2.3, 8.5±2.4 and 10±2.2, 11.4±2.6, 12.4±2.7 respectively in MP and DEXA group at similar time points.

Conclusion: The immediate and short term pain relief following TFESI in lumbar radicular pain remained satisfactory and is comparable between MP and DEXA groups, but the long term benefit is significantly more with the use of MP, as evidenced by the NRS and RMDQ scores.

Keywords: Dexamethasone, methylprednisolone, non-particulate steroids, particulate steroids, transforaminal epidural steroid injection

Introduction

Transforaminal epidural steroid injection (TFESI) is an effective treatment for lumbosacral radicular pain (1), however, the use of particulate corticosteroid preparations (i.e. methylprednisolone, triamcinolone and betamethasone) has been implicated in multiple cases of neurological injury (2, 3). Considering this, the safety guidelines of the Multi-Disciplinary Working Group recommends non-particulate steroid dexamethasone (DEXA) as the initial choice for lumbar TFESI and the only choice for cervical TFESI (4). DEXA has a superior safety profile, but it is still uncertain whether the extent and duration of pain relief by DEXA is comparable to particulate corticosteroids. The majority of recently published literature favours the use of DEXA. Nevertheless, there are studies that revealed a greater degree of pain relief by methylprednisolone (MP) (5, 6), or comparatively shorter duration of effect of

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DEXA (7). The present study was aimed to determine the comparative efficacy between DEXA and MP in terms of pain relief (extent and duration) and improvement of disability, following one-time single- or two-level TFESI.

Methods

Set-up and design

The study was conducted in the Department of Pain Management, Khoula Hopital, a tertiary care hospital in Muscat, following the approval from the Research and Ethical Review & Approval Committee of Ministry of Health, Sultanate of Oman, and after obtaining written informed consent from the individual patients. Seventy-six patients aged between 16-70 years who presented at the hospital between July and December 2017, were enrolled in the study. There were three inclusion criteria. The first was the enrolment of only those patients who understood the nature of the study, available treatment options, the choice to opt out of the study at any stage and who agreed for post-procedure data collection. The second was that the individual's primary complaint was unilateral lower limb pain along with a dermatomal distribution secondary to single- or two-level prolapsed lumbar intervertebral disc (PIVD) causing existing or traversing nerve root compression, the clinical diagnosis of which was corroborated by radiological findings (MRI showed PIVD at the corresponding level). Thirdly, all patients had to have undergone a trial of conservative treatment for at least 3 weeks. The five exclusion criteria were: patients with motor or autonomic disturbances; a history of previous back surgery at same level of current PIVD or evidence of osteophytes, extruded discs, spondylolisthesis or severe spinal deformities; administration of an epidural steroid injection in last 6 months; a history of substance abuse or suspected addiction and all other standard contraindications for percutaneous spinal interventions.

Study protocol

Seventy-six patients were allocated into two groups (MP and DEXA). Patients in the DEXA group received 6 mg of dexamethasone disodium phosphate and those in the MP group received 40 mg of methylprednisolone acetate per injection. For patients in the MP group, 3 mL of 0.25% bupivacaine was added to 2 mL (80 mg) of MP in order to obtain a 5 ml mixture with 16 mg MP mL^{-1}. In a similar manner for patients in DEXA group, 2 mL of 0.25% bupivacaine was added to 3 mL (12 mg) of DEXA in order to obtain a 2.4 mg DEXA mL^{-1} solution. According to the group allocation, 2.5 mL of one of these preparations were injected for each TFESI (maximum 2 injections/patient). The total dose of steroid varied as per the requirements of single or two level injections. All TFESIs were performed by the same pain physician.

TFESI techniques

TFESIs were performed using a 22 gauge, 100 mm spinal needle, with attached standard ASA monitors and while maintaining all aseptic precautions under local anaesthetic infiltration. Optimum placement of the needle was guided by anteroposterior, lateral and oblique fluoroscopic views, using bi-plane digital subtraction angiography (Innova IGS 630, GE Healthcare, IL, U.S.A). The characteristic contrast distribution was used to ascertain the final needle position for TFESI. Both the contrast- (Iohexol 320, up to 2 ml per injection) and steroid-local anaesthetic mixture were injected using an extension tubing under real-time fluoroscopy. Patients were observed for 30 minutes following TFESIs and discharged thereafter. At the time of discharge, all the patients were prescribed celecoxib capsules (200 mg) on a PRN basis. Topical diclofenac cream and hot compression were advised if needed, but no other analgesics were permitted as per the study protocol.

Data collection

Data were collected in the prescribed format by a designated pain nurse. Treatment outcomes were measured by the 11-point Numerical Rating Scale (NRS) and the Roland-Morris Disability Questionnaire (RMDQ). NRS scores were collected pre-treatment, and then at 1-day, 1-month, 3-month and 6-month intervals postoperatively. RMDQ scores were collected at all of the above times except at 1 day postoperatively. The cumulative number of analgesic tablet (celecoxib) consumptions in each group was collected at 1-day, 1-month, 3-month and 6-month intervals following the TFESI. A successful treatment outcome was defined as at least 50% improvement of both NRS and RMDQ scores as compared to the pre-injection scores.

Out of the 76 enrolled patients, 2 from the MP group and 5 from DEXA group opted to withdraw from the study and demanded further treatment prior to 3 months of follow-up. Before the completion of 6 months of follow-up, 1 patient from the MP group and 4 from DEXA group sought to withdraw as well.

Statistical analysis

The results were analysed based on the intention to treat. All results were expressed in mean±SD. For NRS and RMDQ scores, pre-treatment and post-treatment values at different time points were compared with the student's t-test. Nonparametric data were compared with chi-square/Fisher's exact test as applicable. Statistical Package for the Social Sciences software version 16.0 (SPSS Inc.; Chicago, IL, USA) was used for the analysis.

Results

The demographic data, level of nerve root block and type of analgesic use before TFESI were comparable between the

groups (Table 1). Overall, the extent of pain relief (NRS) and quality of life (RMDQ) were significantly better in patients belonging to MP group at 1-month, 3-month and 6-month following TFESI (Table 2). The cumulative consumption of celecoxib was significantly more in DEXA group at 1, 3 and 6-month following injections. Four patients reported unbearable pain during the procedure, 9 patients reported dizziness and 13 patients had mild paraesthesia in the lower limb of the affected side. No motor weakness or any other major procedural complications were noted in any patient. Successful treatment outcome in both groups is shown in Figure 1.

Discussion

The extent of pain relief and improvement in the quality of life was significantly better in patients of the MP group compared to those in the DEXA group throughout the follow-up period. However, a successful treatment outcome was observed in patients of the MP group till 3 months following TFESI, whereas patients belonging to the DEXA group could not achieve the same even at the 1-month postoperative follow-up appointment. Supplementary use of analgesics was also significantly more in DEXA group.

The longer duration of action of MP could be explained by the depot effect of the drug resulting in its continuous release from the injection site over a relatively extended period of time (7). DEXA, being non-particulate, had rapid clearance and consequently a shorter duration of action (8). Two patients in the DEXA group consistently reported a 50% improvement in both NRS and RMDQ scores uptil the last 6-month follow-up appointment. This is unlikely due to DEXA alone, as a similar effect was not observed in other patients of DEXA group. Placebo effect (9), other conservative measures or some unknown factors might have resulted in such improvement.

Scientific evidence is divided, favouring either particulate or non-particulate steroids for TFESI. Kim et al. (10) had shown better results with MP. Similar results were also shown by Noe et al. (11) in their study comparing equipotent betamethasone with DEXA. However, both the studies had a rather short follow-up period (1-2 months) (10, 11). In another study, comparing equipotent doses of triamcinolone with DEXA for TFESI, no difference was observed in pain scores and functional improvements uptil 6 months of postoperative follow-up, but patients who received DEXA had required a significantly higher number of repeat injections to sustain the effects (7). This finding indirectly proved that triamcinolone has better efficacy as compared to DEXA, taking into consideration the patient discomfort caused by multiple injections and the cost-effectiveness that is not afforded by the use of DEXA. Dreyfuss et al. (12) compared different doses of triamcinolone and DEXA but did not observe a significant difference between the patients in terms of pain scores at 1 month postoperatively. Few studies have revealed a better short term pain relief with DEXA as compared to triamcinolone (5, 6). El-Yahchouchi et al. (6) had shown a better functional outcome of non-particulate steroid (DEXA) at 2 months postoperatively. However, it was not apparent from the study how a shorter acting drug administered in a quantity less than the equipotent dose could produce a better functional outcome.

Accidental intravascular injection of the drug causing neurological injury remains a major concern in TFESI when using particulate steroids. Particles of MP or triamcinolone may co-

Table 1. Demographic data

Parameter	MP (n=38)	DEXA (n=38)	p
Age (years)	46.4±13.5	44.3±13.4	0.5
Duration of symptom (months)	7.1±3.2	6.3±2.8	0.24
Level of the nerve roots blocked by TFESI	L4=09 L5=16 S1=28	L4=07 L5=14 S1=25	0.97
Gender (male: female)	24:14	16:22	0.66
Drug use profile as a conservative treatment			
NSAID, paracetamol	38	38	1.00
Tramadol	20	14	0.16
Strong opioids	0	1	1.00
Antiepileptics	35	37	0.61
Antidepressants	15	18	0.48

MP: methylprednisolone; DEXA: dexamethasone; NSAID: non-steroidal anti inflammatory drugs

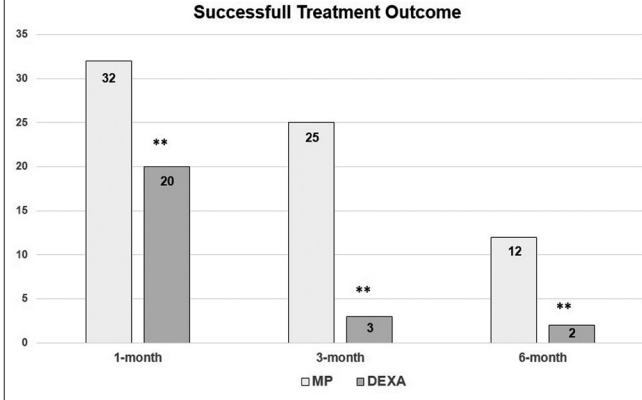

Figure 1. Successful treatment outcome (at least 50% improvement of both in terms of NRS and RMDQ scores as compared to pre-TFESI scores) in MP and DEXA group patients at different times during the follow-up period
RMDQ: Roland-Morris Disability Questionnaire; NRS: numeric rating scale; MP: methylprednisolone; DEXA: dexamethasone

Table 2. Clinical outcomes and improvements in NRS and RMDQ scores

	NRS				RMDQ				Cumulative Celecoxib used			
	MP	DEXA	p		MP	DEXA	p		MP	DEXA	p
Pre-treatment	8.6±0.9	8.4±1	0.41	Pre-treatment	17.1±3.1	16.6±3.2	0.51				
1-day	2.7±1.2	2.6±1.3	0.71					1 day	1±1.2	1.1±1.8	0.76
1-month	2.8±1.2	3.9±1.4	0.0006**	1 month	7.9±2.8	10±2.2	<0.0001**	1 month	9.2±5.4	12±6.3	0.03*
3-month	3.3±1	4.5±1.3	0.0001**	3 months	7.4±2.3	11.4±2.6	<0.0001**	3 months	19.7±10.2	40.1±16.6	0.000**
6-month	5.1±1.6	6.2±1.1	0.0015**	6 months	8.5±2.4	12.4±2.7	<0.0001**	6 months	37.1±14	56.3±13.2	0.000**

MP: methylprednisolone acetate; DEXA: dexamethasone; NRS: numeric rating scale; RMDQ: Roland-Morris Disability Questionnaire. *significant (<0.05); **highly significant (<0.001)

alesce into larger particles having a diameter greater than 100 µm, which could occlude capillaries, metarterioles and even arteries, resulting in infarction of large block of neural tissue supplied by the affected artery (13). DEXA, being non-particulate, has not been associated with any neurological injury up till now, save for one reported case of conus medullaris infarction in which the mechanism of the injury was unclear (14). Another report described a potentially dangerous combination of 1:1 DEXA and ropivacaine (0.75%) resulting in an almost instantaneous formation of crystals large enough to act as emboli (15). Such crystallisation was not observed when DEXA was mixed with lidocaine or bupivacaine (15). The Food and Drug Administration issued a drug safety communication in 2014, warning that injection of corticosteroids into the epidural space of the spine may result in rare, but serious adverse events, including loss of vision, stroke, paralysis and death (16), which resulted in significant concerns and controversies in the scientific community (17). Although TFESI in the cervical region using particulate steroids might cause major disability, they could still be used safely under appropriate image guidance for lumbar TFESI because of a wider transforaminal area in this region (17). A comprehensive risk-benefit analysis favours the use of DEXA as the first-line choice for cervical TFESI and lumbar TFESI at L3 (3rd lumbar vertebrae) and above where the risk of permanent neurologic compromise is greatest (18). Considering this information and the fact that DEXA has been studied for a comparatively shorter period than MP or triamcinolone, it would be too premature to declare DEXA as the ideal choice for TFESI and devoid of any neurological complication. Moreover, in a few studies, the use of faulty or inadequate techniques cannot be ruled out.

The present study had essentially compared the outcomes between MP and DEXA in lower lumbar TFESI (targeting L4, L5 and S1 roots). Therefore, the occurrence of neurological injury was not a major concern in our patients. The results of the present study were comparable with earlier studies that favoured the use of particulate steroids, but this study was distinct in two aspects. First, the follow-up period was relatively longer (6 months) as compared to many previous studies (with a follow-up period of 2-4 months). Secondly, a one-time TFESI protocol was adopted, unlike the repetitive injection techniques used by Kennedy et al. (7) with a similar follow-up period. Hence this study was more unambiguous, which enabled a clear illustration of the differences between MP and DEXA.

The present study had some important limitations. Being a non-randomised single-blind study, the introduction of researcher bias was highly possible. Patient enrolment had been selective and therefore results for radicular pain due to other causes could not be extrapolated. We had followed a one-time injection protocol which may not be the only ac-

ceptable technique in all cases. Further, the total drug dose was not the same and varied as per the number of injections. Patients were also allowed to use topical diclofenac cream due to which the resultant blood level of diclofenac in individual patients could be different. Some patients found it difficult to maintain a correct record of analgesic consumption and might have co-administered other analgesics during the follow-up period. In the present study, DEXA was used in marginally fewer quantity than equipotent methylprednisolone (15 mg DEXA=80 mg MP) (10). Ahadian et al. (19) showed similar efficacy for 4 mg DEXA compared with 8 mg or 12 mg MP used for TFESI.

Conclusion

The immediate and short term pain relief following TFESI in lumbar radicular pain remained satisfactory and comparable between MP and DEXA, but the long term benefit was significantly more in the case of MP, as evidenced by the NRS and RMDQ scores as well as the total cumulative analgesic consumptions. As of now, evidence comparing both the efficacy and complication of particulate (specifically MP) and non-particulate steroids for TFESI is limited. In our opinion, after considering all the complications associated with the use of particulate steroids, and after carefully calibrating the individual risk-benefit ratio along with maintaining all standardised safety recommendations (20), MP may still be used as a drug of choice for lower lumbar TFESI.

Ethics Committee Approval: Ethics committee approval was received for this study from the Research and Ethical Review & Approval Committee of Ministry of Health, Sultanate of Oman (MoH/CSR/16/7462; date of approval 01/05/2017).

Informed Consent: Written informed consent was obtained from the individual patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: The authors have no conflicts of interest to declare.

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