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RESEARCH ARTICLE
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KETAMINE VS DEXMEDETOMIDINE AS AN ADJUNT TO LEVOBUPIVACAINE AND DEXAMETHASONE FOR LUMBAR TRANSFORAMINAL EPIDURAL INJECTION USING HYBRID TECHNIQUE OF ULTRASOUND GUIDANCE + FLUOROSCOPY – A SINGLE CENTERED OBSERVATIONAL STUDY.

Dr. Swathi Gundlakunta[1], Dr. Busetty Prithvi Raj[2], Dr. Chaithanya Kumar[3], Dr. Paavani Andagala[4*], Dr. Haritha Damarla[5], Dr. Krishna Chaithanya [6]

[1]DNB, Assistant professor, Narayana Medical College, Nellore, Andhra Pradesh, Dr.NTR university of health sciences.
[2]MD, Associate professor, Narayana Medical College, Nellore, Andhra Pradesh, Dr.NTR university of health sciences.
[3]MD, Assistant professor, Narayana Medical College, Nellore, Andhra Pradesh, Dr.NTR university of health sciences.
[4*]Postgraduate, Narayana Medical College, Nellore, Andhra Pradesh, Dr.NTR university of health sciences.
[5]MD, Assistant professor, Narayana Medical College, Nellore, Andhra Pradesh, Dr.NTR university of health sciences.
[6]MD, Professor , Narayana Medical College, Nellore, Andhra Pradesh, Dr.NTR university of health sciences.

***Corresponding Author:** Paavani Andagala
*Email: pawaniisekhar96@gmail.com. 7337018627

ABSTRACT:

Introduction: Low back pain is most common in middle age group, which is usually due to nerve root inflammation for which primary treatment often involves medication, physiotherapy and lumbar transforaminal epidural steroid injection. Debate continues regarding the supremacy of one adjuvant over the other in prolonging the analgesic action of lumbar transforaminal epidural steroid injection.
Objective: The present study aims to compare the efficacy of ketamine and dexmedetomidine as an adjuvant to transforaminal epidural injection in terms of pain score, Quality of Life and side effects.

Materials and methods: This single centered study was conducted among a total of 80 patients with chronic low back pain of either sex, aged 18-65 years, with not more than one level of bilateral lumbar foraminal disc protrusion causing radiculopathy were enrolled. Patients who received 10mg of preservative free ketamine were in Group K and those who received 10mcg dexmedetomidine were in Group D, as an adjunct to 2ml of 0.125% levo-bupivacaine with 8mg of dexamethasone. Assessment of Pain was done using Visual Analog score for 24hrs, Quality of Life using Revised Oswestry Disability Score (RODS) at the end of 1,3 and 6 months.

Results: Analgesia and quality of Life improved more in Group D than Group K by the end of 3 months (p=0.024) and 6 months (p=0.009).

Conclusion: The analgesic efficacy of adjuvant therapy with dexmedetomidine is superior in prolonging analgesia and quality of life.

Keywords: - Low back pain, Transforaminal injection, Ketamine, Dexmedetomidine, Oswestry Disability Score

Introduction :

Low back pain and radiculopathy are among the most common conditions caused by a herniated intervertebral disc exerting pressure on nerve root resulting in pain and functional disability.[1] Lumbar transforaminal epidural steroid injection is one of the frequently used approaches for pain control and management of low back pain, as it is more specific and selected nerves are targeted. Fluoroscopy is most commonly used imaging guide in interventional spine procedures for confirmation of needle placement. Although fluoroscopy provide accurate real-time and continuous images this increases the overall exposure time, which puts both physician and patient at the risk of radiation exposure. Considering the constraints and limitations of fluoroscopy, sonography has several advantages like harmonic imaging of tissue, absence of ionizing radiation,better visualization of soft tissues,real time visualization of needle, two dimensional matrix probe technology, imaging with a wider viewing area, greater ease of injection.[2]

So by using hybrid technique of ultrasound guidance and fluoroscopy risk of radiation exposure is decreased and real time visualisation of needle advancement and ability to observe the drug spread is increased.

Epidural steroid injection (ESI) acts by multiple mechanisms like anti-inflammatory, antinociceptive, decreased capillary permeability and reduced intra-neuronal oedema. The local anaesthetics block Na+ channels to affect nerve transmission and dilute the inflammatory mediators. Various adjuvants such as clonidine, tramadol, ketamine have been tried with good results.[3] Low back pain triggering from multiple pathophysiological components or centrally sensitized neuropathic changes (mixed pain disorders) set up intricate neuronal circuits where epidural steroids alone may fail.[4]

Alpha-2 agonists had been shown to reduce chronic allodynia most probably through blocking pre- and postsynaptic α-2 receptors.[5]

In chronic pain, neuropathic aspect occurs due to NMDA receptor sensitisation at pre-synaptic site resulting in increased glutamate release and its phosphorylation at the post-synaptic site, manifesting as wind up phenomenon. Based on this concept, ketamine, an NMDA receptor antagonist with mild opioid receptor action as well as local anaesthetic properties, has been used in a wide range of doses through epidural and intrathecal routes for acute postoperative and chronic neuropathic pain conditions.[3'4]

In this study we compared the efficacy of ketamine versus dexmedetomidine given as an adjunct to lumbar transforaminal epidural steroid injection for selective nerve root block.

Materials and methods

The present observational study was carried out on 80 patients, at Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India, with the approval of Institution's Ethics Committee (IEC/NMC/29.04.2023 /131)for a duration of 9 months. All patients were informed regarding the study protocol during preanaesthetic evaluation, written and informed consent was obtained from every patient. During this study 80 patients were divided into 2 groups of 40 each. Due to technical difficulty and lost to follow up only 36 patients from each group were assessed for this study as depicted in consort flow diagram .

Sample size calculation

Sample size was calculated using the formula :

$n=【2x(Z\alpha+Z\beta)^2(\sigma^2)】 \div 【(X1-X2)^2】$

The mean Oswestry disability index in each group was 6.53 and 1.11, as reported in a previous study.[6] The sample size was calculated using the above formula, assuming a significance level of 0.05(α=1.96) and power of the study of 80% (β=0.84)

$Z\alpha$=1.96

$Z\beta$=0.84

X1= 6.53

X2=1.11

σ =5.86

Thus, n= 【$2 \times (1.96 + 0.84)^2 \times (5.8)^2$】 ÷ 【$(6.53 - 1.11)^2$】

n= 17.955

The sample size was calculated to be 17.95 per group, for better quantification, more number of participants were included in the study, i.e., 40 in each group.

Study population

Patients who receive a lumbar transforaminal epidural steroid injection Dexmedetomidine (10mcg/level) along with dexamethasone 8mg and 0.125% levo-bupivacaine were included in Group-D.

Patients who receive a lumbar transforaminal epidural steroid injection with preservative free Ketamine (10mg/level) along with dexamethasone 8mg and 0.125% levo-bupivacaine were included in Group-K.

Patients aged between 30-70yrs, belonging to ASA I-II, having severe lumboradicular pain for >6weeks, not responding to conservative treatment and positive straight leg raise test (SLR/Lasegue's test) were included in the study.

Patients without valid informed and written risk consent, those requiring transforaminal block for more than one level, those who did not get the effect of the block, pregnant, individuals with bleeding diathesis, those using anticoagulants, those with local skin infections and allergy to study drugs were excluded.

The pre anesthetic checkup included assessment of history, general condition of the patient according to ASA classification, general physical examination, detailed examination of the cardiovascular system, respiratory system, abdomen and neurological evaluation along with various scores, pre procedural vitals, VAS for pain, RODS for QOL were noted. Investigations like complete hemogram, BT, CT, RFT, ECG,MRI

Procedure

With patient lying prepped and in a prone position, standard monitors were connected (non invasive blood pressure, pulse oximetry, ECG),IV line was secured. A pillow was placed under the abdomen to alleviate lumbar lordosis. A portable ultrasound machine (M Turbo, SonoSite) with a curvilinear probe (2-5 MHz frequency) was used for the procedure. Following the sterile technique, the ultrasound transducer was covered in sterile wrapping. After identification of the fifth lumbar spinous process, the desired spinal level for the injection was marked by cephalad counting of the spinous process starting from L5 , with its orientation marker directed cranially.

The probe is moved medially to laterally to visualize the horse head sign (lamina), camel hump (articular processes), and finally trident sign (transverse process).

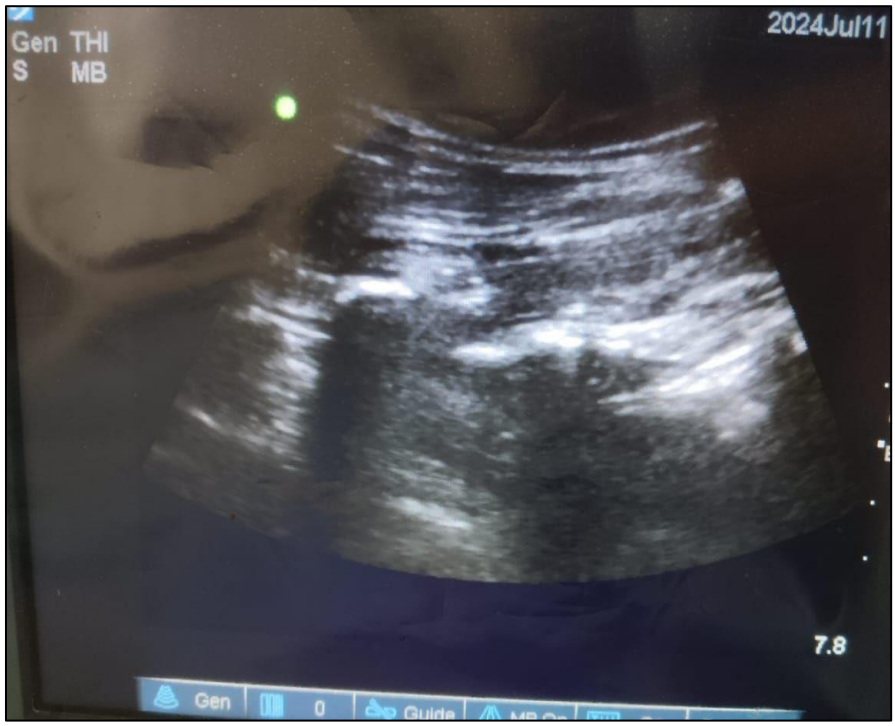
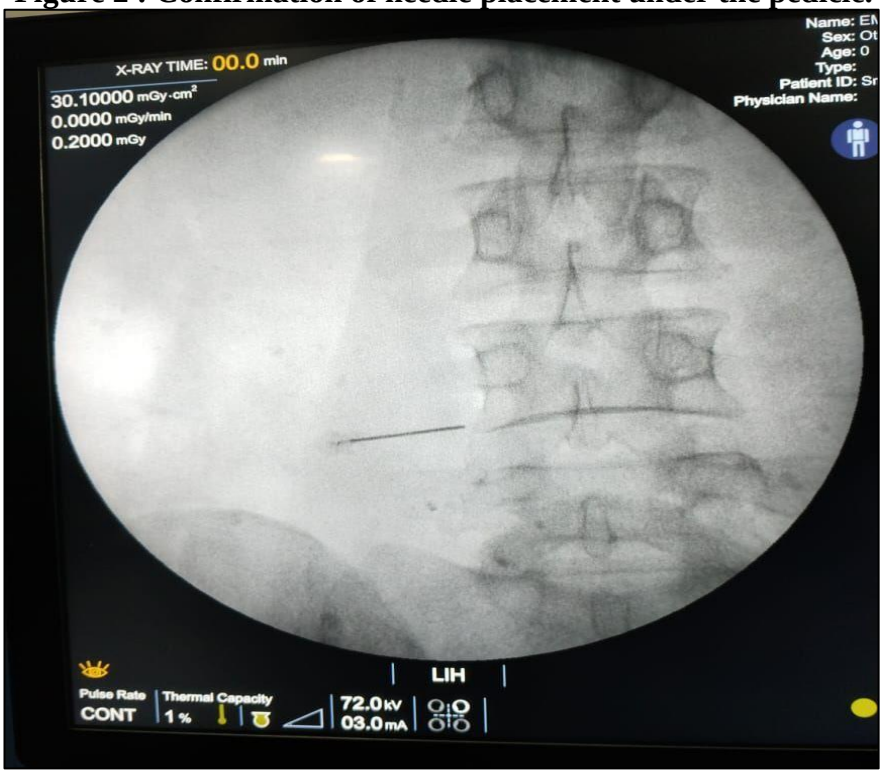


Figure 1 : Ultrasound showing the transverse process

After infiltrating local anesthesia, a 23 gauge, 3.5 inch Quincke tipped spinal needle advanced through the out-plane approach, which enables real-time visualization of tip of the needle. The needle tip was advanced in between two 2 tranverse processes by piercing inter transverse ligament Once satisfactory position of the needle is achieved under ultrasound, fluoroscope (FL) image is taken to confirm needle placement under the pedicle(figure 2) and lateral image to identify the depth of needle (figure 3).

Figure 2 : Confirmation of needle placement under the pedicle.



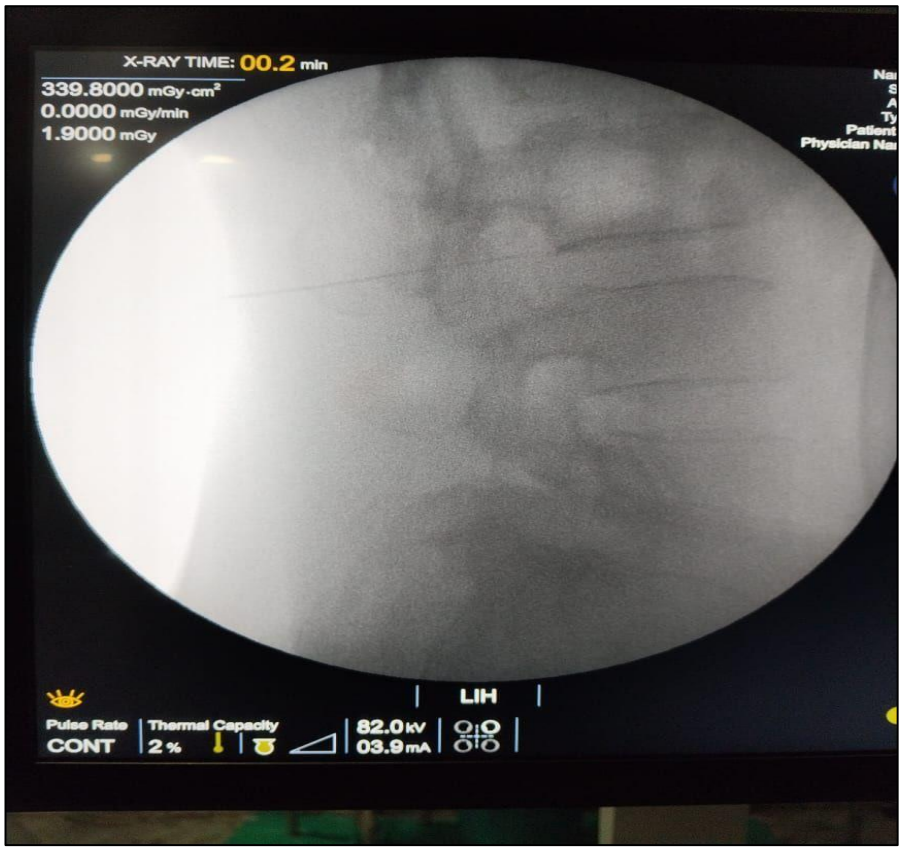


Figure 3 : Confirmation of needle depth in lateral view.

Minor adjustments to position the needle tip were done if required at this stage. One milliliter of iohexol 350 mg I/ml (contrast) was then injected under FL guidance(figure 4). This is done to ensure that there is no intravascular or intrathecal spread .

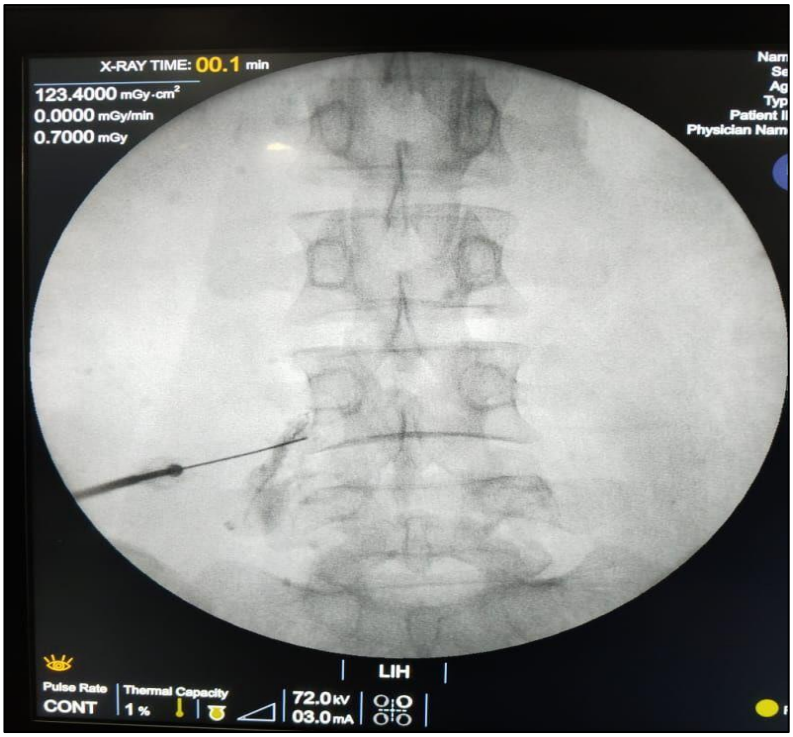


Figure 4 : Confirmation of needle placement by injecting dye under fluoroscopy.

After validation of correct placement of needle, 2ml of 0.125% levo-bupivacaine with 2mg of dexamethasone and 10mg of ketamine (in GROUP K) or 10mcg of dexmedetomidine (in GROUP D) will be given at each level after negative aspiration for CSF or blood.
In case of failure, repositioning of the needle was done by the guide of fluoroscopy. Any complications were noted.
The patients were then transferred to the Peri-Anesthesia Care Unit (PACU) for monitoring vital signs, pain levels, and possible neurological and other adverse events for 60–90 minutes. They were then discharged home (4 hours after the procedure) in the care of a responsible adult and advised not to drive for 24 hours. The pain intensity was evaluated by visual analogue scale scores.
The effects of the procedures were evaluated by measuring the visual analogue scale (VAS) and revised Oswestry disability index (RODS) before the procedures then 1 month ,3 months,6 months after the procedure. Any complications like confusion, hypertension or tachycardia, mental or mood changes, nausea, delirium were to be noted with ketamine. Bradycardia, excess sedation, hypotension were to be noted with dexmedetomidine.

Statistical analysis
Data were presented as mean, standard deviation, frequency and percentage. Categorical variables were compared using the Pearson chi-square test. Significance was defined by P values less than 0.05 using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Science Inc., Chicago, IL).

RESULTS

	Group				P value
	Group K		Group D		
	Mean	Standard Deviation	Mean	Standard Deviation	
Age	44.58	6.04	44.08	4.23	0.669
BMI	25.35	3.07	24.38	0.147	0.147

Table 1 : Comparison of Age and BMI between two groups

No significant difference in age and BMI between two groups.

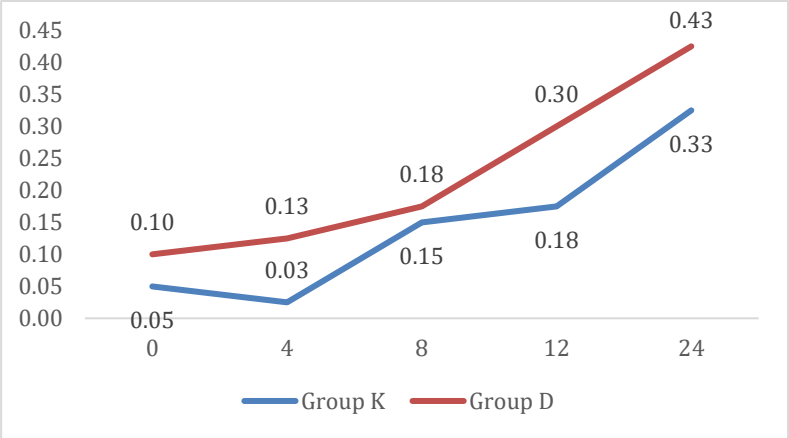
	Group				P value
	Group K		Group D		
	n	**%**	n	%	
Female	26	65%	25	62.5%	0.816
Male	14	35%	15	37.5%	
ASA I	12	30%	17	42.5%	0.245
ASA II	28	70%	23	57.5%	

Table 2 : Comparison of Gender and ASA grading between two groups

No significant difference in gender and ASA grading between two groups.

VAS	Group				P value
	Group K		Group D		
	Mean	Standard Deviation	Mean	Standard Deviation	
Pre procedural	3.48	0.55	3.58	0.64	0.456
0	0.05	0.22	0.10	0.30	0.402
4	0.03	0.16	0.13	0.33	0.092
8	0.15	0.36	0.18	0.50	0.799
12	0.18	0.38	0.30	0.56	0.25
24	0.33	0.53	0.43	0.64	0.446

Table 3 : VAS comparison between two groups at pre-procedural, 0, 4, 8, 12 and 24 hrs



Graph 1 : Graph comparing the VAS between two groups on Day 1

The mean preoperative VAS score for Group K is 3.48 ± 0.55, and for Group D, it's 3.58 ± 0.64. There is no significant difference in pre-operative VAS scores between the groups, with a p-value of 0.456.

At 0 hours, the VAS score for Group K is 0.05 ± 0.22, and for Group D, it's 0.10 ± 0.30, with a p-value of 0.402.

At 4 hours, Group K has a VAS score of 0.03 ± 0.16, and Group D has 0.13 ± 0.33, with a p-value of 0.092.

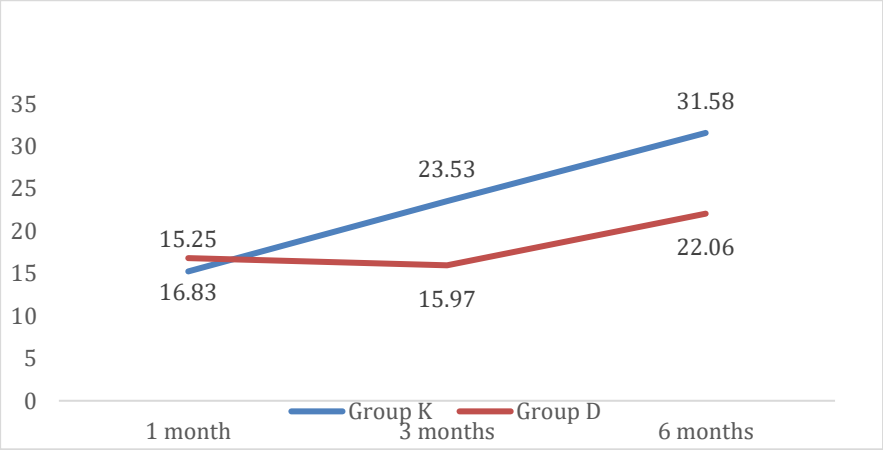
At 8 hours, Group K's VAS score is 0.15 ± 0.36, and Group D's is 0.18 ± 0.50, with a p-value of 0.799.

At 12 hours, Group K's VAS score is 0.18 ± 0.38, and Group D's is 0.30 ± 0.56, with a p-value of 0.25.

Lastly, at 24 hours, Group K has a VAS score of 0.33 ± 0.53, and Group D has 0.43 ± 0.64, with a p-value of 0.446. There is no significant difference in VAS scores between the groups.

RODS	Group				P value
	Group K		Group D		
	Mean	Standard Deviation	Mean	Standard Deviation	
1 month	15.25	13.44	16.83	14.09	0.627
3 months	23.53	15.67	15.97	11.78	0.024
6 months	31.58	16.37	22.06	13.51	0.009

Table 4 : RODS comparison between two groups at 1,3 and 6 months.



Graph 2 : Graph comparing the VAS between two groups during 1, 3 and 6 months

At 1 month, the mean Revised Oswestry Disability Score (RODS) for Group K is 15.25 ± 13.44, and for Group D, it's 16.83 ± 14.09. The difference is not significant between the groups, with a p-value of 0.627.

At 3 months, Group K's mean RODS score is 23.53 ± 15.67, whereas for Group D, it's 15.97 ± 11.78. There is a significant difference between the groups, with a p-value of 0.024.

At 6 months, Group K's mean RODS score is 31.58 ± 16.37, and for Group D, it's 22.06 ± 13.51. Again, there is a significant difference between the groups, with a p-value of 0.009.

No complications were noted during and after the procedure.

Discussion:

Lumbar transformational steroid injections (LTESI) or selective nerve root blocks is one of the age old and gold standard treatment for chronic low back ache.Steroids like particulate Triamcinolone mixed with local anesthetic is the main stay of management. But in the view of accidental intravascular injections and consequent neurological injuries, safety profile of particulate steroids has been questioned. Off late Non particulate Dexamethasone is replacing Triamcinolone for its benefits over non particulate steroids Majority of recently published literature favours use of dexamethasone. David kennedy et al.,[7] published a study comparing dexamethasone to triamcinolone in LTFESIs. They injected 2 mL of 1% lidocaine and 1.5 mL of dexamethasone phosphate 10 mg/mL they concluded that dexamethasone appears to posses reasonably similar effectiveness when compared with particulate steroid triamcinolone but dexamethasone group received slightly more injections than the triamcinolone group to achieve the same.

Byron J. et al.,[8] published that particulate steroids do not achieve greater success rates for pain relief, improved disability or outcomes. In our study we added 8mg of dexamethasone to local anesthetic as dexamethasone do not appear to aggregate as particles are smaller than RBC on microscopic examination and neurologically safe alternative when compared to particulate steroids

Generally the duration of action of this combination works for a limited period. To prolong this duration of pain relief various adjuvants like opioids, magnesium sulphate, clonidine, dexmedetomidine and ketamine were studied but none has proved their superiority over one another. Due to the more complex nature of chronic low back pain ketamine has been studied as an adjuvant to prolong the pain relief due to its neuroprotective actions and NMDA receptor blocking mechanism. Amr YM et al.,[9] observed that epidurally administered ketamine seems to be safe and useful adjunctive to epidural corticosteroid therapy in chronic lumbar pain they observed that oswestery low back pain disability questionnaire score decreased significantly in ketamine group at end of 1 month,3,6,9,12 months respectively. In our study we added 10mg/level of ketamine with local anesthetic and steroid to improve pain relief in low back pain patients.

Dexmedetomidine has gained wide popularity for its synergistic action with local anesthetics in regional blocks. Studies has shown that we can use dexmedetomidine safely in a dose of 1-2 mcg/kg, administered epidurally or caudally for management of post op pain.[10]

Shima zarger et al.,[11] observed that dexmed group has significant reduction in pain scores compare dwith neostigmine in chronic low back pain patients receiving local anesthetics and steroids.

Imani F et al.,[6] observed that dexmed added to triamcilone exerts more pain relief than triamcilone alone.

In current study we added 10mcg/level of dexmedetomidine along with local anaesthetics and steroid. Till now no one compared dexmedetomidine versus ketamine as adjunct to local anesthetic and steroid in LTFEI. So we aimed to compare ketamine and Dexmedetomidine as adjuvants to dexamethasone and levobupivacaine combination.

Fluoroscopy is widely used for LTFESI. Though it's benefits are widely known there is a growing concern about the radiation exposure among the physicians. So Ultrasound was explored for the past few years in this field and is gaining popularity for TFESI. The advantages of USG are no radiation exposure, no requirement of a separate area to perform the block, equipment mobility, and visualization of soft tissue and real-time needle trajectory .

Gofeld M et al.,[12] observed procedural accuracy of ultrasound guided Lumbar transforaminal epidural steroid injection and stated that it is accurate and feasible in the preclinical setting.

Yang et al.,[13] observed that Lumbar TFEI under ultrasound (US) guidance was feasible ,safe and required less radiation to achieve same benefit as FL-guided interventions.The success ratio of the ultrasound guided interventions was 85%. The operation time in the US group was shorter than the FL group .In addition, the radiation dosage in the US group was lower than in the FL group. There was no significant difference in pain relief between the US and FL groups.

P soni et al.,[14] stated description of US-guided transforaminal injection (USTFI) is scarce.This is mainly because of shadowing of the foraminal area with the bony structures, and thus, nonvisualization of the final needle tip position at the desired location. At present, USTFI confirmation with fluoroscopy seems essential.

In current study we have combined both ultrasound and fluoroscopy. Initially with ultrasound level of pathology was identified and needle was inserted, then dye was injected and confirmed with fluoroscopy to rule out any intravascular or intrathecal spread.This hybrid technique allowed us to reduce the radiation hazards.

From.our study we observed that VAS scores were equally reduced in both the groups and there was no significant difference.

There was no significant difference in RODS at the end of 1st month in both groups. At the end of 3rd month and 6th month RODS score was better in Dexmedetomidine group with regards to pain intensity,walking,standing ,and performing daily activities as per RODS questionnaire on daily activities like personal care, sitting, walking, sleeping, etc.,

Our study clearly shows that Dexmedetomidine as adjuvant is highly efficacious in improving the quality of life in people suffering from low back ache.

Conclusion:

We conclude that dexmedetomidine mixed with steroid in LTFESI demonstrated a potential safe and effective adjuvant for analgesia in chronic low back-pain patients with significant improvement in Quality of Life at 3,6 months with no significant adverse effects.

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