International Journal of Clinical Trials
Rajkumari K et al. Int J Clin Trials. 2020 Aug;7(3):188-193
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: http://dx.doi.org/10.18203/2349-3259.ijct20203105

Original Research Article

Comparison of the effectiveness between epidural methylprednisolone injection and intranasal calcitonin in reduction of back pain due to osteoporosis in postmenopausal patients: a randomized controlled trial

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Received: 26 December 2019
Revised: 21 March 2020
Accepted: 31 March 2020

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ABSTRACT

Background: Back pain is a common symptom in osteoporotic patients due to spinal compression fracture. Conservative management like nonsteroidal anti-inflammatory drugs and spinal orthoses has not been able to produce early pain relief. Intranasal calcitonin spray is considered effective because of its analgesic effect and increase in bone density. Role of epidural steroid injection for the treatment of osteoporotic back pain has not been studied. This study was conducted to find out the efficacy of epidural methylprednisolone injection in management of osteoporotic back pain in postmenopausal patients.
Methods: Hundred patients with osteoporotic back pain in postmenopausal subjects were allocated into two groups: epidural and calcitonin. Epidural group received a single dose of interlaminar epidural steroid injection with methylprednisolone 80 mg. Calcitonin group received one puff of 200 IU given through one nostril followed to the other nostril the next day. Visual analogue scale for pain was the outcome measurement used. Pain relief at rest within 7 days was taken as early pain relief and within 21 days as late pain relief. Pain relief after 21st day was considered no response. Test of significance was done by Kaplan Meier, Chi square and Fisher exact tests.
Results: Out of 50 patients, 38 patients in the epidural group got pain relief within 7 days and the finding was statistically significant.
Conclusions: Epidural methylprednisolone gives faster pain relief as early as the first post-injection day with a median value of 2 days against 15 days in case of intranasal calcitonin spray.

Keywords: Epidural steroid injection, Intranasal calcitonin, Osteopororosis

INTRODUCTION

Osteoporosis is a systemic skeletal disease characterised by low bone mass and micro architectural deterioration with a consequent increase in bone fragility and susceptibility to fracture. It is a common skeletal disorder but a silent disease, reflected by a low bone mineral density (BMD), till a fracture occurs. With increasing longevity of Indian population, it is now being realised that osteoporosis and its complications are a major cause of mortality and morbidity as in the west.[1]

World Health Organisation (WHO) defines osteoporosis operationally as BMD that falls 2.5 standard deviation below the mean for normal young adults.[2]

Grading based on T-score of BMD can be classified as normal if score is ≥-1, osteopenia if score is from -1 to -2.5, osteoporosis if ≤-2.5 and severe osteoporosis if <-2.5 with fracture.

Osteoporosis has become a major public health problem of epidemic proportions affecting more than 100 million

people worldwide. Women are most commonly affected i.e. one out of every three postmenopausal women are osteoporotic and a majority of elderly including men too are affected.[3]

In India, 61 million people are osteoporotic and one in every third postmenopausal women is at risk of osteoporosis. Fifty percent of postmenopausal women are osteoporotic.[4] It is calculated that 20% of women and 10% to 15% of men would be osteoporotic in India.[5]

Fracture is the major significant cause of morbidity and mortality in osteoporotic patients. Vertebral compression fracture is the most common fracture in osteoporotic patients accounting >50% of total fracture. The most common site is lower thoracic and upper lumbar vertebra (D-11, D-12 and L-1). It mainly involves the anterior part of vertebra affecting trabecular bone by about 40% by 75 years of age.[3,5] Fracture usually occurs following minimal injury and it causes very severe acute pain in the back. Vertebral fracture also can lead to deformity of spine like reduction in vertebral height, kyphosis, scoliosis etc.[3]

Back pain is a common symptom in osteoporosis mainly due to compression fracture of the spine. Usually the pain is severe and most intense at the site of fracture. It may persist for 2 to 3 weeks and then continue with decrease on severity for 6 to 8 weeks. A vertebral compression fracture can be identified either by a radiograph or as a symptomatic clinical event.[6]

Micro-fracture of the vertebra also causes back pain which cannot be detected radiologically. The pain may be so devastating and disabling that hospital admission is usually required.[3]

The possible mechanisms of bone pain due to osteoporosis are the bone become soften and deformed thereby stretching the periosteum of the bone which is the most painful outer covering of the bone; compression fracture stimulate the nociceptors of the nearby apophysial vertebral joint; mal-alignment of vertebral bodies which disturbs the normal biomechanics of spine and radiculopathy due to compression or irritation of the spinal nerve root following the compression fracture.[7] Other causes of back pain may be secondary to paraspinal muscle spasm, spinal arthritis and costal impingement syndrome.[3]

Osteoporotic back pain causes physical, emotional and psychological consequences to the patients as well as to the family members and also cause a big socio-economic burden to the family.

Treatment modalities of osteoporotic back pain are partial rest, pharmacological interventions (e.g. non steroidal anti-inflammatory drugs, morphine) and immobilization of the fracture site with spinal orthoses. Pain management for chronic back pain in osteoporotic vertebral fracture include a program of strengthening exercises of paravertebral, abdominal and glutei muscles, program to improve balance and faulty posture. Further evaluation and treatment of psychological and social consequences may be required.[8]

It is also important to treat the osteoporosis as a whole and not only the osteoporotic back pain. Pharmacological treatment for osteoporosis includes bisphosphonates, teriparatide- recombinant human parathyroid hormone, supplementation of calcium, vitamin D3 and hormonal therapy e.g. estrogen, raloxifene, testosterone.[7,8]

Intranasal calcitonin spray at the daily dose of 200 IU is considered to be very effective in the relief of back pain due to osteoporosis because of its analgesic effect and increase in bone density. The effect is seen in 2 weeks and lasts for about 4 months.[9] Its mechanisms in reduction of back pain are increase in β-endorphin in plasma suggesting involvement of endogenous opiate system of analgesic and inhibition of substance P release, increase in ACTH level which acts by reducing local inflammation and consequent discharge of nociceptor nerve endings and by inhibiting osteoclast activity.[9]

Epidural steroid injection is also use in low back pain due to compression fracture of lumbar spine with radiculopathy in osteoporosis. Its possible mechanisms of pain reduction are; inhibition of unmyelinated nociceptive C-fibre transmission, inhibition of phospholipase A2 and inflammation and reduction in capillary permeability.

Vertebroplasty and kyphoplasty where polymethyl-methacrylate cement is injected percutaneously into the affected vertebra are the latest minimally invasive techniques in the management of acute and chronic back pain in osteoporotic vertebral compression fracture.[4,5]

Given the frequent necessity of providing analgesia for patients with osteoporotic compression fractures, it is important to find out other treatment modalities for the treatment of pain associated with osteoporotic vertebral compression fracture. Recent studies have suggested the use of salmon calcitonin as an initial and an adjunctive treatment for acute, severe and unrelenting back pain due to osteoporotic fracture because it also exhibits analgesic properties.

The role of epidural methylprednisolone injection for the treatment of osteoporotic back pain has not been studied. Therefore, this study was conducted with the aim to find out the efficacy of low dose epidural methylprednisolone injection in management of back pain due to osteoporosis in postmenopausal patients.

METHODS

A randomized controlled study on 100 postmenopausal women having back pain due to osteoporosis who attended the department of Physical Medicine and

Rehabilitation OPD, Regional Institute of Medical Sciences (RIMS), Imphal, India, was conducted from 1st June 2016 to 31st July 2017.

Approval of the Research Ethics Board, RIMS, Imphal was taken before starting the study and written informed consent were obtained from all the subjects.

Postmenopausal subjects with back pain due to osteoporosis as shown by BMD, without neurological finding, with X-ray spines (Saville index) suggestive of osteoporosis were included in the study. However, patients with back pain due to any reasons other than osteoporosis like disc disease, infection, tumour, sprain and strain, chronic steroid use, uncontrolled diabetes, intolerance or allergic to calcitonin, contrast dyes or anesthetics, post spinal surgery patients and those who refused to take part in the study were excluded.

Considering a response rate (relief of pain) of 70% in 14 days in the standard treatment group with intranasal calcitonin and an expected 90% response rate in the epidural injection of methylprednisolone group with 95% confidence power of 80%, the sample size was calculated to be 50 in each arm.

Patients enrolled in the study were assigned to two groups (group A and B) by block randomization method. Group A (study group) received fluoroscopic guided interlaminar epidural injection with methylprednisolone acetate 80 mg plus paracetamol 1000 mg orally and Group B (control group) received intranasal calcitonin plus oral paracetamol 1000 mg.

Study variables were age, age at menopause, duration of back pain, level of vertebral involvement, intensity of pain (visual analogue scale (VAS)), radiological grading of vertebral osteoporosis, BMD (DXA scan), and pain relief (VAS at rest seen on post initiation days).

Study instruments included pre tested proforma; X-ray spine (AP and Lateral views) – screening of osteoporosis, compression fracture; MRI spines (to exclude patients with back pain due to causes other than osteoporosis), SIEMENS Multimobil 5E C-arm and X-ray bone densitometer (lunar prodigy advance, GE Medical Systems, USA).

Pain was measured by VAS and VAS less than or equal to 2 was considered as pain relief at rest while VAS more than or equal to 3 was taken as no pain relief at rest. Pain relief at rest within 7 days was taken as early pain relief and relief within 21 days was late pain relief. In the study, pain relief on 21st day was considered as no response in both the groups. Pain assessment at rest was done before giving epidural methylprednisolone injection or intranasal calcitonin and on a daily basis following the intervention. Non hospitalised patients were advised to record pain relief on the pretested proforma on daily basis.

Bone mineral density was measured by using Dual Energy X-ray Absorptiometry scan (lunar prodigy advance, GE Medical Systems, USA). T-score and Z-score were estimated from the above data by the system software.

T-score quantifies the difference between the participant's BMD and the mean value for young adults from the reference group. The Z-score is used to compare the participant's BMD with the mean value for individuals of the same age.

For fluoroscopic guided interlaminar epidural steroid injection, patient was placed prone with a pillow under lower abdomen. The area was prepared by antiseptics and draped in sterile manner. After identifying the desired interlaminar space, a guiding needle was placed on the skin and the C-arm was positioned so that the midline of the interlaminar space was correctly identified. Skin was then anesthetized with 1% lidocaine. The epidural needle (20 gauge Tuohy) was placed in the direct midline position. After penetrating the interspinous ligament, the stylet was removed and the needle was connected to a 5 cc, "three ringed" glass syringe that was half filled with air. Using gentle pressure on the plunger of the syringe, the needle was slowly advanced towards the ligamentum flavum, and subsequently into the epidural space, while intermittent lateral fluoroscopic views were obtained to ascertain the needle depth. Once the needle reached the epidural space with appropriate loss of resistance to air, nonionic contrast 1 ml was injected to confirm epidural placement. A lateral fluoroscopic image was obtained as well as an AP image. If no intravascular or soft tissue contrast pattern was seen, injection methylprednisolone 80 mg was given slowly into the epidural space. Then, the needle was removed and covered with a sterile pad. Patient was advised bed rest in supine position for 2 hours.

For intranasal calcitonin spray, patients were instructed about the procedure to inhale and how to use the spray beforehand. With the patients in sitting position and after checking the patency of the nostril, only one puff of 200 IU was given at one time and asked to take a deep inhalation for 10 seconds then exhale. The same procedure was followed on the next day but to the other nostril.

All the patients were followed up for 21 days starting from the day of the intervention.

Statistical analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 21. Descriptive analysis including median, percentage, standard deviation were used. Test of significance was done by employing Kaplan Meier test between the two groups. Chi- square test and Fisher exact test were used to compare between pain

relief and other variables in both the groups. Value of p<0.05 was considered significant.

RESULTS

There were no significant differences in the baseline characteristics of the two groups and hence were comparable with reference to their respective study variables.

Out of 50 patients, 38 patients in the epidural group got pain relief within 7 days and the finding was statistically significant (p=0.000). The median onsets of pain relief were 2±7.8 days in the epidural group and 15±3.7 days in the calcitonin group and pain relief was noted even on the first of post therapy period in the epidural group against the tenth post initiation day in the calcitonin group.

Table 1: Baseline characteristics of the patients.

Variables		Epidural group (n=50)	Calcitonin group (n=50)	P value*
		N (%)	N (%)	
Patients age (years)	≤69	27 (54)	33 (66)	0.22
	≥70	23 (46)	17 (34)	
Menopausal age (years)	≤47	8 (16)	9 (18)	0.79
	≥48	42 (84)	41 (82)	
Duration of back pain (months)	≤3	28 (56)	33 (66)	0.30
	≥4	22 (44)	17 (34)	
Bone mineral density (T-score)	≤-3.5	36 (72)	40 (80)	0.34
	≥-3.6	14 (28)	10 (20)	
X-ray grade of osteoporosis	≤2	17 (34)	17 (34)	1.00
	≥3	33 (66)	33 (66)	

*P value by Fisher exact test and Pearson Chi- square test (p value ≤0.05 was taken as significant).

Table 2: Pain relief in the two groups.

Pain relief	Response (yes/no)	Epidural group (n=50)	Calcitonin group (n=50)	P value*
		N (%)	N (%)	
Early relief (≤7 days)	Yes	38 (76)	0	0.00
	No	12 (24)	50 (100)	
Late relief (≤21 days)	Yes	39 (78)	33 (66)	0.181
	No	11 (22)	17 (34)	
Median onset of pain relief (days±SD)		2±7.8	15±3.7	0.00

yes=VAS<3; no=VAS ≥3.

Table 3: Association between early and late pain relief and the study variables in the epidural group.

Variables		Early pain relief			Late pain relief		
		With pain relief (n=38)	Without pain relief (n=12)	P value*	With pain relief (n=39)	Without pain relief (n=11)	P value*
		N (%)	N (%)		N (%)	N (%)	
Patients age (years)	≤69	24 (63.2)	3 (25)	0.04	25 (64.1)	2 (18.2)	0.00
	≥70	14 (36.8)	9 (75)		14 (35.9)	9 (81.8)	
Menopausal age (years)	≤47	6 (15.8)	2 (16.7)	1.00	6 (15.4)	2 (18.2)	0.82
	≥48	32 (84.2)	10 (83.3)		33 (84.6)	9 (81.8)	
Duration of back pain (months)	≤3	18 (47.4)	10 (83.3)	0.04	19 (48.7)	9 (81.8)	0.05
	≥4	20 (52.6)	2 (16.7)		20 (51.3)	2 (18.2)	
Bone mineral density (T-score)	≤-3.5	28 (73.7)	8 (66.7)	0.71	29 (74.4)	10 (90.9)	0.48
	≥-3.6	10 (26.3)	4 (33.3)		10 (25.6)	1 (9.1)	
X-ray grade of osteoporosis	≤2	16 (42.1)	1 (8.3)	0.03	16 (41)	1 (9.1)	0.04
	≥3	22 (57.9)	11 (91.7)		23 (59)	10 (90.9)	

Table 4: Association between late pain relief and the study variables in the calcitonin group.

Variables		With pain relief (n=33)	Without pain relief (n=17)	P value*
		N (%)	N (%)	
Patients age (years)	≤69	23 (69.7)	10 (58.8)	0.44
	≥70	10 (30.3)	7 (41.2)	
Menopausal age (years)	≤47	5 (15.2)	4 (23.5)	0.46
	≥48	28 (84.8)	13 (76.5)	
Duration of back pain (months)	≤3	20 (60.6)	13 (76.5)	0.26
	≥4	13 (39.4)	4 (23.5)	
Bone mineral density (T-score)	≤-3.5	25 (75.8)	15 (88.2)	0.29
	≥-3.6	8 (24.2)	2 (11.8)	
X-ray grade of osteoporosis	≤2	12 (36.4)	5 (29.4)	0.62
	≥3	21 (63.6)	12 (70.6)	

Early pain relief was noted in 63.2% (n=24) patients in the age group below 69 years which was statistically significant (p=0.04) and late pain relief was noted in 64.1% (n=25) in the same age group which was also significant (p=0.00). Among the early menopausal group (≤47 years), 84.2% (n=32) patients got early pain relief and 84.6% (n=33) got late pain relief against 15.8% (n=6) and 15.4% (n=6) patients respectively of late menopausal age (≥48 years) which was statistically not significant. Out of 38 early pain relief patients, 52.6% (n=20) patients had long duration back pain (≥4 months) while 47.4% had short duration back pain (≤3 months) which was statistically significant. Also, 59% (n=23) patients with X-ray grades 3 and 4 whereas 41% (n=16) patients with grades 1 and 2 got pain relief within 21 days which was statistically significant (p=0.04).

No significant results were found between the late pain relief and the other variables in the calcitonin group.

DISCUSSION

Intense back pain is a common symptom in osteoporosis mainly due to compression fracture of the spine. It may persists for 2 to 3 weeks and then continue with decrease on severity for 6 to 8 weeks.[6] Even micro fracture of the vertebra also cause back pain which cannot be detected radiologically. Again, the pain may be so devastating and disabling that hospital admission is usually required.[3]

The present study clearly revealed that the epidural group fared significantly better than the calcitonin group in terms of onset of pain relief and the finding was statistically significant (p=0.00). It is also found that both the epidural and calcitonin groups have significantly low pain score following the intervention. However, there was a mark difference in the onset of pain relief in the two groups. Median onset of pain relief in the epidural and calcitonin groups were 2±7.8 and 15±3.7 days respectively. This finding is similar to other reports.[7-9]

This study shows that pain relief in the epidural group was better with the younger age group which was statistically significant. This finding may be because of the reason that younger the age of the patients, less severe is the degree of osteoporosis. Pain relief was also better with lesser duration of back pain. The difference in finding can be explained as less duration of back pain meaning thereby lesser duration of osteoporosis. In the patients with X-ray grades 3 and 4 of osteoporosis, 11 out of 12 failed to get early pain relief and 10 out of 11 patients too failed to get late pain relief in the epidural group. The pain relief was less as the grades of osteoporosis increased.

In the calcitonin group, association between late pain relief and the other study variables with reference to age of patients, menopausal age, duration of back pain, BMD and the X-ray grades of osteoporosis were compared by using Chi-square test. However, no significant results were found between the late pain relief and the other variables in this study.

There were no major complications in any of the patients in the epidural group except injection related pain, light headache in 4 patients while in the calcitonin group 3 patients complained of flushing following the nasal spray otherwise there were no serious side effects. Unlike vertebroplasty, epidural corticosteroid injections have some additional advantages as the procedure is simpler and complications are negligible.

The limitations of the study were that the sample size was small and most importantly there was no follow up to highlight the duration of pain relief in both the groups, so also the possible side effects. Study based on self-reported questionnaire regarding pain relief on subsequent days could be another limitation. Therefore, a similar study with an extended follow-up on a bigger sample size is recommended.

CONCLUSION

Epidural methylprednisolone gives better and faster pain relief as early as the first post injection day with a median

value of 2 days against 15 days in case on nasal calcitonin spray. Early onset of pain relief was significant among younger age group, lesser duration of back pain and lower grades of osteoporosis. Further study with a bigger sample size is suggested to find out duration of pain relief and long term side effects of the epidural methylprednisolone injection and intranasal calcitonin

ACKNOWLEDGEMENTS

Authors would like to acknowledge all the participants who participated in the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee, RIMS, Imphal

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Cite this article as: Rajkumari K, Singh AJ, Singh LN. Comparison of the effectiveness between epidural methylprednisolone injection and intranasal calcitonin in reduction of back pain due to osteoporosis in postmenopausal patients: a randomized controlled trial. Int J Clin Trials 2020;7(3):188-93.