

A COMPARATIVE STUDY TO ASSESS THE ROLE OF CALCITONIN IN EARLY FRACTURE HEALING (AS PER RADIOLOGICAL APPEARANCE) IN INTERTROCHANTRIC FRACTURES TREATED WITH INTRAMEDULLARY NAILING

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Abstract:

Background : The objective of this study was to evaluate the outcome of a combined therapy of intramuscular and intranasal salmon calcitonin for treatment of intertrochantric fractures (post-op) leading to early fracture healing and repair, pain relief and functional recovery when compared with placebo drug.

Materials and methods : It is a comparative study in which 40 adult patients between ages of 20 to 75 years with intertrochantric fractures were considered and admitted under the Department of Orthopaedics of KLES Dr. Prabhakar Kore Hospital and MRC, Belgavi from April 2016 to September 2016. Out of these 40 patients, 20 patients were randomly assigned a course of Intra muscular salmon calcitonin 100 IU once a day for 7 days, followed by Intra-nasal spray of salmon calcitonin 200 IU once a day for 3 months along with Calcium 500mg once daily and Vitamin D 60,000 IU once a week and the remaining 20 patients were given placebo along with calcium and vitamin D similar to the first 20 patients. All the patients were followed up post 6 weeks and 10 weeks from the therapy and their radiographs were taken. The callus formation and healing of fracture was determined by radiographic evaluation by RUSH score (radiological union scale of hip) and the pain relief was measured by VAS scale.

Results: Three months after the operation, among patients with internal fixation using DHS or IMIL nailing, fusion of the fracture and disappearance of fracture line was observed in X-rays in 92% of the cases in the salmon calcitonin group and in 63% of the cases in the placebo group. Difference in RUSH scores of the test group and the control group was statistically significant ($P < 0.005$) which indicate that the strength and quality of the callus formation is improved by administering salmon calcitonin following a fracture, leading to better fracture healing. The median intensity of pain ($P < 0.001$) in visual analogue scale was 0 mm (IQR 0.20) in the calcitonin group and 4 mm (IQR 0.33) in the placebo group ($P = 0.15$) and subsequently the need for analgesic intake was reported to have decreased by approximately 60 %

Conclusion : We conclude that a therapy of combined intramuscular and intranasal salmon calcitonin given post operation is useful for early healing and repair of intertrochantric fractures and offers immediate and lasting pain relief.

Keywords: Calcitonin, Early Fracture Healing, Intertrochantric Fractures, Intermedullary Nailing

Introduction

Intertrochantric fractures account for the highest morbidity in the elderly population

and are generally associated with osteoporosis. They are associated with low energy trauma in elderly and high energy trauma in young population (<40 yrs). Low

energy falls from a standing height account for 90% of community hip fractures in above 50 yrs age group and are the commonest fractures in females above 65 yrs.

Gulbarg et al in 1997 has expected the incidence of Intertrochantric fractures to double by 2025 to 2.6 million.

They are the most frequently operated fracture type in the elderly, have the highest post-operative mortality rate and lead to prolongation of hospital stay and late mobilization owing to the population they commonly affect and lead to poor recovery of functional independence after conventional fracture care.

Calcitonin has been used to treat hip fracture patients because it's a potent inhibitor of bone resorption. Old age is the most important risk factor for osteoporosis. Bone loss continues into old age at rate of 1-2% per year and is increased by immobilization. This bone loss may be further increased after hip fracture. Calcitonin is known to decrease pain and promote early mobilization apart from stabilization of callus formation and promoting fracture healing.¹

Intranasal Calcitonin prevents bone loss, the markers of bone formation were increased.¹ It was found that after a 3 month course of intra-nasal Calcitonin in an elderly Intertrochantric fracture treated with CRIF using Nailing improved fracture fusion which was statistically significant.² Animal studies indicate that Calcitonin may augment fracture healing by promoting cartilaginous phase of fracture healing-a prerequisite for endochondral ossification, besides leading to reduction in post-op pain.⁵ Calcitonin shows favourable outcome in spinal pathological fractures with an increase in fracture consolidation and improved quality of life.⁶ Intranasal Calcitonin reduces acute bone loss in patients with intertrochantric fractures and prevents fractures in contra lateral hip of elderly.³ Intranasal Calcitonin has been proven to reduce bone loss and increase markers of bone formation and reduce markers of bone resorption when used in cases of fracture management post-operatively.¹

Calcitonin reduces osteoclastic mediated bone resorption and decreases risk of osteoporotic fractures.¹ CGRP-alpha (calcitonin gene related peptide) signalling had specific effects on periosteal mineralising surface activation in response to mechanical loading leading to earlier mobilization.⁴ Use of calcitonin allowed earlier mobilization

and weight bearing in clinical cases with rigid fixation and the strength and quality of callus formation was improve by administering Calcitonin following a fracture.²

Systematically administered Calcitonin causes calcification of growth plate and an acceleration of skeletal growth and cartilage callous maturation.⁵ By the end of six weeks, subjects using calcitonin could resist significantly larger torsional forces which was due to more mature callus formation.² Calcitonin promotes cartilaginous phase of fracture healing and callus was rich in neutral protease (promotive substances of bone matrix) also vascularisation of callus was increased owing to CGRP-alpha which is the causative neuropeptide for callus angiogenesis; it is direct regulator of osteoblastic functions.² Peptidergic sensory sensory nerve fibres innervating bone and periosteum are rich in CGRP, an osteoanabolic neurotransmitter(4). Salmon Calcitonin can not only increase BMD in osteoporotic bones, but also enhance the bone biomechanical properties and improve the process of fracture healing in fractured osteoporotic bones.⁷

The rate of bone fusion evaluated by x-rays and CT in calcitonin group was significantly higher than bisphosphonates group, there was greater pain relief and faster mobilization in Calcitonin group.⁸

Materials and methods

Adult patients between ages 20 to 75 years with intertrochantric fractures admitted under the Department of Orthopaedics of KLES Dr.Prabhakar Kore Hospital, Belgaum. The aim of our study was to assess whether a combined therapy of intravenous and intranasal Calcitonin can lead to early fracture union when given post-operatively in intertrochantric fractures. Intramedullary nailing was used as a common platform to demonstrate healing in calcitonin and control groups.

The design of this study was as a comparative study. It was conducted from April 2016 to September 2016.

Selection Criteria:

Inclusion criteria: Male and female pts from age 20-75 yrs with intertrochantric fractures.

Exclusion criteria:

Pathological fractures (chronic debilitating liver/kidney disease/cancer/metabolic bone disease/septic arthritis/osteomyelitis/ Marfan’s/ Ehler Danlos syndrome)

Patients not given physician fitness for surgery.

Patients allergic to calcitonin.

Participants not willing to enrol for the study

Procedure-

Forty adult patients, ranged 55-80 yrs participated in the study. The subjects were screened based on the inclusion and exclusion criteria. There were 25 male and 15 female patients. Ethical clearance was obtained from the institutional ethical review board. The purpose of the study was explained and written informed consent was obtained from all the participants. Once the subjects selected for the study, their history was recorded and clinical examination was performed. Also the following investigations were done after admitting the patient - CBC, ESR, RBS, MR, coagulation profile, renal function tests, liver function tests, HIV-1,2, serum. T3, T4, serum uric acid

Treatment Protocol

Allergic testing of calcitonin on patient was first done. Out of the total strength of forty, 20 patients were assigned into the Calcitonin group and 20 were assigned in the control group. Both of the groups were operated by closed reduction and intramedullary nailing. Post operatively, the Calcitonin Group patients were given IM Calcitonin injection 100 IU OD along with Calcium tablet 500mg OD and Vitamin D 60,000 IU once a week from POD-0 TO POD-7 (post-operative day). After POD-7 the patients were given Intranasal Calcitonin formulation 200 IU/day OD which was continued for the next three months.

In the Control group, only Calcium 500mg OD and Vitamin D 60,000 IU once weekly was given for three months. All the procedures were performed in the ward where the patients were admitted.

The patients were followed up at intervals of 6 weeks and

10 weeks from the day of the operation, accompanied by check X-rays which were analysed by the investigator as per RUSH scale to evaluate the amount of fracture healing. Healing of fracture was demonstrated by callus formation. Fusion of fracture was determined by disappearance of 2D fracture line on X-ray.

Statistical Analysis

Outcome was analyzed by using the SPSS program. Data was computed and analyzed by various statistical methods.

Radiographic Union Scale for Hip (RUSH)

Reviewer Name:
 Subject ID:
 Date of Radiograph:
Section 1: General Impression
 Using your overall general impression, has the fracture healed?
 Healed Not Healed

Section 2: RUSH

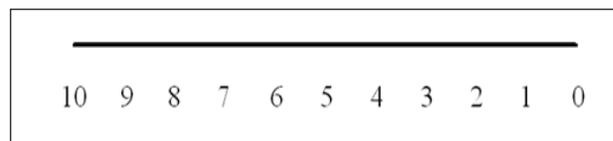
1) Cortical Index - Bridging

Cortex	No Cortical Bridging Score=1	Some Cortical Bridging Score=2	Complete Cortical Bridging Score=3	Total Score (Range, 4 to 12)
Anterior Cortex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Posterior Cortex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Medial Cortex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Lateral Cortex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Overall Score				

2) Cortical Index – Disappearance of the Fracture Line

Cortex	Fracture Line Fully Visible Score=1	Some Evidence of the Fracture Line Score=2	No Evidence of the Fracture Line Score=3	Total Score (Range, 4 to 12)
Anterior Cortex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Posterior Cortex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Medial Cortex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Lateral Cortex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Overall Score				

VAS Pain scale-



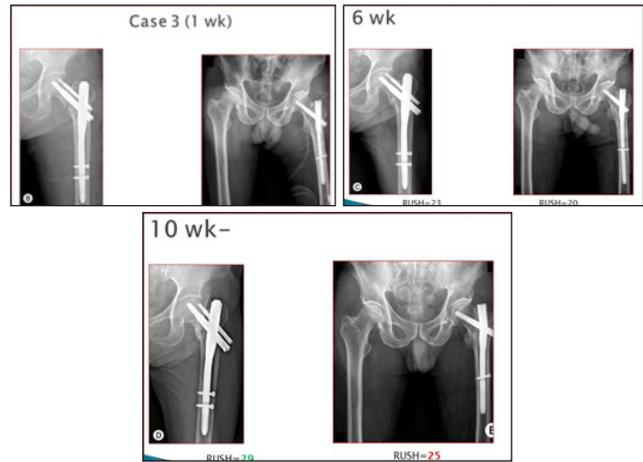
Results:

At baseline, the median age of patients in the 2 groups was similar (67 years [range 55–80 years]). There were no cases of any allergic reaction to Salmon Calcitonin drug. There were no side effects observed from the drug. 10 weeks after the operation, when 20 patients of the calcitonin and control group were examined (all of which were treated with internal fixation using nailing), fusion of the fracture fragments and disappearance of fracture line was observed in X-rays in 92% of the cases in the salmon calcitonin group

and in 63% of the cases in the control group. Difference in RUSH scores of the Test group and control group was statistically significant ($P < 0.005$) which indicate that the strength and quality of the callus formation is improved by administering salmon calcitonin following a fracture, leading to better fracture healing. Increased RUSH score was observed in patients receiving Calcitonin, leading to faster obliteration of the fracture line. The healing was also not dependent on the type of nail used.

The difference in pain relief according to the visual analogue scale was statistically significant ($P < 0.001$) and subsequently the need for analgesic intake was reported to have decreased by approximately 70 %. Another important finding was that by POD-4 the patient was rendered completely pain-free with VAS=1-2 leading to discontinuation of painkillers. This effect continued for the next two months (due to endorphins augmentation effect) and led to a Pain free regimen, which increased faith of the patient in the regimen.

The follow-up x-rays for the cases are as follows-

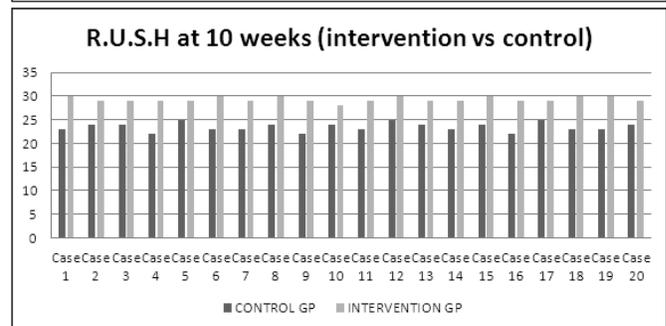
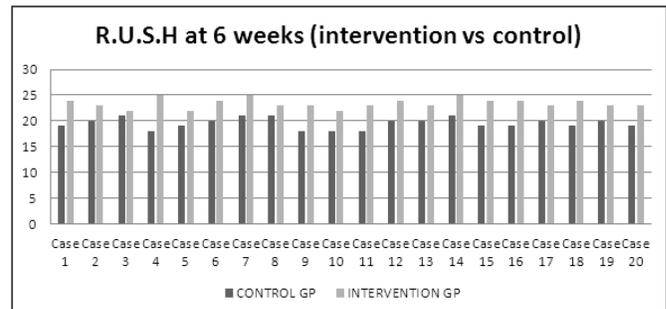


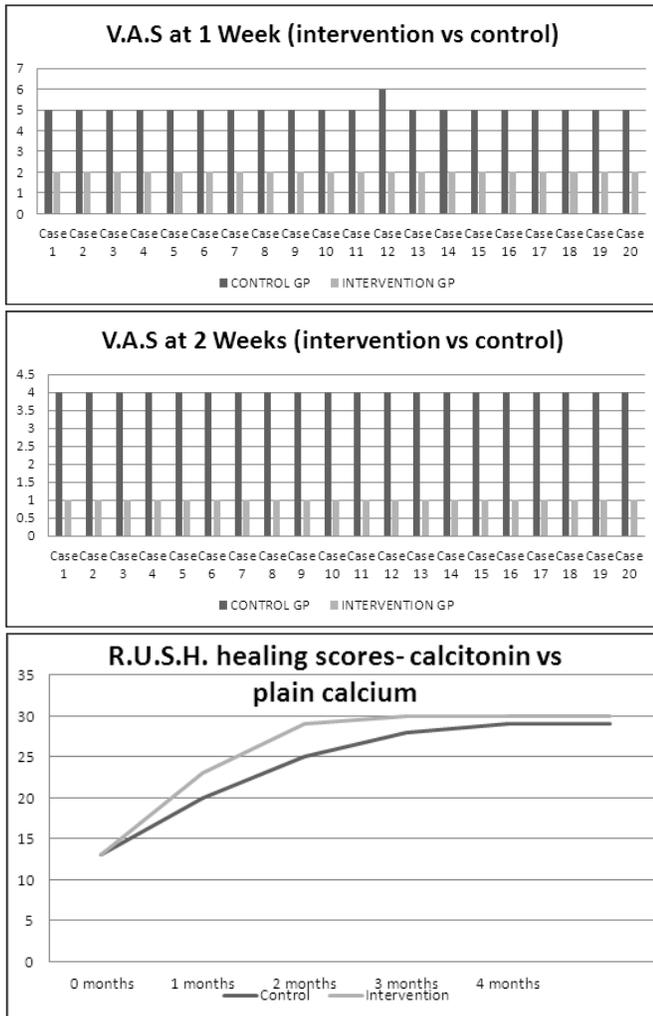
Results- RUSH scores-

Average RUSH score at-	Control group	Intervention group	P-value
6 wks	20	23.33	$P < 0.005$
10 wks	24	29.3	$P < 0.005$

Results- VAS score-

Average VAS score at-	Control group	Intervention group	P-value
1 wk	5	2	$P < 0.001$
2 wk	4	1	$P < 0.001$





increased serum beta endorphin levels.

We thus conclude that a therapy of combined intramuscular and intranasal salmon calcitonin given post-operatively is useful for early and better healing and repair of intertrochantric fractures. Also, calcitonin therapy offers immediate and lasting pain relief and better functional recovery leading to faster and painless mobilization and weight bearing after rigid fixation. Salmon calcitonin has been found effective in early fracture healing in intertrochantric fractures as shown by a significant increase in RUSH fracture healing scores with a dose of 100 IU given intramuscularly and 200 IU given intranasal. Our patients treated with calcitonin also showed a significant improvement in reduction in severity of pain, as observed in the significantly decreased VAS scores soon after starting of therapy. Systematically administered Calcitonin causes calcification of growth plate and an acceleration of skeletal growth and cartilage callous maturation. Calcitonin promotes cartilaginous phase of fracture healing and callus was rich in neutral protease (promotive substances of bone matrix) also vascularisation of callus was increased owing to CGRP-alpha which is the causative neuropeptide for callus angiogenesis; it is direct regulator of osteoblastic functions.

Conclusion

Intertrochantric fractures are the most frequently operated fracture type in the elderly and have the highest post-operative mortality rate and lead to prolongation of hospital stay and late mobilization owing to the population they commonly affect and lead to poor recovery of functional independence after conventional fracture care.

The aim of this study was to assess whether a combined therapy of intravenous and intranasal Calcitonin can lead to early fracture union when given post-operatively in intertrochantric fractures.

Patients included in the present study had beneficial effects on the healing of fractures with concomitant use of the nasal salmon calcitonin leading to early fracture healing, more mature callus formation and faster mobilization. Also calcitonin is suggested to have analgesic effects. Several experimental and clinical studies established the analgesic effects of calcitonin via central serotonergic system and

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