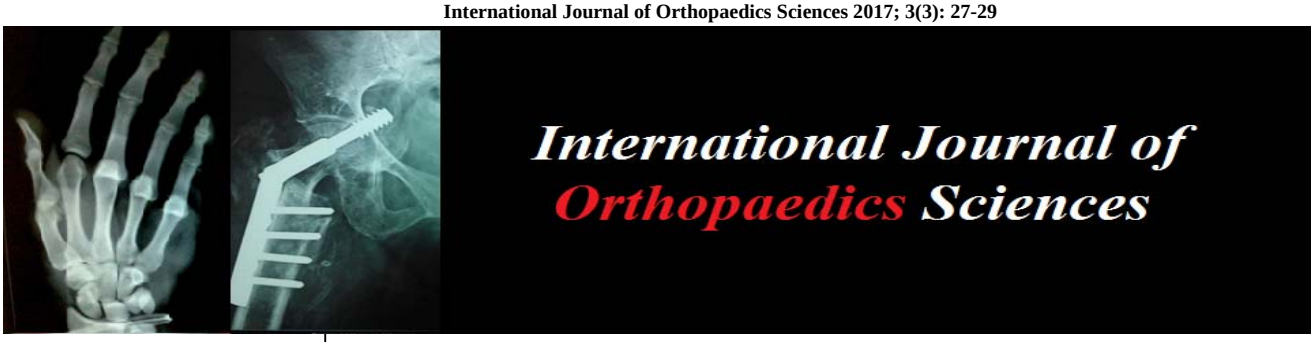

ISSN: 2395-1958
IJOS 2017; 3(3): 27-29

www.orthopaper.com
Received: 06-05-2017
Accepted: 07-06-2017

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Effect of calcitonin in the outcome of distal radial fractures in elderly patients

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DOI: http://dx.doi.org/10.22271/ortho.2017.v3.i3a.06

Abstract
Background: Distal radial fractures are common and produce significant morbidity in elderly osteoporotic individuals. Calcitonin prevents bone resorption in osteoporotic individuals and hence can reduce morbidity in the immediate post fracture period. But scientific evidence regarding its efficacy in improving pain and functional abilities is lacking. Hence this study is being done to assess the clinical and radiological parameters after calcitonin usage in immediate post fracture period.
Methods: 50 elderly patients with distal radial fractures treated conservatively with plaster application were randomly divided into two groups. One group received 400 IU of nasal salmon calcitonin daily for 6 months and the other group did not receive it. Demographic data of patients, co-morbid illnesses, and AO type were recorded. Patients were followed at 2, 4, 6, 8, 12 and 24 weeks post fracture. Their pain score (VAS), functional abilities with Mayo wrist score and radiological union were assessed. Statistical analysis was done with student t test and pearson correlation.
Results: VAS score improved significantly from 9.57 to 2 in calcitonin group compared to 9.31 to 4.42 in non-calcitonin group. Mayo wrist score showed significant difference in calcitonin group. Fracture union and radiological parameters were comparable in both groups with no statistical significance. CRPS was less frequent in patients who took calcitonin.
Conclusion: Calcitonin improves pain and functional outcome in elderly patients with distal radial fractures, reducing the incidence of CRPS. We recommend its routine usage in osteoporotic individuals with distal radial fractures predisposed for CRPS.

Keywords: Calcitonin, CRPS, distal radial fracture, pain score

Introduction
Distal radial fractures are one of the common osteoporotic fractures of elderly. They produce significant morbidity and limitation of activities of daily living [1]. Most of them are managed conservatively even though operative treatment has been on the rise since 2000.Osteoporosis is definitely present in distal radial corticocancellous junction, predisposing these patients. Calcitonin has documented benefits in senile and postmenopausal osteoporosis [2]. It has been proven to reduce the risk of osteoporotic vertebral compression fractures and hip fractures.
Complex regional pain syndrome I, previously known as reflex sympathetic dystrophy is a chronic debilitating condition characterized by pain, swelling, stiffness, discoloration, hyperhidrosis and osteoporosis in the affected extremity. The intensity of pain in CRPS I worsens the expected clinical outcome of distal radial fractures [3]. The resulting stiffness of joints and disuse atrophy produces long term disability. The pathogenesis of this syndrome is not well understood. Hence no single treatment has been proven to be totally effective.
Calcitonin can reduce morbidity in the immediate post fracture period by preventing bone resorption in osteoporotic individuals [4]. Calcitonin by virtue of its analgesic and antiresorptive effect can reduce the incidence of CRPS and improve functional outcome in these patients. But scientific evidence regarding its efficacy in improving pain and functional abilities is lacking. This study is focused at the functional outcome in conservatively treated distal fractures in elderly people treated with nasal salmon calcitonin.

Materials and Methods
50 elderly patients (>60 years) with distal radial fractures treated conservatively by plaster application from 2015 January to May 2016 were included in the study.

They were randomly divided into two groups of 25 each by random table method.

All patients underwent fracture reduction under hematoma block with 5 ml of 1% lignocaine in outpatient department. Below elbow plaster of Paris slab was applied in all patients after closed manipulation and reduction. Patients in first group were given salmon calcitonin nasal spray and the second group was not. Both the groups were supplemented with same calcium, vitamin D3 supplements and vitamin C preparations. Plaster was changed and check x-rays were taken every 2 weeks till fracture union. All patients underwent standard physical therapy program for fingers and shoulder from the first day of treatment.

Epidemiological data of patients, their BMI, occupation, mechanism of injury, velocity of injury, their dominant side, co-morbid illnesses and AO fracture type were recorded. The inclusion criteria of patients were extra-articular fractures, closed fractures. Pathological fractures, open fractures, refractures, concomitant fractures of upper limb were excluded from the study.

Clinical data measuring the range of movements of wrist, elbow, shoulder and evidence of CRPS were recorded. CRPS was diagnosed using Veldman's criteria. Out of the 5 cardinal signs and symptoms namely diffuse pain, diffuse swelling, limited range of motion, abnormal skin color, and temperature relative to the other limb if 4 were present in an area much wider than the primary site of trauma and it increased by use of the limb, diagnosis of CRPS1 was made.

Radiological parameters namely radial length, radial inclination, sagittal plane orientation, ulnar variance were measured. Functional outcome was assessed with Visual Analog Scale and Mayo wrist score. Mayo wrist score uses pain intensity, functional status, range of motion and grip strength for assessing the outcome. Statistical analysis was performed using students' t test and Pearson correlation co-efficient.

Results

The mean age of patients in both the groups was 69 and 68.75 years for non-calcitonin and calcitonin groups respectively. 68% of patients were females in both groups. Low velocity domestic fall was the most common cause of injury. 72% of fractures were of AO type 23A2. Left side (60%) was more frequently injured than right side (40%). Their BMI was comparable between groups, 23.45 and 23.20 in non-calcitonin and calcitonin groups respectively. Diabetes mellitus was the most common co-morbid illness, seen in 24% individuals.

Pretreatment VAS score changed from 9.31 to 4.42 at final follow-up in non-calcitonin group and 9.57 to 2 in calcitonin group. The change in VAS score was statistically significant ($p<0.05$).Final dorsiflexion was 31.15 degrees and 41.25 degrees in non-calcitonin and calcitonin groups. Final palmar flexion was 28.54 and 32.92 degrees in both groups. Supination and pronation were 24.62 and 29.62 degrees in non-calcitonin group. It measured 25.58 and 30.42 degrees in calcitonin group. Range of motion was statistically significant between the two groups. Shoulder Abduction was limited in more patients (28%) in non-calcitonin group than calcitonin group (12%).

The mean values of radial inclination, radial length, sagittal plane orientation at the final follow-up were 15.85 degrees, 11.09mm and 4.50 degrees volar in non-calcitonin group and 15.92degrees, 11.02 mm and 3 degrees volar in calcitonin group with no significant difference.

Fracture union took 8.15 weeks and 7.67 weeks in non-calcitonin and calcitonin groups respectively, and it was not significant statistically. Mayo wrist score was 72.8 and 79.6 at final follow-up in non-calcitonin and calcitonin groups ($p<0.05$). The incidence of CRPS was 36% patients in non-calcitonin group and 12% in patients who took calcitonin ($p<0.05$). Pearson correlation coefficients showed no significant correlation between the radiological parameters, age, side, mechanism of injury, BMI, AO fracture type and the incidence of CRPS.

Discussion

Distal radial fractures are a common cause of morbidity in elderly patients. The soft tissue swelling exaggerates pain and decreases patient satisfaction leading to poor clinical outcome [5]. CRPS is a compounding problem seen in postmenopausal osteoporotic patients with distal radial fractures and nerve injuries.

The incidence of CRPS in distal radial fractures varies from 2% to 39%. CRPS was common in females, poor economic status and in those with hereditary predisposition[6]. In the present study, the incidence of CRPS is 16% and 36% in calcitonin and non-calcitonin groups respectively. The severity of injury, the radiological parameters and psychosocial profile of individuals had no significant correlation to the development of this syndrome in a study by Atkins *et al* [7]. This correlates well with the current study. CRPS and its resultant osteoporosis contribute to delayed healing and nonunion. The delay in fracture healing and the occurrence of nonunion occurs due to demineralisation of bone.

Karnezis *et al*. [8], in their study on distal radial fractures noted that the initial radiographic parameters and the final outcome, incidence of CRPS had no statistically significant correlation as evident by the function and pain scores. But in this study, we found a significant correlation between mayo wrist score and CRPS by person correlation coefficient analysis.

Treatment of CRPS in fractures is largely empirical. Early recognition and treatment of CRPS improves patients' outcomes. The only drug therapy used systemically and evaluated in multiple controlled trials is for that affecting bone resorption. In Randomised Control Trials on CRPS oral, topical, and intravenous drugs which targ*et al*pha-adrenergic receptors and the sympathetic nervous system have proved to be ineffective [9].

Karponis *et al*. [10], in their study noted 50% reduction in pain based on the VAS scores with usage of calcitonin in immediate post fracture period. Calcitonin increases the endorphins level in CNS and produces analgesic effect. Its efficacy to reduce pain is well documented in osteoporotic compression fractures of spine, coccygeal fractures and hip fractures. Pain at rest was reduced and its peak effect was at 4 weeks in their study. Prolonged use of it has reduced therapeutic effect due to antibody formation against its molecules. So they suggested short course of calcitonin can be effective in distal radial fractures for alleviating the pain and facilitating earlier rehabilitation in patients.

Calcitonin was found to minimize the bone loss occurring due to immobilization in patients with hip fractures. Immobilization after fracture due to its stress shielding effects, disuse and vasomotor effects leads to localized osteoporosis [11]. The analgesic effect of calcitonin is attributed to multiple mechanisms like production of β-endorphin, histamine interference, inhibition of prostaglandin

and cytokine production and modulation of pain perception through a central pathway involving serotonin [12].

Nasal Salmon calcitonin is useful in number of painful conditions including reflex sympathetic dystrophy syndrome, adhesive capsulitis, vertebral crush fractures and metastasis and pain due to phantom limb. The intranasal route has less undesirable effects, and a faster, effective analgesia than injectable one [13].

In this study, there is a statistically significant difference in VAS Scores and Mayo wrist score between non-calcitonin and calcitonin groups. Usage of nasal calcitonin in distal radial fractures can reduce the pain effectively and hence improve the final functional outcome in osteoporotic individuals. NSAIDs given to reduce in the post fracture period can delay fracture union by reducing the inflammatory phase essential for fracture healing. These drugs can be avoided or reduced with the usage of calcitonin.

In individuals suffering from CRPS significant improvement in pain scales were seen in patients treated with calcitonin and physical therapy than those treated with physical therapy alone. At least calcitonin was suggested even if physical therapy was not possible[14]. Pain at rest and range of motion improved with calcitonin in patients treated for CRPS. Their ability to work improved significantly.

Gobelet in his study on Calcitonin as an addition to physical therapy in CRPS claimed it is an effective treatment for CRPS type I because of its analgesic effect [15]. Sahin *et al*., in their study comparing paraacetamol and calcitonin in patients with upper extremity trauma with CRPS concluded that calcitonin does not make any favourable contribution in the treatment of patients with acute CRPS [16]. In contrast to their findings, our study shows a significant positive correlation in the incidence of CRPS between both groups. In patients treated with calcitonin, CRPS was less frequent. The decrease in CRPS can be attributed to the ability of calcitonin to reduce pain better since pain is the common inciting factor for CRPS. Its anti-resorptive property in osteoporosis might help these fractures from further demineralisation.

We have a few limitations in our study. The sample size is smaller. The markers of bone turnover are not studied because of the cost constraints. We recommend a study in large scale with a longer followup measuring the indicators of bone metabolism to definitively recommend usage of calcitonin in distal radial fractures.

Conclusion

In osteoporotic distal radial fractures, the functional outcome and pain improves better with the usage of calcitonin in the healing period. CRPS occurs less frequently in those who take calcitonin. Hence calcitonin can be used routinely in osteoporotic individuals with distal radial fractures with predisposition for CRPS.

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