

Role of Vitamin C in Prevention of Complex Regional Pain Syndrome in Patients with Distal End of Radius Fractures

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Abstract: *Introduction:* Fractures of the distal radius are now easily recognized and are the most common fracture of the upper extremity fractures, making up at least one-sixth of fractures encountered in the emergency department. This study aims to investigate whether Vitamin C is useful in decreasing the incidence of CRPS in patients with distal end of radius fractures treated conservatively. *Method:* In a double-blind, prospective study, 150 patients were randomized into two groups, one given a placebo and the other given Vitamin C 500 mg once a day for 6 weeks. They were evaluated at Day 0, 7, 28 and 42. *Results:* The prevalence of Complex Regional Pain Syndrome was 2.7% in the Vitamin C group and 13.3% in the placebo group. Out of the affected patients, 83.3% were women and 16.7% were men. *Conclusion:* This supports our hypothesis that Vitamin C given daily for 6 weeks in patients with distal end radius fractures reduces the incidence of Complex Regional Pain Syndrome.

Keywords: Vitamin C; Distal End Radius Fractures; Complex Regional Pain Syndrome; Colles Fractures; DASH Score

1. Introduction

Fractures of the distal radius are now easily recognized and are the most common fracture of the upper extremity fractures, making up at least one-sixth of fractures encountered in the emergency department. While this injury has likely been common since humans first walked the earth, it was Petit, Pouteau, and Colles who first postulated that the injury may be due to a fracture rather than a dislocation. Dupuytren is credited with popularizing the idea through his lectures, later published by his students. The management of distal radial fractures has changed significantly since Colles' proclamation in 1814. Although distal radial fractures account for up to 20% of all fractures treated in emergency departments, many are not "completely exempt from pain" after treatment. More than 1000 peer-reviewed studies have been published on the subject, yet there is no consensus on which treatment is superior or firm guidelines for treatment decisions. Many confounding variables exist, all of which are somewhat controversial: the level to which the anatomy is restored, the quality of the bone, the emergence of new techniques and devices, the experience and ability of the surgeon, and outcomes in older populations. These fractures have a bimodal distribution with high-energy fractures most commonly occurring in young men and low-energy fractures occurring in elderly women. Distal radius fractures are the second most common fracture in the elderly and the incidence in females is higher than males by a factor of two to three. Furthermore, several studies have found that the incidence of distal radius fractures worldwide has been increasing. The reasons for this are unclear at this stage in time

The risk factors for distal radius fractures are the same as those for other osteoporotic fractures, with the main risk factor being low bone mineral density, which is also a predictor of future fractures. Falls in patients with low bone mineral density often result in fracture, although some patients who have sustained distal radius fractures are in the fitter group of older patients. Studies have shown that these fitter patients have more preserved reflexes, which allow them to outstretch their hand to break their fall, compared with patients who sustain elbow or proximal humerus fractures. Despite being fitter than other patients with osteoporotic fractures, there is evidence that older adults who sustain distal radius fractures have impaired postural stability compared with similar aged individuals who have not sustained fractures. As for other fragility fractures, clinical risk factors such as a history of prior fracture, endocrine disease, and certain medications also place patients at a higher risk of fracture. As expected, innumerable studies have been performed analyzing all aspects of the management of distal radius fractures. However, despite the large volume of research, their treatment remains controversial. The most recent Clinical Practice Guideline (CPG) on the Treatment of Distal Radius Fractures from the American Academy of Orthopaedic Surgeons (AAOS) examines 29 different aspects of their treatment yet is unable to make any strong recommendations. In fact, nearly two-thirds of categories are "inconclusive" or "limited" after review of the evidence. Similarly, the most recent

Cochrane Review concludes "there remains insufficient evidence from randomized controlled trials to determine

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which methods of treatment are the most appropriate for the more common types of distal radius fractures in adults” and further reviews are ongoing. Several studies have reported CRPS resulting from distal radius fractures and Vitamin C has been studied as a possible preventive measure. The 2009 AAOS CPG made a moderate recommendation for the use of Vitamin C in patients with distal radius fractures to prevent disproportionate pain. A more recent randomized controlled trial revealed no difference in outcomes or rates of CRPS in patients treated with Vitamin C versus those who were not. A meta-analysis of the three RCTs concluded that Vitamin C fails to demonstrate a significant benefit, but the overall quality of evidence is low and the problem is difficult to study given its subjective nature. While the evidence remains conflicted and Vitamin C treatment is not routine in our practice, some surgeons argue that there is little downside to prescribing Vitamin C for all patients with distal radius fractures. Complex regional pain syndrome (CRPS) occurs most commonly in elderly patients and those with psychological or psychiatric conditions and has been reported in 8% to 35% of patients with distal radial fractures. A randomized, controlled, multicenter study involving 416 patients with 427 distal radial fractures determined that vitamin C (500 mg daily) can reduce the prevalence of CRPS, and this was listed as having “adequate evidence to support a moderately strong endorsement” in the recent AAOS clinical practice guidelines for distal radial fractures.

2. Literature Survey

Sanjay Meena, Pankaj Sharma reported a significant reduction in prevalence of CRPS with the use of vitamin C. Further high-quality RCTs with standard dosages and common diagnostic criteria are needed to be able to deliver solid conclusions.

Sunitha Malay MPH, Kevin C. Chung MD reported that The number of causal/association criteria met was adequate to support the scientific premise of the effect of vitamin C in preventing CRPS after DRF. Furthermore, vitamin C administration is of relatively low cost and has few complications unless administered in large doses. Owing to sufficient epidemiological evidence availability, the American Academy of Orthopaedic Surgeons recommendation of vitamin C to prevent CRPS has practical merit.

Zollinger, P.E. MD; Tuinebreijer, W.E. MD, PhD, MSc, MA reported that Vitamin C reduces the prevalence of complex regional pain syndrome after wrist fractures. A daily dose of 500 mg for fifty days is recommended.

Evaniew, Nathan MD; McCarthy, Colm MD, CM reported that The evidence for vitamin C to prevent CRPS in patients with distal radius fractures fails to demonstrate a significant benefit. The overall quality of the evidence is low, and these results should be interpreted in the context of clinical expertise and patient preferences.

Paul E. Zollinger, Robert W. Kreis, reported that external fixation doesn't necessarily lead to a higher incidence of CRPS in distal radial fractures. To our opinion vitamin C lowers the incidence of CRPS in non-operatively treated

wrist fractures and may also play a role in operatively treated wrist fractures. This subgroup analysis in operated distal radial fractures showed no CRPS occurrence with vitamin C prophylaxis and gives us further arguments for a new prospective study to gather a large number of patients for sufficient statistical analysis.

Ekröl, Ingri MRCSEd; Duckworth, Andrew D. MSc, MRCSEd reported no significant difference at one year in the DASH score, other functional outcomes, the rate of CRPS, or osseous healing of non displaced or displaced distal radial fractures treated with vitamin C compared with placebo. We conclude that administration of vitamin C confers no benefit to patients with a displaced or nondisplaced fracture of the distal aspect of the radius.

Problem Definition:

Patients with Distal End Radius Fractures treated conservatively with reduction and cast often lead to chronic pain in patients during wrist movements due to CRPS developing in the wrist. Vitamin C is said to be able to reduce the incidence of CRPS in these patients and hence relieve chronic pain and morbidity of such patients.

3. Methodology

The study was conducted at the Department of Orthopaedics, GMC, Kota.

Study Duration: The study was conducted between November 2022 to June 2023..

A primary detailed history regarding name, age, sex, history of injury, residential address, occupational status was recorded.

Patients' general condition and vitals were noted. Any previous history of pain disorders was also taken.

The study included patients attending Orthopaedics Department either in the OPD or the emergency room with complaints of wrist pain following trauma.

Study Design: Hospital based Single Blind Prospective Randomized Control Trial .

Protocol: In the outpatient department/ emergency room of the hospital (MBS and NMCH), the surgeon or orthopedic resident identified the patients eligible for the study. A careful clinico-radiologic assessment was done to exclude associated forearm or hand injuries. The study protocol was instituted. Patients were informed in detail by the treating surgeon regarding the study. The nature of the study was explained to all the patients in their own language and necessary consent obtained after the patients gave their willingness to participate in the study.

Sample Size: The sample size was 150 cases.

Inclusion Criteria:

- 1) Closed injury in the age group of >18 year old, both male and female patients.
- 2) Acute injury not more than 48 hours old.

- 3) Radiological evidence of Distal End of Radius fracture.
- 4) Patients who give consent for the study.

Exclusion Criteria:

- 1) Age <18 years
- 2) Patient had an injury >48 hours old
- 3) Fractures associated with Head injury.
- 4) Those with open fractures and compounding.
- 5) Associated upper limb fractures- associated bony injury to arm/forearm/hand.
- 6) Patient having serious disease of tumor or infection or visceral organ failure.
- 7) Patient not consenting to participate in the study.
- 8) Patients with fracture but no history of trauma.
- 9) Patients with previous history of pain disorder.
- 10) Patients on any medication affecting pain.
- 11) Patients having fractures secondary to metastasis or other systemic illnesses.

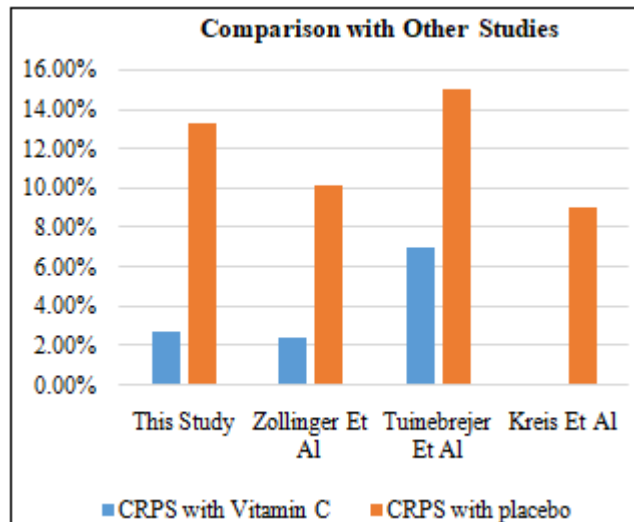
The statistical analysis of whole data was done using the Unpaired T Test to determine the significance of the results obtained.

PROCEDURE -All patients received in the emergency room or Outdoor were evaluated for any associated major injuries such as chest injury or head injury etc. The main symptoms and signs of the patient were asked and a primary survey done. The patients underwent a thorough clinical and neurological examination. All the cases were clinically assessed. Then, X-ray of Wrist with forearm in Antero Posterior (AP) view and Lateral View was taken. The distal end of radius fracture was diagnosed based on the following criteria: a clear history of trauma, Tenderness +; Deformity +/-; Distal end Radius fracture shown by radiography; Crepitus +. The fracture was reduced and an Above Elbow Slab was applied which was converted into an Above Elbow Cast on Day 3. An Informed consent was be obtained from each patient.

4. Results/ Discussion

150 patients with distal end radius fractures were randomized to receive Vitamin C, with 75 patients being given Vitamin C and 75 patients being given a placebo. The incidence of CRPS (Complex Regional Pain Syndrome) was 2.7% (2 out of 75) in the Vitamin C Group and 13.3% (10 out of 75) in the placebo group.

Study	Sample Size	CRPS with Vitamin C	CRPS with placebo
This Study	150	2.7%	13.3%
Zollinger Et Al	416	2.4%	10.1%
Tuinebrejer Et Al	123	7%	15%
Kreis Et Al	48	0%	9%



No. of Patients	Male	Female
150	24	126

5. Conclusion

From this study we are able to conclude that:

- 1) CRPS is a recognized complication of distal end radius fractures which lead to increased morbidity in patients in the form of chronic pain and disablement.
- 2) Vitamin C definitely has a role to play in reducing the incidence of CRPS in patients treated conservatively with reduction and casting for distal end radius fractures and hence decreasing morbidity in such patients.
- 3) A daily dose of 500 mg of Vitamin C given for 6 weeks is effective in reducing incidence of CRPS in patients with distal end radius fractures treated conservatively.

6. Future Scope

Vitamin C can be a game changer if used optimally as it can lead to significant decrease in morbidity of patients suffering from CRPS. This study shows that Vitamin C has a definitive role in preventing CRPS. Further studies are required to elaborate the optimum dosing and duration of Vitamin C to be given to patients to be able to reach the therapeutic level without compromising on functional outcome of the drug. Further studies are also required to ascertain whether this reduction in CRPS is only seen in patients treated with closed reduction and casting or such results are also reciprocated in patients treated with operative procedures. Furthermore, more studies are needed to find any drug interactions with Vitamin C that can have a synergistic / antagonistic effect on the body with this drug in reducing CRPS.

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