Role of Anti-Oxidant Vitamin C in Post Operative Pain Relief in Foot and Ankle Surgery

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Abstract
Aims and Objectives: The primary objective of the study is to assess the efficacy of Anti-oxidant Vitamin C in postoperative pain relief in foot and ankle surgery.

Materials and Methods: This is a Randomized Comparative double blinded study. A minimum of 60 subjects were selected for the study. Study subjects were systematically and randomly allocated into two groups of 30 each (Group A and Group B) receiving either Vitamin C or Placebo depending upon randomization by closed envelope technique. Patients who had foot and ankle surgery received a course of tablets for a period of 6 weeks, starting from first postoperative day.

Results: The mean VAS Score at first week in group 1 was 63.33±14.70 and in group 2 was 69.33±14.33 while at second week the VAS Score in group 1 improved to 20.37 ± 19.11 and in group 2 improved up to 31.03 ± 17.6. The VAS Score at six week in group 1 was 0.67 ± 2.54 and in group 2 was 3.33 ± 8.44. Patients on further follow ups had occasional pain at rest. The functional outcome evaluation using “FOOT AND ANKLE CORE SCORE” at final follow up in group 1 in terms of standardized mean was 72±3.95 and group 2 was 62.45±9.2. The normative score at final follow up in group 1 was 32.79±3.09 and in group 2 was 25.55±6.30.

Conclusion: vitamin C is an effective prophylactic agent following trauma to extremities and also after scheduled surgeries to decrease postoperative pain and decrease the need for analgesia and for better functional outcome of the patient for early rehabilitation of the patient.

Introduction
The complex regional pain syndrome (CRPS) type 1, also known as sudeck’s dystrophy, is a complex pain disorder which occurs after trauma or surgical management of fractures. It is characterized by a combination of autonomous, sensory and vasomotor symptoms(1). Pain, temperature difference, restricted motion, colour change, hyperaesthesia, hyperalgesia, hyperpathy, tremor, involuntary movement, muscle spasms, paresis, pseudoparalysis, atrophy of skin, muscle and bone, hyperhidrosis and changes in hair and nail growth have all been described as associated with CRPS-I. CRPS-I is one of the most important...
causes of invalidation after an injury to long bones of arm, leg and after surgical management of such fractures.

Complex regional pain syndrome remains a poorly understood chronic pain disorder. Little data has been published assessing the epidemiology of CRPS. When a complication such as CRPS-1 occurs, it may develop into a chronic disability, meaning that the simple fracture is no longer marginal for the patient in question, but also for his relatives, social and working environment and there is a great public health impact resulting in increase in sick leave and absence from work. Allen G et al(2) assessed epidemiological variables in 134 CRPS patients and found that these patients had seen on average 4.8 different physicians before referral to the pain centre and had received an average of five different kinds of treatments both prior to and during pain clinic treatment. The mean duration of CRPS symptoms prior to evaluation at “Pain Centre” was 30 months. The duration of CRPS symptoms and the involvement of the upper extremity were significantly associated with the presence of myofascial dysfunction. Thus, this study found that most CRPS patients were referred to a pain specialty clinic after several years of symptoms and many failed therapies. The data also suggest the lack of utility of a diagnostic bone scan and highlight the prominence of myofascial dysfunction in a majority of CRPS patients.

The emphasis of treatment of such a disabling complication should therefore be on prevention of this complication after injury and surgery of long bones of arm and leg. Dijkstra PU, et al (3) found incidence of CRPS-1 in wrist fractures to be 1 to 37%. Rewhorn MJ(4) in his retrospective cohort study of 390 patients observed the incidence of CRPS to be 4.36% after foot and ankle surgeries.

Vitamin C or ascorbic acid is a water soluble vitamin. For humans, vitamin C is an essential nutrient with a daily advised dose(5) of 60 milligram for adults. Ascorbic acid is an organic acid with antioxidant properties(6, 7). Vitamin C has been shown to be effective in preventing CRPS I secondary to wrist fracture, but few data are available with respect to foot and ankle cases. Cazeneuve et al(9) found role of vitamin C as a preventive measure for CRPS-1 by giving one gram of vitamin C for 45 days in wrist fractures postoperatively. Zollinger PE, et al (9,10) reported decrease in the incidence CRPS-1 after giving 500mg vitamin C daily for 50 days in wrist fractures after surgical management. The literature supporting the role of vitamin C as a preventive measure for CRPS-1 after foot and ankle surgery is very little. Besse JL, et al(11) found that incidence of CRPS-1 is more in control group without vitamin C than in group with one gram vitamin C daily for 45 days and found that one gram of vitamin C daily for 45 days is effective in decreasing the incidence of CRPS-1 in elective foot and ankle surgery. Naohiro, et al(12) in their systematic review and meta-analysis also demonstrated the efficacy daily vitamin C of at least 500 mg initiated immediately after the foot and ankle surgery or injury and continued for 45 to 50 days. Thus, vitamin C seems to offer its role as an antioxidant as a preventive measure for CRPS-1 after foot and ankle surgery.

Materials and Methods

This is a Randomized Comparative double blinded study. The primary objective of the study is to assess the efficacy of Anti-oxidant (Vitamin C) in postoperative pain relief in foot and ankle surgery. A minimum of 60 subjects were selected for the study. Study subjects were systematically and randomly allocated into two groups of 30 each (Group A and Group B). Group A received either Vitamin C or Placebo depending upon randomization by closed envelope technique. Group B received either Vitamin C or Placebo depending upon randomization by closed envelope technique. Healthy patients (>18 yrs and <60 yrs) undergoing foot and ankle surgery were included in the study. Patients suffering from Renal Calculi, Diabetes, glucose-galactose malabsorption, glucose-6-phosphate dehydroge-
nase (G6PD) and pregnant and breast feeding ladies were excluded from study. Patients taking Fluphenazine and those who are already taking Vitamin C or multi-vitamin supplementation were also excluded. Patients who undergone foot and ankle surgery received a course of tablets for a period of 6 weeks, starting from first postoperative day. These tablets were either Vitamin C or placebo. The patients were assessed for their pain scores, function outcome and analgesia requirements. The patients were followed up to 6 months postoperatively. Patients were assessed on the basis of Visual analogue scale

Ankle and foot outcome score (AFOS) (Validated by AAOS)

Requirement for analgesia.

Statistical analysis done using paired t-test.

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Continuous variables were presented as mean±SD or median if the data is unevenly distributed. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student’s t test. Nominal categorical data between the groups was compared using Chi-squared test or Fisher’s exact test as appropriate. Non-normal distribution continuous variables were compared using Mann Whitney U test. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference. Interpretation and analysis of data was done by paired t–tests.

Results

An independent researcher after randomization divided Patients into two groups of 30 each. Group 1 patients had received vitamin C from first postoperative day for a period of six weeks and Group 2 patients had received placebo tablets for a period of six weeks starting from first postoperative day.

The majority of the patients (40%) in group 1 were between 20 to 30 years of age whereas 36.7% of the patients in group 2 were between the ages of 31-50 years. The mean age of the patient was 37.17 ±11.58 years and 39.83 ± 8.69 in group 1 & group 2 respectively (p=0.317). Majority of patients in both the groups were males, group 1 having 86% and group 2 66% (p= 0.125). Mode of injury in majority of patients was road traffic accidents in patients of both the groups (p=0.237) followed by fall from height. The mean BMI in group 1 was 21.7±4.64 and in group 2 was 22.03±3.8 (p=0.7). The mean VAS Score (Table 1) at first week in group 1 was 63.33±14.70 and in group 2 was 69.33± 14.13 (p=0.112) while at second week the VAS Score in group 1 Improved to 20.37 ± 19.11 and in group 2 improved up to 31.03 ± 17.6 (p=0.034). The VAS Score at six week in group 1 was 0.67 ± 2.54 and in group 2 was 3.33 ± 8.44 (p=0.103). Patients on further follow ups had occasional pain at rest (figure 1). The functional outcome evaluation using “FOOT AND ANKLE CORE SCORE” (Table 2) at final follow up in group 1 in terms of standardised mean was 72±3.95 and group 2 was 62.45±9.21 (p < 0.0001). The normative score at final follow up in group 1 was 32.79±3.09 and in group 2 was 25.55±6.30 (p < 0.0001) (Figure 2).

### Table1: Distribution according to Visual analogue scale (VAS).

<table>
<thead>
<tr>
<th>Visual analogue scale(VAS)</th>
<th>Group 1 (n=30)</th>
<th>Group 2 (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At first week</td>
<td>Mean± SD</td>
<td>Min-Max</td>
<td>Mean± SD</td>
</tr>
<tr>
<td>At first week</td>
<td>63.33 ± 14.70</td>
<td>20 - 80</td>
<td>69.33 ± 14.13</td>
</tr>
<tr>
<td>At second week</td>
<td>20.37 ± 19.11</td>
<td>0 - 50</td>
<td>31.03 ± 17.6</td>
</tr>
<tr>
<td>At sixth week</td>
<td>0.67 ± 2.54</td>
<td>0 - 10</td>
<td>3.33 ± 8.44</td>
</tr>
<tr>
<td>At three months</td>
<td>0 ± 0</td>
<td>0 - 0</td>
<td>0 ± 0</td>
</tr>
</tbody>
</table>
Figure 1: Line diagram showing comparison of visual analogue scale between group 1 and group 2.

![Comparison of Visual analogue score Between Group 1 and Group 2](image)

Table 2: Distribution according to Foot and ankle outcome score (FAAOS) at three months.

<table>
<thead>
<tr>
<th>Group Statistics</th>
<th>GROUP</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot and Ankle core scale: Standardized mean at three months</td>
<td>1</td>
<td>29</td>
<td>72.00</td>
<td>3.955</td>
<td>0.734</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>31</td>
<td>62.45</td>
<td>9.215</td>
<td>1.655</td>
<td></td>
</tr>
<tr>
<td>Foot and Ankle core scale: Normative score at three months</td>
<td>1</td>
<td>29</td>
<td>32.79</td>
<td>3.098</td>
<td>0.575</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>31</td>
<td>25.55</td>
<td>6.303</td>
<td>1.132</td>
<td></td>
</tr>
</tbody>
</table>

Figure 4: Bar diagram showing correlation between foot and outcome score between group 1 and group 2.

![Bar diagram showing correlation between foot and outcome score between group 1 and group 2](image)
Discussion

Complex regional pain syndrome (CRPS) is a devastating condition common after foot and ankle injuries and surgeries. CRPS causes diffuse pain in the extremities that is not isolated to the area of injury or surgery. The condition usually initiates from some form of traumatic stimuli, including injury and surgical intervention. Patients with this condition often complain of edema, erythema, sudomotor, and motor dysfunctions. Prognosis of this condition is fair when treated early, but becomes poor when it becomes chronic. Use of high-dose vitamin C has been recommended by the Evidence Based Guidelines for Type 1 CRPS for wrist fractures. The recommended intervention consists of a daily, 500-mg dose of vitamin C for a duration of 50 days.

Cazeneuve et al. in 2002 reported a 10% incidence of CRPS I in his surgically managed control group (not receiving vitamin C), and Zollinger et al. in 1999 reported a 22% rate in his orthopedically managed control group (likewise, not receiving vitamin C). In the experimental groups, receiving vitamin C, Zollinger reported a 7% incidence of CRPS I (relative risk: 0.17) and Cazeneuve 2.1%.

Jean-luc Besse et al carried out a “before–after” quasi-experimental study comparing two chronologically successive groups without (Group I) and with (Group II) prophylactic vitamin C treatment. Four hundred and twenty feet (392 patients) were included. Group I without vitamin C, having surgery from July 2002 to June 2003, comprised 185 feet: 177 patients (44 males, 133 females). Mean age at time of surgery was 47.1±17 years; range 16–78 years. Group II receiving prophylactic vitamin C treatment, having surgery on between July 2003 and June 2004, comprised 235 feet: 215 patients (49 males, 166 females). Mean age at time of surgery was 51±16 years; range 15–87 years. There were no significant inter-group differences on general Characteristics. CRPS I occurred in 9.6% of Group I patients (n = 18), as against 1.7% (n = 4) in Group II (p < 0.0001).

In this double blind comparative study, patients were evaluated for pain score on visual analogue scale, analgesic requirement and functional outcome at various intervals during their treatment. The majority of the patients (40%) in group 1 were between 20 to 30 years of age whereas 36.7% of the patients in group 2 were between the age of 31-50 years. The mean age of the patient was 37.17 ± 11.58 years in group 1 and 39.83 ± 8.69 year in group 2. The p value of 0.317 suggests that the age of patients in both the groups were comparable.

Majority of patients in both the groups were males. The p value of 0.125 suggests that the difference of gender between two groups was not biased.

The mean value of body mass index in both the groups was comparable and the p value of 0.812 suggests that the body mass index of patients in two groups were comparable. The Visual analogue score at first week was not statistically significant between two groups (p value = 0.112) which means pain score was comparable in patients of both the groups at first week. The difference of visual analogue score at second week was statistically significant (p value=0.034) which means patients of group 1 who had taken vitamin C tablets had less amount of pain at the end of second week as compared to patients of group 2 who had taken placebo tablets. The difference of visual analogue score at the end of six weeks, 3 months and 6 months was not statistically significant (p value=0.103) which means amount of pain in patients of both the groups was comparable. The functional outcome was assessed using American academy of orthopaedic surgeon’s (AAOS) “Foot and ankle outcome instrument” at the end of three months. The p value of less than 0.001 in both the groups in relation to standardized mean and normative score suggest that the difference in functional outcome at the end of six months was statistically significant. It shows that patients of group1 who were given vitamin C had better functional outcome in comparison to patients of group 2 who
were given placebo. Total amount of analgesia required in patients of group 1 was 3.46 grams and in patients of group 2 was 6.25 grams. The p value of 0.001 suggests that the amount of analgesia required in two groups was statistically significant which means patients of group 1 who had taken vitamin C tablets had less amount of analgesia requirement as compared to patients of group 2.

Thus Vitamin C as an antioxidant was found to have a significant role in postoperative pain relief and reduction in amount of analgesia requirements in foot and ankle surgery. It is also helpful in better functional outcome post foot and ankle surgery.

**Conclusion**

We recommend vitamin C, being a cheap and safe medicine, as a prophylactic agent following trauma to extremities and also after scheduled surgeries to decrease postoperative pain and decrease the need for analgesia and for better functional outcome of the patient for early rehabilitation of the patient.

**Conflicts of Interest:** NIL

**Source of funding:** Independant

**References**

12. Naohiro Shibuya, Jon M. Humphers, Monica R. Agarwal, Daniel C. Jupiter