Randomized Trial

Long-term Prednisolone in Post-stroke Complex Regional Pain Syndrome

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Background: There is no study on the long-term use of prednisolone in post-stroke complex regional pain syndrome-1 (CRPS1).

Objective: To evaluate the efficacy and safety of long-term low dose prednisolone in post-stroke CRPS-I.

Study Design: Open-labeled randomized controlled trial.

Setting: Tertiary care teaching institute.

Methods: Seventy-seven out of 396 (19.4%) patients with stroke had CRPS-1 and 58 met the inclusion criteria. Their clinical details and CRPS, Visual Analogue Scale (VAS), modified Rankin Scale (mRS), and Barthel Index (BI) scores were noted. The patients were prescribed 40 mg prednisolone for 2 weeks followed by tapering in the next 2 weeks. Patients who responded were randomly assigned prednisolone 10 mg daily (group I) or no prednisolone (group II). They were followed up for the first and second month of randomization and their CRPS, VAS, mRS, and BI scores were noted. The primary outcome was improvement in CRPS score and secondary outcomes were VAS, mRS, BI scores, and severe adverse events (SAE).

Results: Fifty-six of fifty-eight (96.5%) patients responded to the initial high dose prednisolone and 26 each were assigned group I and group II treatment. Group I patients had further improvement in CRPS score. Fifty percent of patients in group II had deterioration at one month and needed reinstitution of prednisolone; following which 77% of them improved in the next month. The improvement in CRPS score paralleled the VAS score but not mRS and BI scores in the first and second months in group I compared to group II. There was no SAE necessitating withdrawal of prednisolone.

Limitation: The design of the study is not double blind.

Conclusion: In post-stroke CRPS-I, continuation of low dose prednisolone for 2 months is safe and effective.

Key words: Shoulder hand syndrome, CRPS, corticosteroid, prednisolone, stroke, Visual Analogue Scale

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Complex regional pain syndrome (CRPS) is characterized by pain in combination with sensory, autonomic, trophic, and motor changes (1,2). When there is no identifiable nerve injury, it is termed as CRPS-I, and if it is associated with a nerve injury, it is termed CRPS-II. The annual incidence of CRPS is widely variable, ranging from 5.5 to 26.2/100,000 person-years (3,4). The most common triggering event is fracture (45%), followed by sprain (18%), and elective surgery (12%), and it

can be spontaneous in less than 10% of patients (5,6). In a study of 596 patients with CRPS-I following fracture, the median time from trauma to peak of CRPS symptoms was 3 months (7). The incidence of CRPS-I following stroke has been reported in a few studies only. In one study, 82 patients who had a stroke were followed up for 28 weeks and 48.8% of them developed CRPS. The occurrence of CRPS correlated with the Ashworth score, subluxation, and loss of range of movement and muscle strength (8). Stroke is the second leading cause of death and third leading cause of disability-adjusted life-years (DALYs) worldwide (9,10). The major advances are focused on the acute stroke treatment resulting in better survival but disability. For the activities of daily living, a full range of painless movement, especially of the upper limb, is essential. Occurrence of CRPS-I may limit physiotherapy which results in increased spasticity and reduced muscle strength and contracture. Multiple pharmacological and non-pharmacological therapies for CRPS have been evaluated, mostly directed to fracture and other orthopedic conditions. After the stroke, biomechanical factors and microtrauma to the hemiparetic shoulder may contribute to the genesis of CPRS. The exact pathophysiology that links these triggers to the CRPS manifestation remains uncertain. Sympathetic dysfunction, somatic nervous system dysfunction, inflammation, hypoxia, and psychological factors are also likely contributors to the genesis of CRPS (11). Three major pathophysiological pathways are identified, including abnormal inflammatory and vasomotor response and aberrant neuronal plasticity (1). High levels of pro-inflammatory cytokines have been reported in patients with CRPS (12-14). Corticosteroids are the key drugs for immunological disorders, immune suppression, and immunomodulation. Studies in CRPS have shown remarkable results in reducing edema and pain following corticosteroid treatment (15-18). Most of these studies are limited to a few weeks of treatment. Prescribing high dose corticosteroids for a long duration may not be appropriate, especially to stroke patients who are likely to have diabetes mellitus, hypertension, and osteoporosis. There is no study evaluating low dose of corticosteroids after one month of standard prednisolone treatment. In this open label randomized controlled trial, we report the efficacy and safety of 2 months of low dose prednisolone after one month of standard prednisolone therapy in the patients with post-stroke CRPS-I.

Methods

Study Design

This is an investigator initiated open label randomized controlled trial with a cross-over design evaluating the efficacy and safety of continuing low dose of prednisolone beyond one month of standard treatment. The project was formulated by JK and the study was approved by the Institute Ethics Committee (code 2013-92-IP-72 dated August 16, 2013). Informed consent was obtained from the patient or their first degree relatives.

Inclusion criteria: The patients with CRPS following a stroke treated by a neurology service of a tertiary care teaching institute of North India from 2013 to 2015 were included. A diagnosis of CRPS-I was based on the following features (16).

a. Pain and tenderness during humeral abduction, flexion, and external rotation.
b. Pain and dorsal swelling over the carpal bones.
c. Moderate fusiform edema of metacarpo-phalangeal and inter-phalangeal joints.
d. Change in temperature, color, and dryness of skin.
e. Loss of dorsal skin lines and change in nails.

The severity of CRPS was assessed on a 0 – 14 point scale, 0 being the lowest and 14 being the highest score (16). Stroke patients with a CRPS score ≥ 8 were included.

Exclusion Criteria

The stroke patients with uncontrolled hypertension (BP > 150/90 mm of Hg), poorly controlled diabetes mellitus, hemiplegia due to other causes, rheumatoid or seronegative arthritis, history of shoulder dislocation, trauma, traumatic brachial plexus injury, gastrointestinal bleeding, peptic ulcer disease, septicemia, pregnancy, malignancy, liver and kidney failure, children (< 15 years), and CRPS score < 8 were excluded. Those patients unwilling to give consent were also excluded.

Sample Size Calculation

Considering the reported improvement of 80% following prednisolone treatment, 24 patients with CRPS in each arm would be required for 95% power of the test at a 5% level of significance.

Clinical Evaluation

The demographic details of the patients were noted, including stroke risk factors such as hypertension, diabetes, hyperlipidemia, cardiac arrhythmia, coronary

artery disease, smoking, tobacco chewing, life style, and dietary habits. The severity of the stroke was assessed by National Institutes of Health Stroke Scale (NIHSS) score and depth of the coma by Glasgow Coma Scale (GCS). Muscle power at stroke onset, tone, reflexes, and sensory abnormalities were noted from the computerized hospital record system. The clinical parameters were also recorded when the patient developed CRPS-I. The time from stroke to development of CRPS was noted.

In all the patients, complete blood counts, hemoglobin, ESR, fasting and postprandial blood sugar, and serum creatinine, sodium, potassium, bilirubin, transaminase, calcium, phosphorous, and alkaline phosphatase were measured. Electrocardiogram and radiograph of the chest and the affected shoulder joint were carried out.

All the patients underwent a cranial computerized tomography (CT) and/or magnetic resonance imaging (MRI) study at the time of stroke onset. The type of stroke (ischemic vs intracerebral hemorrhage), location, volume, and evidence of midline shift were noted. The size of the lesion was divided into small, medium, and large (19,20).

Severity Assessment

The following parameters were used to assess the severity of CRPS-I and activity of daily living (ADL). The scores of the above-mentioned parameters were noted at baseline, one month after standard treatment, and at one and 2 months after randomization.

1. Severity of CRPS was assessed on a 0 – 14 scale including 4 domains (15,16).
   a. Sensory: pain and hyperalgesia (0 = none; 1 = mild; 2 = moderate; 3 = distinct; 4 = severe; 5 = spontaneous).
   b. Autonomic: distal edema (0 = none; 1 = mild; 2 = distinct; 3 = severe).
   c. Motoric: painless passive range of motion – humeral abduction (> 120° = 0, < 120° = 1, < 90° = 2, and < 45° = 3) and humeral external rotation (> 30° = 0, < 30° = 1, < 20° = 2, < 10° = 3).
2. Visual Analogue Scale (VAS): Severity of pain was assessed on a 0 – 10 scale, 0 being no pain and 10 being extreme pain.
3. Modified Rankin Scale (mRS) score was used for functional recovery with score ranges between 0 and 6.
4. Barthel index (BI) score on a 0 – 100 scale. Zero being the lowest and 100 being the highest score meaning independent ADL.

Treatment Protocol

Pre-randomization

All the patients fulfilling the diagnostic criteria of CRPS-I having a severity score of ≥ 8 were prescribed 40 mg prednisolone after breakfast for 14 days then tapered to 10 mg by 30 days.

Randomization

The patients who responded to standard prednisolone therapy were randomly assigned to a prednisolone continuation group (Group I) or discontinuation group (Group II) using computerized random numbers. Group I continued to receive 10 mg prednisolone for the next 2 months and in group II prednisolone was stopped.

The patients were followed up at one month of randomization and those with a recurrence of CRPS in group II were crossed over to prednisolone 10 mg daily for the next month. Patients were followed up at one and 2 months after randomization.

Outcome

Outcome was defined at one and 2 months of randomization. The primary outcome was improvement in CRPS severity scale. The secondary outcome measures were improvement in VAS, mRS, and BI scores, and severe adverse events (SAE). Analysis of the improvement in the different domains of the CRPS severity scale was also done.

Statistical Analysis

The baseline characteristics of patients in the 2 treatment arms were compared by Fisher exact test for categorical variables and independent t- test or Mann Whitney U test for continuous variables. The CRPS, VAS, mRS, and BI scores in the group at different time points were compared by one way ANOVA and the difference of scores at different time points between the groups were also compared by one way ANOVA. The number of patients having a ≥ 2 point improvement in CRPS severity scale and ≥ 20% improvement in VAS score between the 2 treatment arms was compared by Fisher exact test. The side effects between the 2 treatment groups were compared by using the Chi square test. A variable was considered significant if the 2 tailed *P* value was < 0.05. The statistical analysis was done by SPSS 16 version software and graphs were prepared by Graph Pad prism 5.

Results

During the study period, 396 stroke patients were examined and 77 (19.4%) who had post-stroke CRPS who were evaluated for possible enrollment in the trial. Nineteen patients were excluded: 8 for low CRPS score (< 8), 2 for uncontrolled hypertension, 3 for diabetes mellitus, 3 for shoulder dislocation, and one each for chronic liver disease, extra hepatic portal vein thrombosis, and hematemesis. The results therefore are based on 58 patients (Fig. 1). The age of the patients ranged between 35 and 85 (mean 55.15 ± 10.84, median 55) years and 43.1% were women. The time from stroke to development of CRPS ranged between one and 24 (median 10, mean 9.52 ± 5.72) weeks. Fifteen (25.9%) developed CRPS-I within one month, 29 (50%) within one to 3 months, and 14 (24.1%) within 3 to 6 months.

Pre-randomization Treatment Response:

After receiving standard prednisolone treatment for one month, 52 (89.7%) patients improved in CRPS score (> 2 points) and 6 (10.3%) did not. The CRPS score declined from 9.10 ± 1.01 to 4.88 ± 1.70 at one month ($P < 0.001$) and improvement was noted in all 4 CRPS severity domains, including pain, edema, abduction, and external rotation of the shoulder joint. There was also significant improvement in BI, mRS, and VAS scores (Fig. 2). Fasting blood sugar (86.2 ± 16.5 vs 92.9 ± 19.8 mg/dl; $P < 0.01$), postprandial blood sugar (141.1 ± 28.0 vs 160.3 ± 2 9.9 mg/dl; $P < 0.01$), and body weight (62.6 ± 10.6 vs 63.2 ± 10.7; $P < 0.01$) at one month increased compared to the baseline.

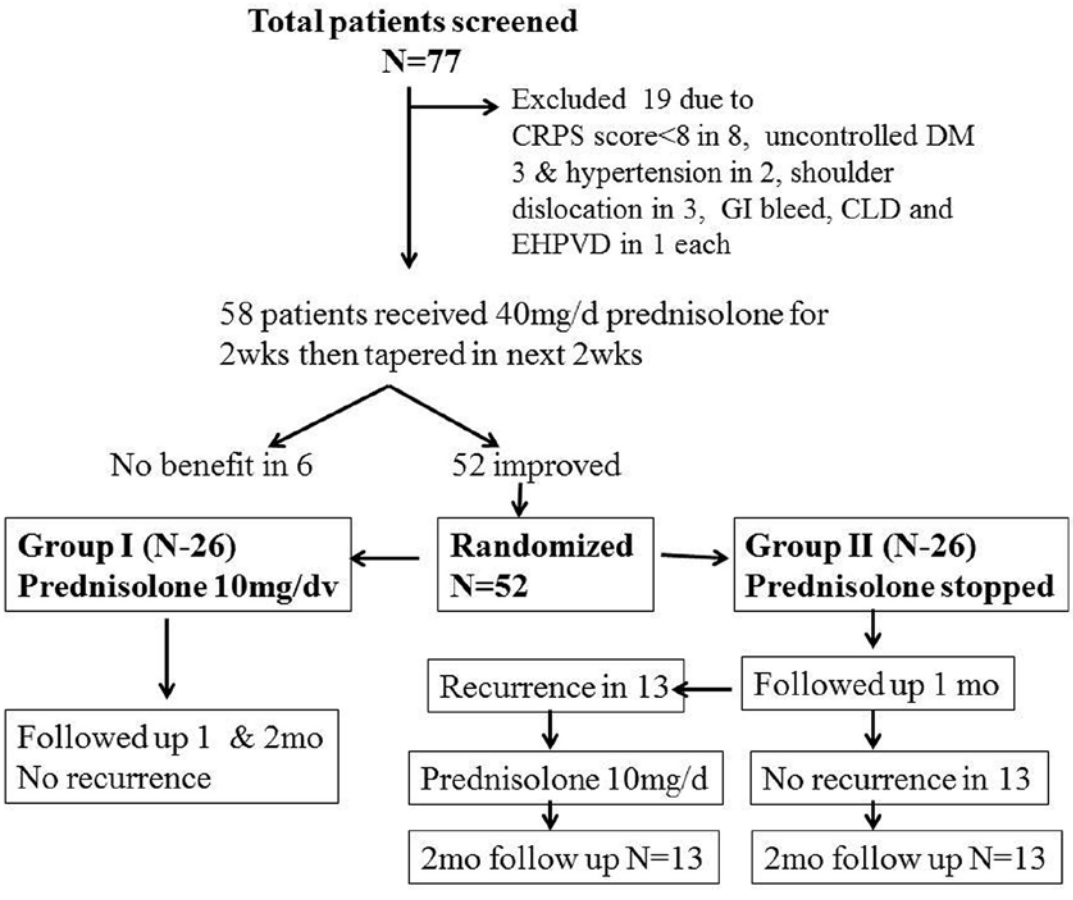

Fig. 1. *Flow chart of treatment protocol.*

Post-randomization Treatment Outcome:

Fifty-two patients who improved were randomized to group I (10 mg prednisolone) and group II (no prednisolone group). The baseline characteristics of group I and group II patients were comparable (Table 1). Group I patients had further improvement in CRPS score at one month and 2 months compared to baseline especially in pain and autonomic scores. The improvement in CRPS score was associated with improvement in VAS score but not with mRS and BI scores (Table 2). In group II, the CRPS score deteriorated at one month (4.6 ± 1.5 to 5.8 ± 2.5; $P < 0.003$) which was mostly in pain score (1.2 ± 0.6 vs 2.1 ± 1.2; $P < 0.001$). The deterioration in CRPS score was associated with deterioration in VAS score (3.5 ± 1.0 vs 4.9 ± 2.1; $P = 0.003$). The mRS score, however, improved from the baseline even in group II patients (2.0 ± 0.8 vs 1.8 ± 0.7; $P = 0.02$) but not the BI score (74.6 ± 21.1 vs 75.2 ± 19.7; $P = 1.00$).

After one month, none of the patients in group I deteriorated with respect to CRPS score, but in group II, 13 (50%) had deterioration in CRPS score by > 2 ($P < 0.001$) and prednisolone 10 mg/day was restarted (Group IIA). The remaining 13 patients in group II remained steroid free (group IIB). In the next month, the CRPS score in the group IIA reduced significantly compared to group IIB (Fig 3).

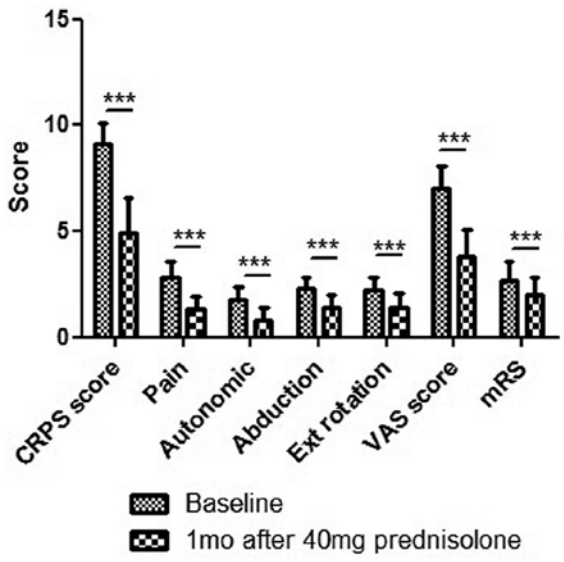

Fig. 2. *The complex regional pain syndrome (CRPS) score, its different components and Visual Analogue Scale (VAS) score improved following one month standard prednisolone (40 mg daily for 2 weeks then tapered in next 2 weeks) treatment. This was associated with improvement in modified Rankin Scale (mRS) and Barthel Index score (not shown). Ext = external. ***P < 0.001.*

Table 1. *Baseline characteristics of group I (prednisolone 10 mg continued) and group II (prednisolone discontinued) patients with post-stroke complex regional pain syndrome.*

Variable	Steroid continued (n = 26)	Steroid stopped (n = 26)	*P*
Age years	56.6 ± 12.5	52.5 ± 8.9	0.17
Women	12	11	0.78
Diabetes	10	6	0.23
Hypertension	22	24	0.38
UL Spasticity Grade			
0/1/2/3	3/14/8/1	4/13/8/1	0.98
Upper Limb Power			
Gr II/III/IV/V	2/12/11/1	2/9/14/1	0.86
Hemorrhage/Infarct	9/17	19/7	0.005
mRS score	1.8 ± 0.9	2.0 ± 0.8	0.42
Barthel Index score	77.5 ± 21.8	74.6 ± 21.1	0.63
VAS Score	3.6 ± 1.1	3.5 ± 1.0	0.71
CRPS Score	4.3 ± 0.9	4.6 ± 1.5	0.31
Pain score	1.3 ± 0.6	1.2 ± 0.6	0.38
Autonomic score	0.6 ± 0.5	0.7 ± 0.5	0.57
Abduction score	1.2 ± 0.4	1.4 ± 0.6	0.17
External rotation score	1.2 ± 0.7	1.4 ± 0.9	0.43

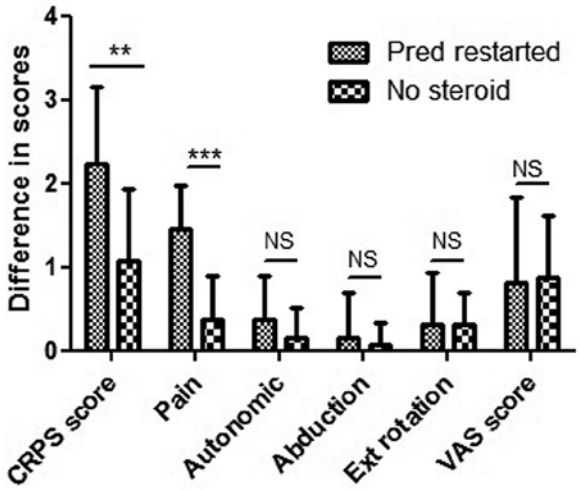

Fig. 3. *Comparison of group II patients who had recurrence of complex regional pain syndrome (CRPS) needing retreatment with prednisolone 10 mg/day (N = 13) with those who did have recurrence at one month post randomization (N = 13). Error bar diagram shows significant reduction in CRPS total score and pain score in prednisolone retreatment group (group IIA) than prednisolone discontinued group (group IIB) at 2 months. The scores are the change in scores between one and 2 months post randomization. Ext = external. VAS = Visual Analogue Scale. *P < 0.01.*

Comparison between group I and group II at the end of one month revealed significant improvement in CRPS score and VAS score in group I but not in mRS and BI scores (Table 2). At 2 months the improvement in CRPS score was significantly better in group I compared to those patients in group IIA (Table 3).

After completion of the defined end point, the patients were contacted by telephone until a median of 428 (range 127 – 1,320) days. Out of 41 patients who could be contacted, 9 (22%) had a recurrence of symptoms after a mean duration of 40.55 ± 17.62 (median 45, range 14 – 60) days. Out of these 9 patients, 3 were in group I and 6 in group II.

Adverse Events

At the end of standard prednisolone treatment, there was a significant increase in fasting blood sugar (86.24% ± 16.52 vs 92.91 ± 19.81 mg/dl; $P < 0.002$), postprandial blood sugar (141.10 ± 27.98 vs 160.33 ± 29.93 mg/dl, $P < 0.001$), and body weight (62.63 ± 10.62 vs 63.17 ± 10.67 kg, $P < 0.001$).

After randomization, the prednisolone continuation group (group I) did not have a rise in blood pressure, fasting blood sugar, postprandial blood sugar, and body weight. Three patients in the steroid continuation

Table 2. *Comparison of outcome and side effects between group I (prednisolone continued) and group II (prednisolone discontinued) at one month of randomization.*

Variables	Group I (n = 26)	Group II (n = 26)	*P*
CRPS score	2.7 ± 0.8	5.8 ± 2.5	< 0.01
Pain score	0.8 ± 0.5	2.1 ± 1.2	< 0.01
Autonomic score	0.1 ± 0.3	0.7 ± 0.7	< 0.01
Abduction score	1.0 ± 0.2	1.5 ± 0.6	< 0.01
Ext rotation	0.9 ± 0.6	1.5 ± 0.8	0.04
VAS score	2.4 ± 1.0	4.9 ± 2.1	< 0.01
BI score	79.0 ± 21.0	75.2 ± 19.7	0.50
mRS score	1.6 ± 0.8	1.8 ± 0.7	0.21
Side effects			
SBP mmHg	133.8 ± 7.5	131.1 ± 1.0	0.28
DBP mmHg	81.9 ± 4.6	80.7 ± 7.0	0.46
FBS mg/dl	92.04 ± 17.49	86.77 ± 14.75	0.25
PPBS mg/dl	154.96 ± 23.85	146.77 ± 24.46	0.23
Weight (kg)	61.73 ± 10.01	63.81 ± 10.88	0.48

BI = Barthel Index, BP = blood pressure, CRPS = complex regional pain syndrome, Ext = external rotation, FBS = fasting blood sugar, mRS = Modified Rankin Score, PPBS = postprandial blood sugar, VAS = Visual Analogue Scale.

Table 3. *Comparison of outcome parameters at 2 months between group I (prednisolone continued group), group IIA (prednisolone restarted at one month due to recurrence) and group IIB (prednisolone discontinued) patients with complex regional pain syndrome (CRPS).*

Variables	Group I N = 26	Group II A N = 13	Group II B N = 13	Gr I Vs IIA	Gr I Vs II B	Gr IIA Vs B
CRPS score	2.10 ± 1.10	5.40 ± 2.00	2.80 ± 1.10	< 0.01	NS	< 0.01
Pain	0.58 ± 0.58	1.6 ± 0.77	0.78 ± 0.44	< 0.01	NS	< 0.01
Auto	0.78 ± 0.27	0.69 ± 0.63	0.15 ± 0.37	< 0.01	NS	< 0.01
Abduction	0.73 ± 0.45	1.69 ± 0.63	1.08 ± 0.28	< 0.01	NS	< 0.01
Ext Rotation	0.65 ± 0.74	1.46 ± 0.97	1.00 ± 0.71	< 0.05	NS	NS
VAS Score	1.54 ± 1.34	3.98 ± 1.23	2.19 ± 1.03	< 0.01	NS	<0.01
mRS score	1.35 ± 0.56	1.77 ± 0.83	1.46 ± 0.52	NS	NS	NS
B1 score	81.54 ± 19.58	77.92 ± 20.05	80.77 ± 20.80	NS	NS	NS

BI = Barthel Index, BP = blood pressure, CRPS = complex regional pain syndrome, Ext = external rotation, FBS = fasting blood sugar, mRS = Modified Rankin Score, PPBS = postprandial blood sugar, VAS = Visual Analogue Scale.

group and one in the discontinuation group had gastrointestinal symptoms. None had any infection during the follow-up. One patient had a cataract at base line. None of the patients withdrew from the study due to SAE.

Discussion

In the present study 89.7% of patients with post-stroke CRPS-1 improved following high dose prednisolone. Continuation of 10 mg prednisolone for a further 2 more months resulted in no recurrence of CRPS-1; whereas, 50% had a recurrence in the group in which prednisolone was stopped. Seventy-seven percent of these patients with recurrence also responded following reintroduction of 10 mg prednisolone. The improvement was noted in all 4 domains of CRPS and paralleled improvement in VAS scores at all-time points. Activities of daily living measured by mRS and BI scores improved at the end of the standard treatment. Subsequent improvement in ADL was not different between the groups. The study drug did not have to be withdrawn in any of the patients because of SAE. This is the first study reporting the beneficial effect of long-term use of low dose prednisolone in patients with post-stroke CRPS-1. A number of drugs such as nonsteroidal anti-inflammatory drugs, gabapentin, opioids, α-adrenergic blockers (clonidine), antidepressant, anxiolytic, COX-2 inhibitors, TNF-α inhibitors, free radical scavengers, corticosteroids, calcitonin, bisphosphonate, and nerve blocks have been used for the management of CRPS with variable results (21). Only a few studies have evaluated the efficacy of corticosteroids in CRPS (15-17,22,23). Of these, only 2 studies were randomized controlled trials on stroke patients. In one study, 34 patients were randomly assigned 32 mg methylprednisolone for 14 days which was tapered in the next 14 days. Thirty-one (91.2%) patients significantly improved in CRPS score (16). In another randomized controlled trial on 60 patients with post-stroke CRPS-1, prednisolone 40 mg for 14 days followed by taper in next 14 days was compared with piroxicam 20 mg daily. Eight-three point three percent of patients in the prednisolone arm improved at one month whereas only 16% improved in the piroxicam arm (15). Both these studies however used corticosteroids for one month only. The recurrence of CRPS-1 subsequently is not evaluated in these studies. The benefit of long-term use of prednisolone has been reported in a randomized placebo control trial in patients with CRPS of varying etiology. In this study, 23 patients with CRPS were prescribed 10 mg prednisolone 3 times daily until the clinical remission was achieved for a maximum of 12 weeks. All 13 patients receiving prednisolone had more than 75% clinical improvement within 12 weeks, but only 20% (2/20) of patients improved on placebo (17). In this study, prednisolone was given for a variable period. Prednisolone has also been reported to be better than stellate ganglion blocking in CRPS due to various causes (22). Despite the unequivocal benefit of corticosteroid treatment for CRPS, it has not been endorsed for treatment of CRPS-1 (24). In stroke patients, the presence of CRPS-1 adversely affects the activities of daily living and also interferes in physiotherapy resulting in increased spasticity resulting in contracture.

The median duration of occurrence of CRPS from

the onset of a stroke in our patients was 10 weeks and about 75% developed CRPS-I one month after a stroke. Post-traumatic CRPS, however, occurs earlier than the observed time lag in post-stroke CRPS in our study. In a large study including 506 patients with post-traumatic CRPS, 57% had CRPS within one month, 23% within one to 3 months, 10% within 3 to 6 months, and another 10% after 6 months of inciting trauma (25). The longer time lag to post-stroke CRPS may be due to altered sensorium in the initial stage or different pathophysiological mechanisms (11).

The pathophysiological basis of CRPS has been attributed to multiple factors such as neurogenic inflammation, altered local immune and sympathetic response, impaired central inhibitory control, and defective cerebral reorganization of the affected body part (1,11). Conglomeration of signs and symptoms of inflammation with trophic changes and mechanical hyperalgesia suggests a predominant role of neurogenic inflammation in CRPS (26). The activation of the primary afferent results in the release of calcitonin gene-related peptide (CGRP) and substance P from the nerve ending. CGRP results in vasodilation of the arteriole, and substance *P* leads to extravasation of plasma protein from the venules (27). Denervation hypersensitivity of the nociceptors may be responsible for enhanced neurogenic inflammation. Skin biopsies however revealed a slightly greater α adreno-receptor but not in the blood vessels (28,29). Hyperalgesia has also been attributed to recruitment of "sleeping nociceptors" (30). On the other hand, there are strong views about the central theory based on PET and fMRI studies (31,32). An unequivocal response to corticosteroids in the treatment of CRPS suggests the predominant role of inflammation. Corticosteroids may improve CRPS symptoms and signs by inhibiting production of inflammatory mediators and reducing the transcription rate of neuropeptides in the dorsal root ganglion (DRG) and facilitating degradation of neuropeptides (17,33). Pericapsular soft tissue of CRPS joints in stroke patients revealed perivascular leukocytic infiltration in synovium and granulation tissue in the capsule (16). During an acute stroke, there may be undetected trauma during positioning, especially in a cerebral shock state when the limb is hypotonic. Continuation of low dose prednisolone for another 2 months may suppress the above mentioned mechanisms giving rise to long-term benefits. In the present study, CRPS recurred in 22% patients after completion of the study after a median duration of 45 days, which raises the question about the need for low dose prednisolone in this group of patients. Prednisolone 10 mg in our patients was safe, and none had significant aggravation of diabetes, hypertension, weight gain, or other complications.

The present study is limited by its open label design. An identical looking preparation of a placebo tablet was not possible as it was an investigator-initiated trial without financial support. The strengths of the study are its single center desing, lack of inter-rater variability, adequate sample size, and lack of drop out.

Conclusion

Discontinuation of prednisolone at one month of standard treatment results in a recurrence of CRPS in 50% of patients within one month. Continuation of low dose prednisolone for another 2 months is safe and effective in preventing recurrence of CRPS.

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Conflict of Interest

There is no conflict of interest to declare.

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