Physical therapy and cognitive-behavioral treatment for complex regional pain syndromes

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Complex regional pain syndromes (CRPS; type 1, reflex sympathetic dystrophy, and type 2, causalgia) involve persistent pain, allodynia, and vasomotor signs. We conducted a prospective, randomized, single-blind trial of physical therapy (PT) and cognitive-behavioral treatment for children and adolescents with CRPS. Children 8 to 17 years of age (n = 28) were randomly assigned to either group A (PT once per week for 6 weeks) or group B (PT 3 times per week for 6 weeks). Both groups received 6 sessions of cognitive-behavioral treatment. Assessments of pain and function were repeated at two follow-up time periods. Outcomes were compared at the three time points through the use of parametric or nonparametric analysis of variance and post hoc tests. All five measures of pain and function improved significantly in both groups after treatment, with sustained benefit evident in the majority of patients at long-term follow-up. Recurrent episodes were reported in 50% of patients, and 10 patients eventually received sympathetic blockade. Most children with CRPS showed reduced pain and improved function with a noninvasive rehabilitative treatment approach. Long-term functional outcomes were also very good. (J Pediatr 2002;141:135-40)

Complex regional pain syndromes (CRPS) type 1 (reflex sympathetic dystrophy) and type 2 (causalgia) are forms of neuropathic pain that occur in the extremities. Diagnostic criteria include severe pain, allodynia (pain evoked by light touch), and autonomic dysfunction. If the extremity is not mobilized, atrophy and limb contractures may ensue. In 1994, a consensus group proposed standard diagnostic criteria.[1]

CRPS has been described in adults since 1860. Pediatric case reports were rare before 1970[2-4]; 331 cases were identified in Medline from 1970 to 1999. There are no prospective, controlled, descriptive or interventional studies of pediatric CRPS. Physical therapy (PT) is used for a range of musculoskeletal conditions and is often advocated for treatment of CRPS. Pediatric retrospective case series suggest a more favorable response to conservative therapies such as PT in pediatric CRPS in contrast to adults.[4-8]

CBT	Cognitive-behavioral therapy
CRPS	Complex regional pain syndrome
PT	Physical therapy
VAS	Visual analogue scale

The objectives of this study were to prospectively examine (1) effects of a structured PT and cognitive-behavioral treatment (CBT) program on pain and function, (2) the impact of frequency of PT on outcome, and (3) whether measures of psychological distress are significantly elevated in patients with CRPS compared with published normal values.

METHODS

Patient Population and Enrollment Criteria

A prospective, randomized trial was conducted from October 1997 to January 2001 at Children's Hospital, Boston. Protocols were approved by the Clinical Investigation Committee at Children's Hospital. Eligibility criteria were patient assent, parental consent, age 8 to 17 years, and diagnosis of CRPS by previously established criteria.[1,9] Exclusion criteria were active participation in a PT program (more than two sessions of PT), systemic neurologic or major psychiatric illness, or previous sympathetic blockade.

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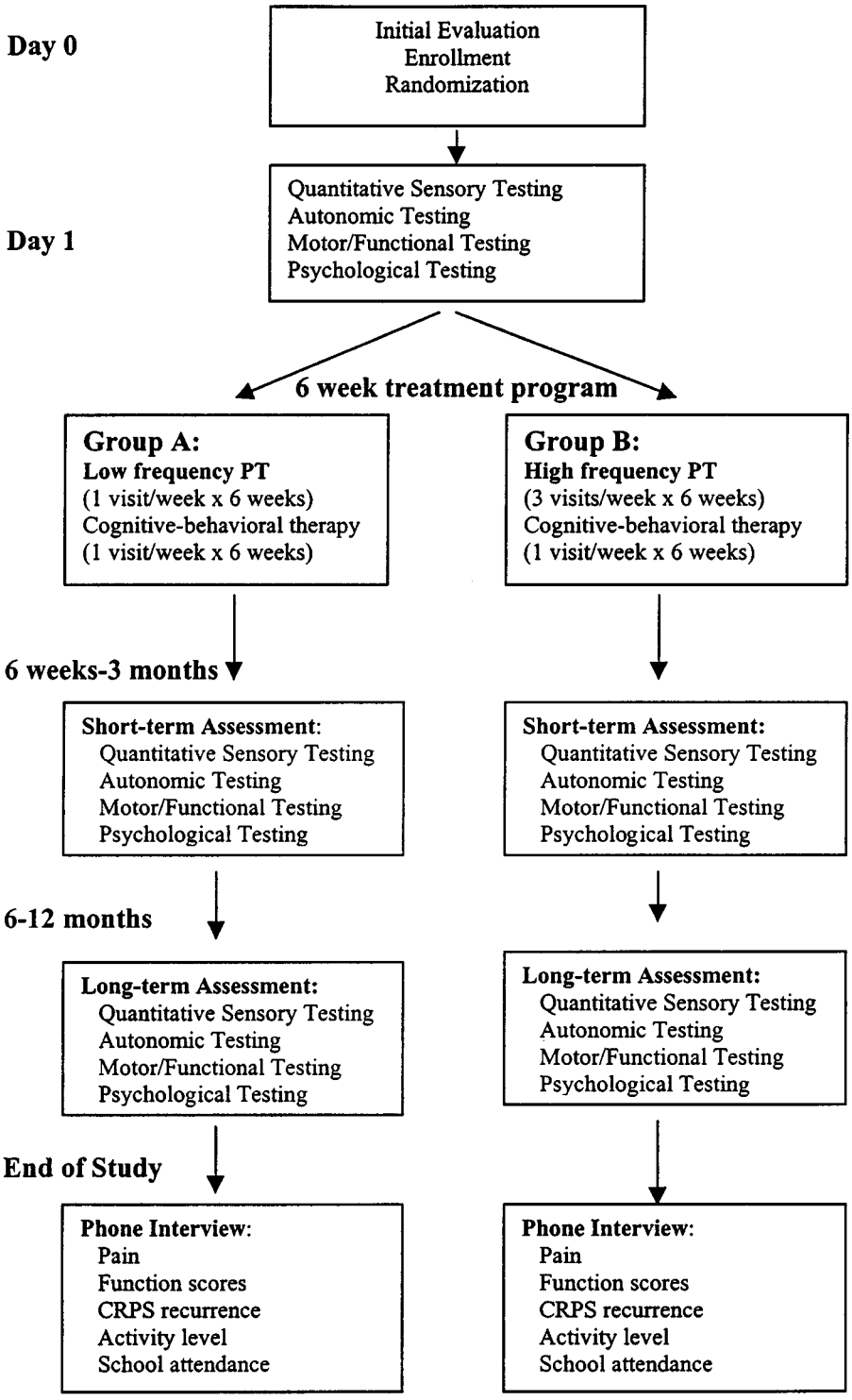

Fig 1. Flow chart of time course study assessments and treatment sessions for the two groups.

Study Design

Once enrolled, participants were randomly assigned by means of a random-number table to one of two treatment groups (Fig 1). Group A received a 1-hour session of PT once per week for 6 weeks (6 sessions) and group B received a 1-hour session of PT 3 times per week for 6 weeks (18 sessions). All patients received the same CBT regimen, which consisted of six 1-hour sessions.

Pain intensity and measures of physical functioning were assessed at 3 time points: (1) pretreatment; (2) short-term follow-up after completion of the treatment program; and (3) long-term follow-up at 6 to 12 months after treatment.

An additional end-of-study follow-up structured telephone questionnaire assessment was conducted at a mean of 133 weeks after treatment (range, 29-180 weeks). Data collected included current level of pain (a verbal 0 to 10 scale), recurrent exacerbations of CRPS, participation in school and activities, and lower extremity function scores.[9] The 11-point verbal pain rating scale is an ordinal scale in contrast with the continuous visual analogue scale (VAS) scale and has been widely used in pain outcomes research. All investigators performing follow-up assessments were not the treating clinicians and were blinded to patients' group assignments. An intention-to-treat analysis was used.

Assessments and Outcome Measures

PAIN ASSESSMENT. Pain intensity and pain affect (psychological distress caused by pain) were assessed with the use of a 10-cm horizontal VAS. Allodynia (pain evoked by light touch) was assessed by means of an ordinal scale ranging from 1 (extreme allodynia) to 7 (no allodynia).

PHYSICAL THERAPY ASSESSMENT. A standardized physical assessment was performed along with two quantitative PT outcome measures.[10] A standardized gait impairment score was determined by having patients walk on a level surface for an untimed 9.1 meters (30 feet), with the least amount of assisted support, and return to the starting line. Major and minor gait deviations are summed to derive a composite gait impairment score.[10] The stair climbing impairment score quantifies the patient's unassisted ability to climb and descend stairs. Higher scores (to a maximum value of 15) indicate more severe functional impairment. Pilot testing with the use of videotaped

Table I. Demographic and clinical characteristics of patients with CRPS in the two study groups

Variable	Group A: PT 1 session/wk (n = 15)	Group B: PT 3 sessions/wk (n = 13)	*P* value*
Patient age (y)	12.5 ± 2.2	13.3 ± 2.8	.39†
Sex			1.00
Female (%)	14 (93)	12 (92)	
Male (%)	1 (7)	1 (8)	
Duration of pain (mo)	2 (1–4)	5 (2–18)	.08‡
Previous PT (%)	10 (67)	7 (54)	.70
History of previous CRPS (%)	3 (20)	3 (23)	.98
Inciting trauma (%)	10 (67)	9 (69)	.99
Location of pain (%)			.37§
Foot or ankle	6 (40)	8 (61)	
Knee	4 (27)	1 (8)	
Leg	2 (13)	3 (23)	
Bilateral lower extremities	3 (20)	1 (8)	

Age is expressed as mean ± SD and onset of pain as median with interquartile range in parentheses.
*Fisher exact test except where otherwise indicated.
†Unpaired Student *t* test.
‡Mann-Whitney *U* test.
§Pearson χ^2 test.

Table II. Status of patients at end-of-study telephone follow-up interview

	Group A (n = 13)	Group B (n = 12)	*P* value
Pain score* (median, interquartile range)	0 (0–0)	0 (0–5)	.40
Recurrence of CRPS	5 (38%)	7 (64%)	.22
Function scores† (median, interquartile range)	5 (4.5–5)	5 (3–5)	.48
CRPS pain in another limb	3 (33%)	2 (22%)	.60
Participation in sports	8 (67%)	7 (70%)	.87

*Numeric rating scale (0 = no pain; 10 = worst pain ever).
†Function scores are ranked from 0 to 5: 0, wheelchair bound; 1, walking with crutches; 2, walking with a cane, partial weight-bearing; 3, unrestricted walking; 4, able to cycle or swim, some restriction on higher-impact activities; 5, no restrictions with full activities.

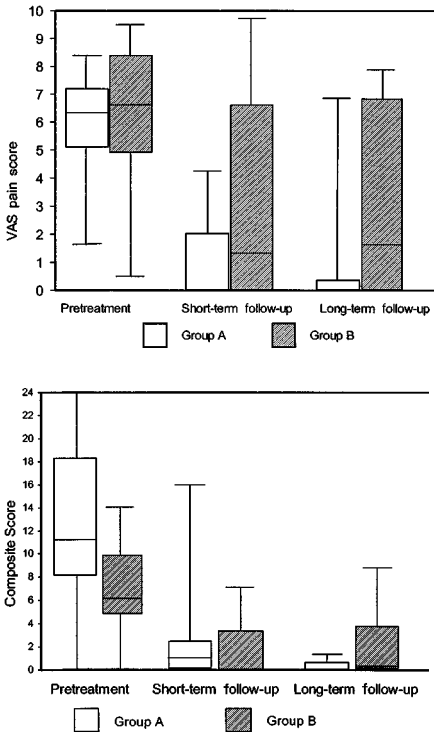

Fig 2. Patients in both treatment groups showed significant improvements in VAS pain scores **(A)** and gait impairment scores **(B)** during the course of treatment, which were maintained at follow-up ($P < .01$ for each comparison relative to before treatment). Median values are presented as *horizontal lines*, *boxes* depict interquartile ranges, and *upper and lower bars* denote ranges. In each panel, the *open box* refers to treatment group A; *dashed boxes* refer to treatment group B.

sessions confirmed excellent interrater agreement (>90%) for both measures.

PSYCHOSOCIAL ASSESSMENT. Participants completed the following questionnaires:

1. The Child Health Questionnaire (CHQ-CF87)[11] comprises 14 subscales including physical functioning, limitations caused by emotional, behavioral, and physical problems, body pain, general behavior, mental health, and self-esteem. Subscales range from 0 (lowest) to 100 (highest).
2. The Child Depression Inventory is a downward extension of the Beck Depression Inventory for adults and uses the child's self-report.[12] T-scores (standardized with a mean of 50 and standard deviation of 10) were derived from published tables.[13]
3. The Revised Children's Manifest Anxiety Scale[14] is a 37-item self-report instrument. Total anxiety scores range from 0 to 28. T-scores were calculated according to the published manual.

Treatment Program

PHYSICAL THERAPY. The PT treatment program was individualized for each participant, based on specific interventions for specific impairments noted in the initial evaluation. Content of treatment varied and reflected strategies appropriate to the patient's status and complexity. Specific modalities included transcutaneous electrical nerve stimulation, progressive weight bearing, tactile desensitization, massage, and contrast baths. All were instructed in home practice regimens with goals to be achieved between scheduled visits.

COGNITIVE-BEHAVIORAL THERAPY. Subjects received 6 weekly sessions of individual CBT incorporating pain management strategies, including relaxation training, deep breathing exercises, biofeedback, and guided imagery. Treatment emphasized problem-solving and identifying and coping with stressful life events. Audiotapes of relaxation techniques were provided for daily home use.

EDUCATIONAL PROGRAM. A standardized educational program reviewed (1) differences between nociceptive and neuropathic pain, (2) differences between protective and nonprotective pain, (3) the importance of physical and psychosocial rehabilitation, and (4) the importance of active participation in treatment. Patients with persistent severe pain and motor and circulatory dysfunction after the 6-week treatment protocol were considered for a separate clinical trial of inpatient treatment with continuous lumbar sympathetic blockade/continuous epidural blockade.

Compliance was assessed both as the individual patient's ratio of kept PT or CBT visits to scheduled PT or CBT visits, respectively, and as the percentage of a study group's patients that kept at least 80% of scheduled visits.

Statistical Analyses

For nonnormally distributed data, between-group comparisons used Kruskal Wallis tests followed by Mann-Whitney *U* tests, and within-group comparisons at repeated time points used Friedman tests followed by Wilcoxon signed-rank tests. Between-group comparisons for normally distributed variables used analysis of variance followed by 2-sample Student *t* tests. Comparisons between time points within each group or for the combined study sample were evaluated by paired Student *t* tests. A Bonferroni-corrected value of $P < .05$ was considered statistically significant. Statistical analysis was performed with the SPSS software package (version 11.0, SPSS Inc, Chicago, Ill).

Power analysis (nQuery Advisor 4.0, Statistical Solutions, Boston, Mass) determined that a total sample size of 26 patients (13 in each group) would provide 80% power for detecting a difference, with an effect size of 1.0 in gait impairment scores and VAS pain scores by using a 2-tailed Bonferroni correction of $P < .017$ (.05 divided by 3 time-point comparisons).

RESULTS

Study Group Characteristics at the Time of Pretreatment Assessments

The study included 26 girls and 2 boys with a mean age of 12.8 ± 2.2 years (Table I). There were no significant group differences in age, duration of pain, and psychological questionnaire scores. All patients had lower extremity involvement, and 4 (14%) of the 28 patients had bilateral involvement. Six patients had reported symptoms of CRPS on previous occasions, though limited medical information made it impossible to confirm diagnostic criteria for CRPS. All patients were using assistive devices (wheelchairs, one or two crutches, or cast-boots) at initial presentation; none could ambulate freely without assistive devices. Most (61%) had previously consulted with a physical therapist; exclusion criteria limited participation to those who had received less than two PT sessions.

Although all patients were referred with a presumed diagnosis of CRPS type 1 (CRPS1), detailed neurologic testing at enrollment confirmed CRPS type 2 (CRPS2) in 10 patients. There was no difference in response to treatment and clinical outcome measures in patients with CRPS2 compared with those with CRPS1; thus, there is no distinction between these syndromes in the reported analyses.

As expected, the psychologic questionnaires revealed altered physical functioning (mean, 46.2; SD, 28.6) and body pain (mean, 21.9; SD, 28.0) scores on the Child Health Questionnaire ($P < .01$ for both 1-sample *t* tests). Interestingly, the mean *t* scores for the Child Depression Inventory (50.9; SD, 12.0) and the Revised Children's Manifest Anxiety Scale (42.5; SD, 12.5) were within normal range, indicating that these children and adolescents did not tend to report elevated depression or anxiety symptoms. Similar results have been reported elsewhere.[6]

Responses to Treatment

Compliance with the treatment regimen was generally good, with 22 (79%) of 28 patients attending at least 80% of scheduled PT sessions and 23 (82%) of 28 attending at least 80% of scheduled CBT sessions. There was no difference between the treatment groups in compliance, despite the difference in the number of PT sessions assigned to the groups. Three participants (2 in group A, 1 in group B) did not complete treatment but were included in the intention-to-treat analysis.

Twenty-five individuals participated in the short-term follow-up evaluation (mean follow-up time, 10 weeks; range, 6-25 weeks) and 24 participated in the long-term follow-up (mean, 66 weeks; range, 29-158 weeks). At the short-term follow-up, both groups showed improvement in all five outcome measures related to pain and physical functioning ($P < .001$ for all measures with a change in median values as follows: VAS pain, 6.4 to 0.6; VAS effect, 5.4 to 0.6; allodynia, 5 to 7; stair climbing impairment score, 9-1; and gait impairment score, 9-0.5) (Fig 2). There were no between-group differences in any of these measures at baseline or at either follow-up assessment. Improvements were maintained at the long-term follow-up, and there was statistically significant additional improvement in pain effect and stair climbing impairment scores between the short-term and long-term follow-up assessments.

One patient dropped out of the study before short-term assessment. Two participants completed short-term assessments but were unable to complete the 6-week PT treatment regimen; one failed to complete the 6-week PT course because of intense pain during the PT exercises and the other failed because of cellulitis of the foot that initially did not clear with antibiotic therapy. Eight additional patients who had shown good improvement at short-term assessment later had severe episodes of recurrent pain and dysfunction that failed adequately to respond to PT during the subsequent follow-up period. These 10 patients (2 early, 8 late; 4 in group A, 6 in group B) eventually received treatment within 1 year with combined continuous lumbar sympathetic and continuous lumbar epidural infusions of the local anesthetic bupivacaine. There were no differences between these 10 patients and the remaining 18 patients who did not receive invasive treatment on any of the pretreatment outcome variables, and there were no differences in long-term outcome between those who did and did not receive lumbar sympathetic/lumbar epidural infusions (P = not significant for each comparison). Treatment with lumbar sympathetic/lumbar epidural infusion was conducted under the aegis of a separate clinical trial (manuscript in preparation).

End-of-study follow-up data were obtained from 25 patients and their families through a phone interview. There were no group differences in pain scores, recurrent episodes of CRPS, and participation in school or activities (Table II). Although recurrent episodes were frequent, in the majority of cases they responded more quickly to PT and related treatments than the original episode. All study participants were attending school and reported improvement in function. All were ambulating without assistive devices at the end of the study.

DISCUSSION

Children and adolescents with CRPS show reduced pain and improved function with a 6-week program of PT and CBT. At the end-of-study follow-up assessment, all patients who could be reached (89%) had excellent improvement in functional status: No patient required crutches or a wheelchair, and no patient had severe atrophy, limb contractures, or vascular compromise.

The results from this trial agree in several respects with previous pediatric retrospective series. Previous studies, including our own,[9] showed generally good recovery with a rehabilitative approach, with a minority of subjects having some persistent or episodic pain and/or limitation in physical activity at 2- to 5-year follow-up. Stanton et al[15] reported resolution of pain in 25 (69%) of 36 children with reflex sympathetic dystrophy treated with an inpatient rehabilitation program including PT, transcutaneous electrical nerve stimulation, biofeedback, and analgesics. Sherry et al[5] reviewed experience with an intensive exercise program in 103 children with CRPS. Ninety-five (92%) children became symptom-free at initial follow-up. Long-term telephone follow-up of a subgroup of 49 patients at a mean duration of 5 years showed either some persistent pain or recurrent episodes in 14 of 49 patients but overall very good functional recovery, with only 1 patient having pain that impaired normal functioning.[5] The findings of Sherry et al suggest that there may be additional benefit from a very high intensity and duration of therapy (5 hours daily) that we were unable to assess with a protocol using 6 to 18 outpatient PT sessions over 6 weeks. The question of what is the optimum frequency and intensity of PT is an issue that may be addressed in future research. In addition, our protocol contained two interventions that were identical in both treatment groups (CBT and education). We cannot, therefore, draw conclusions regarding PT treatment outcome alone.

Enrollment was restricted to subjects who had not received either any substantive PT or nerve blocks. This tended to exclude patients with long-standing disease, as they would generally have received extensive PT and/or nerve blockade. Therefore our results cannot be generalized beyond children and adolescents with a short duration of symptoms.

In previous studies, CRPS recurrence rates ranged from 28% to 33%.[5,15,16] Our findings were similar, with 36% of patients having a recurrence between enrollment and long-term follow-up. Since treatment was not standardized after the 6-week protocol, we cannot draw definite inferences regarding which factors most influenced long-term outcomes. In the future, large-scale multicenter clinical trials with larger numbers of patients may help to elucidate these factors.

The psychological questionnaire scores reflected children and adolescents in the normal range for all of the measures used, with the exception of subscales that assessed physical functioning and body pain. Future studies should also incorporate measures of activities of daily living and functional disability measures to determine the more specific aspects of daily life that are affected by CRPS and improved with treatment.

Compliance with attendance of PT sessions was good in both groups, and there was no apparent difference between a group of individuals receiving 6 PT sessions and those receiving 18 sessions. There was inadequate compliance with recording of "homework" (eg, doing the exercises at home and listening to the relaxation tapes), and thus we were unable to examine if there were any differences in home practice between the groups or any differences in outcomes between those children who were more compliant with homework versus those who were not.

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REFERENCES

1. Stanton-Hicks M, Janig W, Hassenbusch S, Haddox JD, Boas R, Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. Pain 1995; 63:127-33.
2. Mitchell S, Morehouse G, Kean W. Gunshot wounds and other injuries of nerves. New York: Lippincott; 1989.
3. Fermaglich DR. Reflex sympathetic dystrophy in children. Pediatrics 1977; 60:881-3.
4. Richlin DM, Carron H, Rowlingson JC, Sussman MD, Baugher WH, Goldner RD. Reflex sympathetic dystrophy: successful treatment by transcutaneous nerve stimulation. J Pediatr. 1978;93:84-6.
5. Sherry DD, Wallace CA, Kelley C, Kidder M, Sapp L. Short- and long-term outcomes of children with complex regional pain syndrome type I treated with exercise therapy. Clin J Pain 1999;15:218-23.
6. Sherry DD, Weisman R. Psychological aspects of childhood reflex neurovascular dystrophy. Pediatrics 1988;81:572-8.
7. Ruggeri SB, Athreya BH, Doughty R, Gregg JR, Das MM. Reflex sympathetic dystrophy in children. Clin Orthop 1982:225-30.
8. Bernstein BH, Singsen BH, Kent JT, Kornreich H, King R, Hicks R. Reflex neurovascular dystrophy in childhood. J Pediatr 1978;93:211-5.
9. Wilder RT, Berde CB, Wolohan M, Vieyra MA, Masek BJ, Micheli LJ. Reflex sympathetic dystrophy in children: clinical characteristics and follow-up of seventy patients. J Bone Joint Surg Am 1992;74:910-9.
10. Gronley JK, Perry J. Gait analysis techniques: Rancho Los Amigos Hospital gait laboratory. Phys Ther 1984; 64:1831-8.
11. Landgraf JAL, Ware JE. Child Health Questionnaire: a user's manual. Boston: The Health Institute, New England Medical Center; 1996.
12. Beck A, Ward C, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-71.
13. Kovacs M. Children's Depression Inventory. North Tonawanda, NY: Multi-Health Systems; 1992.
14. Reynolds CR, Richmond BO. Revised Children's Manifest Anxiety Scale (RCMAS) manual. Los Angeles: Western Psychological Services; 1985.
15. Stanton RP, Malcolm JR, Wesdock KA, Singsen BH. Reflex sympathetic dystrophy in children: an orthopedic perspective. Orthopedics 1993;16: 773-80.
16. Murray CS, Cohen A, Perkins T, Davidson JE, Sills JA. Morbidity in reflex sympathetic dystrophy. Arch Dis Child 2000;82:231-3.