

# THE MANAGEMENT OF COMPLEX REGIONAL PAIN SYNDROME (CRPS)

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**Abstract.** *The first step in the management of complex regional pain syndrome (CRPS) is coming to the arrival at an accurate diagnosis. CRPS is diagnosed by inclusion and not by exclusion. No laboratory tests can diagnose CRPS 100% of the time. The use of scintigraphic triphasic bone scans (STBS) may help diagnose CRPS in approximately 55% of the cases in the first six months(1). The research of Chelimsky et al., found STBS to be abnormal in no more than 25% of CRPS patients(2). The use of infrared thermal imaging (ITI) is useful in the diagnosis and management of CRPS pain. It provides an overall picture of temperature changes in superficial and deep structures (27 mm) (3-5). ITI provides useful clinical information when applied with proper technique. It provides diagnostic and therapeutic information limited to diseases involving autonomic, neurovascular, and neuroinflammatory changes(3,6,7).*

*CRPS is a clinical diagnosis corroborated by test such as laser doppler, STBS, and ITI. Early diagnosis is essential for successful treatment of CRPS(8-10).*

**Descriptors.** *complex regional pain syndrome (CRPS), epidural nerve block, early diagnosis, infrared thermal imaging (ITI), scintigraphic triphasic bone scans (STBS), sympathetic ganglion block (SGB)*

## INTRODUCTION

Complex regional pain syndrome (CRPS) is best managed by a multi-disciplinary therapeutic approach in early stages of the disease.

The successful formula in the treatment of CRPS can be summarized as early diagnosis, early physical therapy, early sympathetic nerve blocks, discontinuation of addictive narcotics, benzodiazepines(BZ), and treatment with antidepressants(analgesics of choice for chronic pain)(8,11).

The best method of diagnosing CRPS requires the following four principles:

- (i). A practically constant allodynic and hyperpathic pain at times is superimposed by stabbing or causalgic pain.
- (ii). Pathologic motor response to the pain in the form of vasoconstriction of the skin resulting in, a cold extremity. In more advanced cases, the patient can develop symptoms such as flexion deformity, tremor, and dystonia(8,12-20).
- (iii). The symptom of inflammation can be in different degrees. The inflammation may be in the form of soft tissue swelling, skin rash, spontaneous black and blue discoloration of the skin, purplish skin, neurodermatitis, swollen, shiny, or sweaty skin, and in more advanced cases trophic changes involving hair, nails, skin, and lymphoethic circulation. The inflammation and its varied manifestations fluctuate from day to day(21-23).
- (iv). The stimulation of the limbic system can be caused by the constant neuropathic pain. This is manifested by insomnia, agitation, irritability, depression, chronic fatigue, and poor judgment(8,11).

Once the patient meets the above four criteria(which may be present in different degrees and different severity), the diagnosis of CRPS is established.

## MANAGEMENT OF CRPS

In the treatment of CRPS the administration of a multi-disciplinary management approach discussed below is quite helpful in the management of CRPS patients.

*(i). Detoxification:* By the time the patient is referred to a pain clinic for the management of CRPS, they are already on a series of addicting medications. The use of addicting medications should be discontinued and the patient should be detoxified at the onset of treatment.

*(ii). Detoxification from addicting Benzodiazepams:* Most commonly, such patients have been treated on a long term basis with medications such as Valium as a muscle relaxant, Xanax, Ativan, or Tranxene as anxiolytic, Halcion, Dalmane, or Restoril as a sedative.

Realizing that there are two forms of benzodiazepams available which are not addicting (they do not suppress the cerebral endo-benzodiazepams formation). These two medications can be used to replace the addicting benzodiazepams. These consist of Klonopin (Clonazepam), and Serax. The patient can be withdrawn quite rapidly in the matter of five to seven days as long as Klonopin is used in generous doses to prevent withdrawal. In the case of Halcion and Valium, it may take up to two to three weeks to achieve the same goal because of their strong potential of dependence.

*(iii). Detoxification from addicting narcotics:* Invariably, such patients have been exposed to medications such as Lortab, Lorcet, Percodan, Percocet, Demerol, and a large list of other Morphine agonists which can suppress the cerebral endorphines on a long term basis.

Realizing that no CRPS patient will see any type of improvement as long as their pain is not under control, and realizing that no CRPS patient will get better as long as the cerebral endorphines are absent, the patients should be “cold turkey” withdrawn from the above mentioned addicting narcotics. This immediate withdrawal can be achieved by providing the patient with Morphine antagonists, non-addicting type of narcotics that provide complete pain relief without withdrawal complications enabling the patient to discontinue the strong narcotics that they have been on. This is achieved by treatment with Stadol (nasal spray is preferred to IM form) alternated with one to two tablets of Ultram every four hours as needed. Between these two non-addicting strong narcotics, the patient will not suffer from withdrawal pain. If the patient for any reason cannot take one or the other of the above-mentioned two medications, then there are alternative analgesics with the same characteristics as the above-mentioned medications. These consist of Nubain or Buprenorphine (Buprenex).

Realizing that Stadol is not even a controlled substance and realizing that it has only the potential abuse of psychological rather than physical nature, the patient should sign a contract that they will not seek pain medication from another source. In addition, even if the patient tries to abuse the system and tries to take the old addicting narcotics along with Stadol, then they will become quite nauseated and that gives the clue to the clinician regarding purposeful drug abuse in early stages.

*(iv). Treatment with newer Antidepressants:* The treatment of choice for CRPS is the use of antidepressants. Every CRPS patient should be started on antidepressants from the beginning of their course of treatment. The patient should be educated that the use of antidepressants is not for the purpose of counteracting depression. Antidepressants have three major functions which consist of first of all providing analgesia, secondly providing natural sleep, and thirdly improving cerebral function to better control depression.

The antidepressant of choice in order of preference for CRPS patients is Trazodone (which provides excellent REM sleep and accelerates recovery along with providing excellent analgesic effect), Prozac, Paxil, and Desipramine.

The older tricyclic antidepressants such as Elavil and Tofranil should be avoided due to the fact that they can cause weight gain, inactivity due to aggravation of fatigue, and can aggravate cardiac arrhythmia.

The patient's compliance should be monitored with the help of obtaining serum levels of antidepressants. The dosage of the medication should be adjusted according to the patient's tolerance and their sleep pattern. The dosage of antidepressants is quite variable from patient to patient.

(v). **Treatment with muscle relaxants:** The constant component of CRPS is hypertonicity of the muscles in the form of vasoconstriction, flexion spasm, or movement disorder(8,12-20). It is imperative to treat the patient with muscle relaxants. The use of addicting muscle relaxants such as Soma should be avoided. Soma is metabolized in the body and is transformed to meprobamate which is quite addicting and causes withdrawal with recurrence of muscle spasms. Flexeril which some have has the reputation of being an antidepressant, is quite depressing and aggravates fatigue. It is quite effective in somatic type of muscle spasm, but not the sympathetic type.

The ideal muscle relaxant which works quite selectively on anterior lateral horn cells of the spinal cord is Lioresal(Baclofen). This medicine should be started in small doses and gradually increased to a larger dose. The limiting factor is nausea. Once the patient develops nausea, then the dosage should be cut down by 5-10 mg and not increased any further.

Another effective muscle relaxant is Norflex. If the patient has muscle spasms along with jerky movement and dystonic motion of the extremity, the use of anticonvulsants such as Klonopin, Neurontin, Tegretol, Depakene and Trileptal may be beneficial.

After achieving enough relaxation of the muscles in the extremity, the use of assistive devices such as crutches, wheelchair, braces, canes, and walkers should be discontinued. As long as the extremity is inactive due to the use of assistive devices or due to the application of a cast, the "sleeping nociceptive nerve fibers" become activated causing more inflammation and deep pain.

## **PITFALLS IN THE MANAGEMENT OF CRPS**

The lack of a multi-disciplinary therapeutic approach can cause major pitfalls in the management of CRPS. Depending on the specialist who first starts treating the patient, the treatment method is eschewed toward the role of that specialty. This simple neuropathologic fact has become a point of contention and argument among physicians. This has deprived a lot of patients from proper treatment just because in the chronic stages of their pain, it is not purely sympathetic in nature.

The more chronic the disease, the more the treatment should be addressing the control of both sympathetic and non-sympathetic pain.

Also, the lack of understanding of the disease can cause major pitfalls in the treatment and management of CRPS.

## **USEFUL TOOLS IN THE MANAGEMENT OF CRPS**

The use of infrared thermal imaging (ITI) can facilitate early diagnosis of CRPS, and can achieve a higher recovery rate among CRPS patients by virtue of early diagnosis of the disease. CRPS cannot be accurately diagnosed by a single test. CRPS is a clinical diagnosis when the following four principles are met (7-9,24-26):

- (i). Neuropathic, hyperpathic, or causalgic pain;
- (ii). Vasomotor disturbance, flexor spasm, or tremor;
- (iii). Inflammation at some point in the course of the disease;
- (iv). Limbic system dysfunction in the form of insomnia, agitation, depression, and poor memory (7,11,27).

Tests such as ITI are mainly helpful to obtain information regarding the nature and extent of the disease, and to guide the clinician in proper management of pain (7,8).

ITI is helpful in identifying the areas of thermosensory nerve damage, and as well as diagnosing the phenomenon of CRPS spread.

Another commonly applied test of choice for the diagnosis of CRPS is the scintigraphic triphasic bone scan (STBS). Lee and Weeks, in their meta-analysis of STBS showed this test to be positive in no more than 55% of CRPS patients (1, 28). Chelimsky et al., found STBS to be abnormal in no more than 25% of CRPS patients(2).

The use of anatomical tests such as magnetic resonance imaging (MRI), computed tomography (CT), and physiological tests such as electromyography (EMG) and nerve conduction velocity (NCV) tests have been the main diagnostic tools applied in the management of somesthetic (somatic) pain. The above tests usually are not informative in the diagnosis of neuropathic pain(3).

The neurovascular involvement in neuropathic pain requires tests such as ITI and Quantitative sudomotor axon reflex test (QSART) that address the autonomic (e.g., thermal) changes for a more accurate diagnosis and treatment(3).

## **NERVE BLOCKS**

The use of sympathetic ganglion blocks (SGB) is not helpful in the treatment of late stages of CRPS. This is because the patient's pain is not sympathetically maintained pain (SMP), but the pain is sympathetically independent pain (SIP). In the early stages of the disease, when the pain is SMP in nature, SGB temporarily help calm down the disease. They are mainly used as a diagnostic tool rather than a therapeutic tool. In late stages of the disease, the use of SGB can be more harmful by being traumatic to the sympathetic nervous system(11,29,30).

In contrast, in late stages of CRPS, the only form of nerve blocks that are helpful and improve the pain are epidural, caudal, and paravertebral nerve blocks. These blocks have nothing in common with SGB. The SGB is done by inserting a needle into the sympathetic ganglion. Each time this is done, several nerve cells are destroyed and excessive repetitive SGB can cause "virtual sympathectomy" due to permanent damage to the sympathetic ganglia (3,6,7,11).

The use of an epidural nerve block is the last resort type nerve block in patients with late stage CRPS. The reason for administration of epidural and paravertebral nerve blocks is the fact that the pathology is chronic and is affecting both sympathetic and somesthetic systems. These blocks help relieve the pain and improve the circulation in the target area. This block is done by insertion of the needle into the epidural space (the space between the spinal cord and spinal canal). This is done under x-ray guidance. After the epidural space is identified, a combination of 4/5 Marcaine local anesthetic and a minuscule amount of Depo-Medrol® is injected in the epidural space. The Depo-Medrol® itself consists of a large inert and innocuous protein attached to a small amount of Methylprednisolone. The use of local anesthetic Marcaine and a small amount of a corticosteroid helps relieve the pain and reduces the inflammation.

Because of the heavy molecule of protein attached to the corticosteroid, the blood circulation cannot readily absorb the Depo-Medrol®. As a result, the beneficial effect of pain relief and anti-inflammation lasts approximately two to three months. During the same period of time, physical therapy, massage therapy, and other treatments are applied. In 90% of such patients do not need more than one complete course of nerve blocks. In 10% of the patients who have been quite chronic and have had permanent nerve damage may need a reinforcement course of nerve blocks every three to four months.

The side effects of this treatment are nil or negligible. The molecule of protein does not allow the corticosteroid to spread to other organs of the body, and helps the beneficial effect of the treatment to last up to two to three months.

If the chronic, complicated patients are not treated with epidural blocks, the patient becomes inactive and immobilized due to severe pain. In contrast, these blocks provide relief lasting up to three months as well as reducing the neuroinflammation of CRPS. The prolonged inactivity and bed rest are the two cardinal sins in the management of CRPS, and are counteracted with these blocks.

If we go according to current concepts of diagnosis and management of CRPS, the patients are doomed to be in severe chronic pain and are loaded with strong narcotics that make them even more inactive. This is the main reason for the very high percentage of failure in the management of CRPS.

On the other hand, in our study of 824 CRPS patients, we have found that more than 50% of the patients return to work after they have been detoxified and treated with epidural and paravertebral nerve blocks versus less than 20% treatment success in patients who were not treated effectively or were treated with unnecessary surgical procedures(11).

## **MANNITOL IN THE TREATMENT OF CRPS**

In, 1969 and 1972 the research by my colleagues and I showed the efficacy of the use of Mannitol, in counteracting intracellular edema(31,32).

Over the past decade in our clinic, we have noted the beneficial effect of I.V. Mannitol in neuroinflammation. This is especially true in patients suffering from post-herpetic neuralgia, CRPS, and other forms of neuropathic pain. The common denominator in the various neuropathic pain is involvement of thermoreceptor sensory nerves and the sympathetic system at some stage of the disease. The sympathetic nervous system has three main functions. *(I)*. Thermal regulation; *(ii)*. Control of vital signs; *(iii)*. Regulation and modulation of the immune system function. In the neuropathic pain patients, it is not that unusual for the dysfunctional immune system to cause neuroinflammation accompanied by intercellular and axonal edema. If such patients are treated with plasma diuretics such as Hydrochlorothiazide or Lasix, these diuretics reduce the plasma volume which can have the potential of causing edema ex-vacuole and aggravate the neuroinflammatory edema.

The use of I.V. Mannitol (which is an inert sugar, and is a selective strong diuretic) selectively helps counteract neuroinflammation and reduces the intracellular edema of CRPS. On the basis, in our clinic as well as Doctor Veldman and his colleagues from the Netherlands have applied I.V. Mannitol to counteract the neurogenic edema of CRPS (33). This neurogenic edema is especially more prominent in patients who have undergone surgery for sympathectomy, infusion pump treatment, and spinal cord stimulator (SCS). At times the neuroinflammation is severe enough to cause such symptoms as skin rash and neurodermatitis as well.

I.V. Mannitol is very well tolerated. The only contraindications are in patients who have practically total renal failure and in patients who already have a dead space of an intracerebral hemorrhage or necrotic brain tumor, which can cause entrapment of the Mannitol in the dead space.

As long as the patient has normal renal clearance (no protein in the urine), the I.V. Mannitol is quite safe in the treatment of CRPS. As the Mannitol has a tendency to crystallize, the IV should be applied in 1-1 ½ hours. If the IV drip is prolonged up to 4-6 hours, there is the risk of crystallization of the Mannitol. Certainly, a filter should help prevent any such risk as well. The usual dose is 100gm Mannitol in 500cc D5W (depending on the patients weight). This treatment can be done on an out patient basis.

Usually, it only takes one to three treatments of I.V. Mannitol to help reduce the neuroinflammation of CRPS. Also, I.V. Mannitol treatment is quite successful and would help eliminate the necessity for unnecessary surgery in CRPS.

## **PHYSICAL THERAPY**

"There have been references in the literature that physical therapy can aggravate the patient's pain. Yet in every outline of treatment for CRPS, the use of physical therapy is emphasized. These two statements seem to be contradictory."

Both statements are absolutely true. Excessive exercise and physical therapy that causes fatigue, pain, and distress to any part of the body, only flares-up aggravates the inflammation and pain of CRPS. On the other hand, the commonest aggravators of CRPS are bed rest, inactivity, application of ice, and the use of assistive devices (8,34). In CRPS, the best treatment is eustress and not distress (8).

Distress refers to the stress of prolonged bed rest and inactivity. Like any other machine, prolonged idling of the body is distressful and causes damage to the body. Especially in CRPS, the prolonged bed rest results in aggravation of pain and insomnia. These patients also suffer from severe, chronic insomnia due to the constant allodynic pain as well as due to the aggravation of constriction of blood vessels secondary to inactivity. One of the earliest signs of CRPS is a restless night with the patient constantly being fidgety and changing position all night as well as having to get up and walk to get some relief.

The second form of distress is too much exercise, and prolonged physical therapy.

The CRPS patient has to learn that they will have pain with too much exercise, and the patient will have more pain without exercise. The patient will have to find a happy medium. The patient will have to rest and exercise frequently. Three days a week in the P.T. Department is not enough. The patient should continue the instructions of the physical therapist from morning to night with equal periods of rest and exercise. The patient should learn from the human heart which beats approximately once a second for 80 to 90 years without taking a vacation. The reason is the heart beats half a second and rests half a second. The same principle should apply to physical therapy in CRPS.

## **MASSAGE THERAPY**

Massage therapy is practically indispensable for the treatment of CRPS, especially if the patient is undergoing trigger point injections, occipital nerve blocks, and paravertebral nerve blocks. Applying massage therapy immediately after having the above-mentioned nerve blocks disseminates the irritating chemicals (e.g., nitric oxide (NO), substance P, and calcitonin gene-related peptide (CGRP)) away from the area that the nerve block insertion has released the encapsulated chemicals and thus helps the elimination of the irritating chemicals by massage as well as application of moist heat. This is similar to trying to clean a swimming pool that has not been touched for a year. Obviously, the pool is full of residuals of chemicals that have been accumulated in the pool. It is not enough to partially clean the toxic chemicals, but it also needs the flushing of the chemicals out of the pool. The massage does the job of flushing of the chemicals out of the encapsulated areas making the chemicals accessible to capillaries, which absorb the chemicals and excrete them through the kidneys.

## **PROPRIO THERAPY**

Proprio therapy refers to the patient applying physical therapy onto themselves. For example, one of the best treatment modalities for pain is treatment of allodynia (proprioceptive touching and applying massage) applied by the patient in the form of gentle massage to the skin. If another person tries to do the massage in the same sensitive area, the pain may get worse, but the patient can usually perform the proprioception with far less pain. Application of Emla cream (lidocaine 2.5% and prilocaine 2.5%) also helps. This is not a sign of malingering or anything like that. It is noted in animals suffering from neuropathic pain of CRPS that animals avoid any contact with people or other animals. On the other hand, when the pain is severe, cats or dogs try to get relief by licking and even gently biting the extremity. We don't expect any patient to bite their extremity, but otherwise proprioceptive therapy is very effective. The patient should use the proprio therapy for treatment of allodynia, as well as for treatment of inactivity causing deep pain.

## **AVOIDANCE OF SURGERY**

The major contributors to failure of CRPS management are application of ice, the use of addicting medications, bed rest, inactivity, the application of a cast, and the performance of unnecessary operations(8,11,34).

The commonest forms of surgical procedures that cause permanent damage and permanent intractability of CRPS are: Carpel tunnel surgery, tarsal tunnel surgery, rotator cuff surgery, ulnar nerve decompression, surgical exploration of the knee, neuroma, or ankle, thoracic outlet syndrome surgery, or removal of a bulging disc or herniated discs in the distribution of spasm and pain secondary to CRPS.

Realizing that CRPS is invariably accompanied by different degrees of inflammation, it is not at all uncommon for the patient to have a clinical picture simulating carpal tunnel or tarsal tunnel syndrome. Instead of operating on the patient, the best things to do are to use epsom salt with warm water, nerve blocks, and I.V. Mannitol to help take away the inflammation.

The clinician should be reminded that it is not the so-called entrapment neuropathy which is the cause of CRPS. The reverse is invariably the case.

Other surgical treatment methods such as sympathectomy is invariably a failure. Its application should be limited to the patients who have less than five years of life expectancy(8). In such late stages of CRPS, the nervous system has lost its plasticity and cannot respond properly to surgical sympathectomy (11,35). More over, the disease has spread, to other parts of the body and a regional sympathectomy will not be of any benefit to the patient (3,11,36-39).

Chemical sympathectomy (Alcohol blocks) which are chemical blocks in the form of phenol, alcohol, etc., are the most dangerous and destructive forms of nerve blocks.

The use of alcohol blocks, sympathectomy, or neurectomy (cutting nerve fibers) only adds assault to the injury. Such destructive procedures relieve the pain for a few weeks to a maximum two months, only for the pain to return with more intensity and in a larger area of the body.

The use of radiofrequency sympathectomy (nerve ablation and block) is the most traumatic and invasive form of treatment. The radiofrequency electrode causing a boiling hot temperature at the target area which coagulates, destroys and kills the nerve fibers and nerve cells.

Treatment with sympathectomy, be it surgical, chemical, or radiofrequency is useless for advanced cases of CRPS. It will cause rapid spread of CRPS to other parts of the body and cause more pain for the patient.

## **DIET**

Even though the majority of clinicians do not consider eating habits important in CRPS patients, certain foods such as chocolate (which contains phenylethylamine and it directly stimulates the formation of dopamine and norepinephrin), hot dogs, and foods rich in tyrosine (red meats) which is the precursor of norepinephrine should be avoided.

We devised this method of behavior modification more than 17 years ago. This diet is not aimed at losing or gaining weight. It excludes foods that are harmful to your health and aggravate chronic pain (i.e., Five C's: cookies, cakes, chocolate, cocktails and candy. Other foods to avoid are internal organ meats such as Liver, sausage, and hot dogs). It also emphasizes the intake of foods that help the inhibitory nerve cells that suppress the pain input (4 F's: Fresh fruit, fresh vegetables, fish, and fowl)(8).

By doing so, the patient's weight normalizes itself automatically: overweight or underweight extremes normalize close to the patients ideal weight(8).

## **CONCLUSION**

CRPS patients should be diagnosed early, treated early; the treatment should be multi-disciplinary and affirmative. The only hope for the patient is better education of the physicians in regards to the mechanism of CRPS, and the importance of early diagnosis, early physical therapy, and the use of nerve blocks, as well as detoxification from harmful medications. Also, it is important to spare the patient from unnecessary surgical procedures that can cause more pain and spread of CRPS.

There are no standardized diagnostic methods and no universal treatment plan that have been available, and the success rate of the treatment has been quite low.

At, the present time there are enough methods available to keep these patients comfortable and give them a better quality of life.

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