

Complex Regional Pain Syndrome (CRPS) – Order or Chaos?

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Introduction

Causalgia was first described in survivors of gunshot wounds who survived the American Civil War. Since then, despite the efforts of the International Society for the Study of Pain (IASP) in codifying the diagnostic criteria for CRPS, therapy remains problematic and bedevilled by the presence of many case reports and small series but sparse level-one evidence in the form of randomised control trials (RCTs).

Diagnosis

CRPS may affect children of any age but is most common in middle age and is four times more common in females. There is a particular association with stress, both at home and work, typified by the fact that CRPS has never affected a successful professional athlete or an independently wealthy individual. Any part of the body may be affected but the limbs are most frequently involved with an equal incidence in upper and lower limbs. The IASP published a classification of and diagnostic criteria for CRPS in 1994⁽¹⁾.

The major criterion for diagnosis of CRPS is the presence of an initiating noxious event that results in reduced mobility and continuing pain / allodynia / hyperalgesia disproportionate to the initiating injury. The initiating trauma may be so trivial as to have been forgotten.

The two types of CRPS are defined by:

- The absence (CRPS 1 previously reflex sympathetic dystrophy [RSD])
- Or presence (CRPS 2 previously causalgia) of a coexisting nerve injury

Supporting evidence of CRPS in the early stages includes:

- Oedema
- Changes in skin blood flow (or colour)
- Abnormal sweating (sudomotor activity)
- The diagnosis is excluded by the presence of conditions which would explain the symptoms.

With progression of CRPS further symptoms and signs may be noted:

- Atrophy of the hair, nails and other soft tissues.
- Loss of joint mobility.
- Impairment of motor function including weakness, tremor and dystonia.

- Possible presence of sympathetically maintained pain revealed by diagnostic blocks.

The diagnostic criteria were modified by Bruehl in 1999⁽²⁾ to include continuing pain out of all proportion to the inciting event but noting that 10% of cases may have the vaso- and sudomotor changes with reduced mobility but mild or absent pain. The new classification was based on symptoms and signs as follows:

The patient must report at least one **SYMPTOM** in each of the following categories.

- Sensory:** Hyperaesthesia / allodynia.
- Vasomotor:** Temperature changes, skin colour changes and/or skin asymmetry.
- Sudomotor:** Oedema, sweating changes or asymmetry.
- Motor/Trophic:** weakness or loss of range of motion.

The clinician must elicit at least one **SIGN** in two or more of the following categories.

- Sensory:** Hyperalgesia (pinprick) or allodynia.
- Vasomotor:** Temperature and/or skin colour changes and/or asymmetry
- Sudomotor:** Oedema or sweating alteration.
- Motor/Trophic:** Evidence of decreased range of motion or power.

The clinician must maintain a high index of suspicion and involve a pain practitioner early to confirm the diagnosis by means of response to sympathetic block that is best elicited as early as possible in the progression of CRPS.

TREATMENT

Systemic Medication

NSAIDs – are used early in the disease together with opioids and paracetamol to exclude the presence of nociceptive pain. COX 2 specific agents (coxibs) have been advocated for long term treatment due to their lesser side effect profile but the cost of these agents is significant and improved efficacy over the cheaper non-selective NSAIDs has yet to be demonstrated in CRPS. Gastric side effects may be reduced as long as patients are not on aspirin for prophylaxis of coronary and cerebrovascular disease⁽³⁾. Coxibs have similar renal effects to non-selective NSAIDs and both may impair hypertensive control by causing fluid retention⁽⁴⁾.

Tricyclic antidepressants – have never been formally tested in CRPS but have shown some effectiveness in small series.

Amitriptyline is the most widely used, especially where sleep disturbances are prominent. Dothiepin has a similar mode of action but fewer anticholinergic side effects. Doses used start at 10mg nocte and may be escalated to 75mg nocte after which further analgesic response is unlikely to be seen. Desipramine may be more appropriate for agitated patients and may cause moderate weight loss. The SSRIs such as fluoxetine are ineffective in pain management but may be used to treat coexisting depression. Venlafaxine may be useful in patients who are unable to tolerate the tricyclics ⁽⁶⁾.

Tramadol – has combined antidepressant and mu agonist activity making it a very useful agent for long term management of CRPS. There is a very low abuse potential compared to other opioids. A slow release preparation should be used to minimise troublesome nausea and dysphoria associated with high peak levels. Typical doses start at 100mg of the SR preparation 8-12 hourly to a maximum of 300mg 8 hourly or 400mg 12 hourly ⁽⁶⁾.

Trifluoperazine – Is a phenothiazine with anxiolytic, anti emetic and anti-psychotic activity. This drug seems to be effective in CRPS in early stages but the mechanism is uncertain, possibly related to effects on the alpha receptors peripherally and at a spinal level. Dose should start at 0.5-1 mg BD increasing to a maximum of 5mg BD ⁽⁷⁾.

Anticonvulsants – may be particularly important for the neuropathic component of CRPS 2 with the associated lancinating pain in a nerve or root distribution. Gabapentin is the most effective and least toxic alternative but is also the most expensive and is only funded by a small number of medical aids after extensive motivation. The initial dose of gabapentin is 200mg BD and further effect is unlikely above doses of 1200mg TDS.

The suggested alternative is carbamazepine, which has a lower acquisition cost but may actually result in an increase utilisation of medical resources due to the unpredictable pharmacokinetics (requiring regular blood levels) and toxicity (requiring regular FBC and LFT monitoring).

Clonazepam is a reasonable alternative in doses of 0.5-3mg BD. Sedation with concomitant tricyclic therapy may be problematic but the drug is cheap and effective ⁽⁸⁾.

Sympathetic blocks

IVRA – A Bier's block is an easy and effective technique to manage CRPS of both the upper and lower limbs. Unfortunately the most effective adjunct to the local anesthetics used in IVRA, guanethidine and bretylium are no longer manufactured due to limited demand in their primary roles in anaesthesia and cardiology. The effectiveness of guanethidine has been questioned but appeared effective in limited experience at Westville ⁽⁹⁾. IV clonidine has been used but is also not available in SA ⁽¹⁰⁾. The Pain Clinic at Westville has been using a combination of labetalol 60mg and ketorolac 30mg in 40ml (arm) or 60ml (leg) 0.5% lignocaine ⁽¹¹⁾. Limited patient numbers has made evaluation of the combination difficult but the initial impression is that the combination is somewhat less effective than guanethidine. Safe performance of IVRA requires meticulous attention to detail.

IVRA requires IV access in the limb to be blocked, as distally as possible, as well as the unblocked limb, to treat adverse effects that may arise during cuff inflation.

The cuff used should be an orthopaedic tourniquet rather than a baumanometer cuff due to the more secure fixation possible with the orthopaedic tourniquet. The pressure of the cuff should be monitored and should be at least 50mmHg greater than the patient's systolic BP. A standard pressure (commonly 250-300 mmHg) may be excessive, especially in younger patients.

The recommended local anaesthetic for BB is prilocaine, but this drug is not freely available in South Africa. Bupivacaine (both racemic and levo) and ropivacaine **SHOULD NEVER** be used for BB as cardiac arrest is likely after cuff deflation. The most appropriate drug for BB in South Africa is lignocaine at a concentration of 0.5%. This concentration is achieved by mixing 5ml of 2% solution in 35 ml diluent to a total volume of 40ml. The volume required is 30-40ml for an arm BB and 60-80ml for leg BB. The diluent used may include 0.5 ml 8.5% NaHCO₃ per 40ml to reduce burning and hasten onset.

The limb to be blocked should be exsanguinated, using an Eschmark bandage to improve block effectiveness by limiting dilution of injectate. Exsanguination may be omitted, or limited to limb elevation, if it is likely to cause significant patient discomfort.

Following exsanguination and cuff inflation injectate should be administered slowly (over 3-5 minutes). Rapid injection may cause venous hypertension sufficient to overcome cuff pressure with potential toxicity and loss of block efficacy.

The cuff should remain inflated for at least 20 minutes to allow distribution and fixation of the drugs used.

Cuff deflation should be done incrementally by completely deflating the cuff for 20 sec and reinflating for 10sec over a period of 1-2 minutes (3-4 cycles). This reduces the peak level of lignocaine released into the circulation ⁽¹²⁾.

Plexus Blockade – The upper limb may be blocked at the interscalene, supra- and infraclavicular levels and at an axillary level. The leg may be blocked at the lumbar and sacral plexuses, femoral nerve and proximal and distal sciatic nerves. At each of these sites a single shot block may be done or a catheter may be inserted to prolong the duration of blockade. The level and duration of limb blockade for CRPS has yet to be determined. Winnie first advocated a single shot block to define the level of nociceptive pathology in 1968 as follows ⁽¹³⁾:

- No relief** – indicates a central pain syndrome. This is extremely difficult to treat but further blocks ARE NOT indicated.
- Relief for the expected duration of Local Anaesthesia** – indicates a nociceptive pain syndrome. A continuous block may be effective but further single shot blocks ARE NOT indicated.
- Relief significantly in excess (3hrs +) of expected duration of Local Anaesthesia** – indicates CRPS /

Sympathetically Maintained Pain (SMP). This is the situation where repeated single shot blocks MAY BE indicated.

While this classification may seem intuitively attractive it has not been widely accepted⁽¹⁴⁾. Plexus blockade has been used in a single case of CRPS but the role of continuous somatic blocks for CRPS has yet to be defined⁽¹⁵⁾.

Ganglion Blockade – The sympathetic nervous system may be blocked at a number of levels, most commonly the stellate ganglion for CRPS affecting the arm. Long lasting relief is diagnostic for CRPS / SMP level⁽¹⁶⁾. Successful ganglion block may be followed up by permanent sympathectomy, with the largest series in the world literature reported from Durban⁽¹⁷⁾.

The most important role of interventional pain management in CRPS may be to facilitate physio- and occupational therapy and thus prevent the progressive immobility and muscle atrophy responsible for most of the disability in CRPS⁽¹⁸⁾.

The latest algorithm for management of CRPS is shown in Appendix 1 from Stanton-Hicks. The progression shown is from least invasive / lowest risk to most invasive / high risk procedures depending on clinical response.

There are a number of experimental treatments in case reports or small series for which references are available on request.

Topical treatment with capsaicin is now possible at high doses due to advances in patch technology and drugs such as ketamine and lignocaine may also be effective topically. Systemic lignocaine, either IV or subcut and later orally (as mexelitine) has also proven surprisingly effective.

Many therapeutic modalities are being explored, most with significant monetary (hyperbaric O₂, IV Immunoglobulin, spinal cord stimulation) and / or physiological (corticosteroids, α blockers (impotence), Ca channel blockers) costs.

Conclusion

The management of CRPS in the coming years will hopefully be defined more by RCTs than case reports and small series. Should this happen, order will hopefully appear from the current chaos⁽¹⁹⁾.

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