Intravenous regional sympathetic block: Past, present and future?

Alfred PJ Lake BSc MBBS FFARCS

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Intravenous regional sympathetic block is a valued component of the pain clinician's armamentarium for the management of the complex regional pain syndrome type 1. Treatment of this multifaceted condition is multimodal, and despite a lack of convincing supporting evidence from clinical trials, the author makes the case for retaining the technique while recommending both appropriate guidance and further study.

Key Words: *Complex regional pain syndrome type 1; Guanethidine; Intravenous regional block; Reflex sympathetic dystrophy*

The intravenous regional sympathetic block (IRSB) with guanethidine, or other sympatholytics such as reserpine, has been performed by pain clinicians all over the world since it was first described by Hannington-Kiff (1). It has resulted in significant benefits for patients with reflex sympathetic dystrophy, now relabelled chronic regional pain syndrome (CRPS) type 1. Overall, the clinical management of neuropathic pain syndromes remains challenging, and patient's needs are persistently unmet (2). CRPS is one of the most difficult pain syndromes to treat, with uncertain etiology and mechanisms. Perez and colleagues (3) reviewed studies of variable quality and found major differences in treatment methods, ranging from IRSB to steroid or calcitonin administration.

A systematic review combined with a double-blind evaluation by Jadad et al (4) failed to support IRSB as an evidence-based treatment; however, the study only looked at 10 patients. A review of sympathetic nerve blocks for pain therapy by Boas (5) concluded that further use of intravenous regional blocks remains questionable, but recommended further study to establish a role for the procedure. In addition, a double-blind study of patients with symptoms for 2.5 months to eight years looking at both upper and lower limbs, showed no difference between IRSB treatment and normal saline; however, the study reported benefit for longer than 12 weeks in three of the 14 patients receiving guanethidine (6). Kaplan and colleagues (7) were unable to demonstrate benefit in a series of 55 patients who received guanethidine in local anesthesia which, along with a review of the literature, led them to conclude that the

Le bloc sympathique régional intraveineux : Le passé, le présent et l'avenir ?

Le bloc sympathique régional intraveineux est un précieux élément de l'arsenal du médecin contre la douleur pour prendre en charge le syndrome algodystrophique de type 1. Le traitement de cette maladie à multiples facettes est multimodal, et malgré l'absence de preuves à l'appui convaincantes tirées d'essais cliniques, l'auteur établit le bien-fondé de conserver cette technique, tout en recommandant à la fois un encadrement pertinent et des études plus approfondies.

technique could not be considered useful for the long term relief of CRPS type 1. However, the patients in that study were so varied with respect to the precipitating event and duration of symptoms, and the documented treatments previously received, that such a conclusion is difficult to support despite which the accompanying editorial considered that without adequate studies, the routine use of IRSB could not be justified (8). In a well-conducted study, Livingstone and Atkins (9) examined 57 patients with CRPS type 1 nine weeks after suffering a closed fracture. The study assessed features of sympathetic nervous system dysfunction and randomised patients to receive either IRSB or normal saline. No significant short term benefit was demonstrated and in the long term, disbenefit was identified in the group receiving guanethidine. Individual patients, however, are reported as deriving very significant benefit, in a typical case, 18 months of pain relief after two treatments (10).

How can this be? Should pain clinicians be required to abandon IRSB or can we reconcile what at first appears to be a quandary and allow the retention of an intervention considered to be useful for selected patients?

Following the original description by Hannington-Kiff (1), the approaches to IRSB have become many and varied, without any agreement on technical factors, composition of the injectate, symptoms for which it is carried out, the stage of the illness when it might be appropriate or the psychological preparation of the patient at the time of the block. The frequency and number of interventions together with the interval between them,

Glan Clwyd Hospital, Bodelwyddan, Denbighshire, United Kingdom

Correspondence: Dr Alfred PJ Lake, Glan Clwyd Hospital, Bodelwyddan, Denbighshire LL18 5UJ, United Kingdom.

Telephone +44-1745-534969, fax +44-1745-534993, e-mail apjlake@aol.com

and even tourniquet time, are a matter of debate. For example, the early performance of IRSB in CRPS type 1 (eg, just nine weeks in one study [9]), may serve to inhibit pain centralization and the fixation of pain memories to limit chronicity. In addition, the substitution of the α_2 adrenergic agonist clonidine for guanethidine led to significant benefit in patients with symptoms for less than three months (11).

Lignocaine, commonly included as part of a technique based on intravenous regional analgesia, may or may not be appropriate because it has been described as preventing the beneficial effects of guanethidine, however, the "technique should still be available" (12). However, *in vitro* results using the rabbit isolated ileum preparation suggested that lignocaine did not inhibit the ability of guanethidine to deplete noradrenaline stores (13), and in experimental models of nerve injury, systemic sodium channel blockers such as lignocaine have been shown to silence the spontaneous activity of neuromata and the dorsal root ganglion at low concentrations and may also block glutamate-evoked activity (14). An effect on nociceptors through N-methyl-D-aspartate via membrane receptors in the primary afferent fibre, locally mediated (15), would be expected to be beneficial in a situation of peripheral nerve damage, which is applicable to CRPS type 1. A central effect of released lignocaine after tourniquet deflation may also occur. Tourniquet-induced analgesia due to an effective ischemic nerve block as part of the technique may itself be beneficial (6).

Various adjunctive treatments as part of an overall mixed approach must also be considered. Physiotherapy, which is difficult to perform in patients with CRPS type 1 owing to their unwillingness to have the limb touched or manipulated, can be beneficially carried out, and good results have been reported when performed during or after (as is our clinic's practice) the local anesthetic block (16). Passive mobility exercises and the encouragement of active movement associated with reduced pain through the local anesthetic effect can be most beneficial. The use of hypnotherapy has also been described in CRPS type 1 (17,18) and may be of real benefit when incorporated into a treatment plan including IRSB. Even electroconvulsive therapy, the effect of which may have a scientific basis (19), may be particularly effective, although further research is needed (20).

CRPS type 1 is a multifaceted condition. The management of patients and their treatment must be flexible, interdisciplinary and multimodal, with agreement between pain clinicians on the need to ensure that a favourable outcome for the patient by boosting the ability to cope is delivered through their intervention. The many and varied approaches to a condition notable for its diversity should come as no surprise; indeed, they may be expected. Although gabapentin, as an example of an intervention for CRPS type 1 is indeed useful, it is not universally effective for this or any other chronic pain condition, yet physicians prescribe large amounts at a significant side effect cost. IRSB has side effects too, often related to dose and frequency, but can it really be considered dangerous in comparison? Most individual interventions for this and other forms of chronic pain should not realistically be expected to deliver a better than 50% improvement in more than half the patients.

The pain of CRPS type 1 can be extremely distressing to patients and is often difficult to relieve. The benefit derived from even a short period of pain relief should not be underestimated, and we are all aware of the advantages that accrue from 'cycle breaking'.

Some forms of sympathectomy have been considered fundamental in the management of CRPS type 1, but IRSB, as usually performed, is much more than just an interruption of the sympathetic outflow. It is a simple, repeatable and broadly safe procedure that may be effectively used to control pain either alone or in combination with other treatment modalities, and is one procedure that should be tried (10).

IRSB may not have satisfied the demands of rigorous scientific evaluation, but as it remains a useful and valued component of the planned staged approach to the management of CRPS type 1, many pain clinicians will continue to include it or an equivalent intervention in their armamentarium.

A final answer to the question of efficacy is unlikely unless all of the many confounding variables are stratified. Although this would be a considerable undertaking, more study of the effects of alternative treatments for CRPS type 1, as well as more fundamental research with placebo controls, may provide us with new insight into this illness (3).

Now may indeed be the time for a change of name and strategy (2) with respect to CRPS type 1's treatment by IRSB, the production of appropriate guidelines to address issues of safety and risk management, and ensuring long term relevance should be the next steps. To avoid IRSB becoming sidelined as a futile procedure (21) and to ensure its availability for those who may benefit from the procedure, we need to adopt a fresh approach by promoting a correct understanding and selection of treatment options with the use of appropriate outcome measures (2) to better identify individuals or groups of patients who may respond to IRSB, particularly, those patients with marked features of sympathetic overactivity, suggesting a different underlying pathophysiology.

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