

# Effective but overlooked treatments some doctors miss

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## ABSTRACT

The results of published novel research in a specific field of medicine are the basis for changing the existing, recognized diagnostic or therapeutic paradigm. Over the last 20–30 years, there have been many examples of such changes. Most often, no one misses them, because new forms of diagnosis and treatment are usually much more precise and effective. However, there are some treatments that have been abandoned despite having been used for many years with good results, and their fate was decided by the results of novel research showing that their effectiveness is similar to placebo. There are several examples of such

therapies, including the use of regional intravenous blockades with guanethidine and free radical scavengers in the treatment of the acute phase of complex regional pain syndrome (CRPS), treatment of distal radial fractures by percutaneous fixation with K-wires, and conservative treatment of hand fractures. In this article, the authors recall these methods and discuss their advantages, despite the fact that evidence-based medicine (EBM) has considered them ineffective.

**Keywords:** unfashionable treatments; CRPS treatment; regional guanethidine blocks; free radical scavengers; distal radial fractures treatment; hand fractures treatment.

## INTRODUCTION

In medicine, the principles and standards for diagnosing and treating diseases or injuries are only valid for a limited time. The progress of technology and scientific research forces changes in established paradigms, which are sometimes very significant and may occur either shortly after or long after the introduction of previous standards. The standards of diagnosis and treatment are determined by the concept of evidence-based medicine (EBM). Knowledge updates are based on the results of evidence-based studies (prospective, randomized, involving a sufficiently large sample size and reliable interpretation), both clinical and experimental. In this process, meta-analyses and systematic reviews of the literature are helpful, as they analyse (according to set criteria) the results of published research in a specific field of medicine and formulate conclusions that may serve as the basis for changing the existing, recognized diagnostic or therapeutic paradigm.

Over the last 20–30 years, there have been many examples of such changes. In surgery, this has included the treatment of neoplasms (lung, breast, prostate), inflammatory diseases (acute pancreatitis, acute appendicitis, peptic ulcer), or injuries. Many surgical methods have been forgotten, and an equal number of pharmacological treatments have been proven ineffective. Most often, they are not missed, because new forms of diagnosis and treatment are usually much more precise and effective. Perhaps only older doctors (especially surgeons), who have become accustomed to certain methods over the years, will sometimes express a sense of nostalgia and say that the old ways were not so bad.

However, there are some diagnostic and therapeutic schemes and methods that have been abandoned despite having been

used for many years with good results, and their fate was determined by the results of several scientific studies indicating that their effectiveness is similar to that of placebo. There are several examples of such therapies, including the use of regional intravenous blockades with guanethidine and the use of free radical scavengers in the treatment of the acute phase of complex regional pain syndrome (CRPS). A similar situation applies to the surgical technique of treating distal radial fractures by percutaneous fixation with K-wires, which has been in use for over 40 years.

The objective of this study is to recall methods of diagnosing diseases and injuries of the hand that have been abandoned – perhaps prematurely – and which many physicians still value and continue to use, despite the fact that EBM has assessed them as ineffective.

## REGIONAL, INTRAVENOUS GUANETHIDINE BLOCKS FOR COMPLEX REGIONAL PAIN SYNDROME

This method of treating acute CRPS was introduced by Hannington-Kiff in 1974 [1]. The sympatholytic drug is administered intravenously into an exsanguinated limb (from which blood has been squeezed using a rubber band, and a pneumatic tourniquet has been inflated on the arm). In this way, a high concentration of the drug is achieved at the site of the disease, which is impossible to attain with systemic (intravenous) therapy. Three sympatholytic agents were most commonly used: guanethidine (10–20 mg), reserpine (1–2 mg), and phentolamine (10 mg). Guanethidine is a false neurotransmitter that occupies the place of norepinephrine at its storage sites in the postganglionic nerve endings of the sympathetic nervous

system. In this way, the activity of these nerves is completely blocked – a process called “chemical sympathectomy”. The primary use of guanethidine was in the treatment of hypertension resistant to standard therapy.

Treatment of CRPS with this method was popular in the 1970s and 1980s, when it was reported to be highly effective [1, 2, 3, 4]. However, subsequent publications of controlled trials launched in the late 1990s showed that treatment of CRPS with regional intravenous sympathetic blockades was no more effective than placebo [5]. Guanethidine, as a drug for the treatment of hypertension, was eventually abandoned due to its relatively numerous adverse effects when safer and equally effective drugs were developed. Treatment of CRPS with regional intravenous guanethidine blockades continued to be used in clinical practice until guanethidine was discontinued in the early 2000s. To this day, however, many physicians – especially in the UK – miss this drug, as they consider this method more effective than currently used CRPS therapies.

### **TREATMENT OF ACUTE COMPLEX REGIONAL PAIN SYNDROME WITH FREE RADICAL SCAVENGERS**

Treatment of acute forms of CRPS with oxygen and hydroxyl free radical scavengers was introduced by Rene Jan Goris in 1985 [6]. The rationale for this therapy referred to the concept of the inflammatory aetiology of CRPS, introduced by Paul Sudeck in 1900 [7]. Goris further developed this theory and discovered that, in the acute phase of CRPS, there is increased production of free radicals, which leads to inflammation. Treatment with substances that inactivate these free radicals (called “free radical scavengers”) is intended to alleviate symptoms and prevent disease progression.

Several substances with such properties are known, e.g.: mannitol, vitamin C, steroids, N-acetylcysteine, and dimethyl sulfoxide. Goris and his successors treated acute CRPS with intravenous mannitol and topical dimethyl sulfoxide compresses, with good results [8, 9]. Other substances have also been successfully used to treat early forms of CRPS. Results of clinical experiments at the authors’ institution using a combination of a radical scavenger (mannitol) and a steroid (dexamethasone) showed that this treatment significantly enhanced the resolution of the symptoms and signs of the disease compared to the use of either drug alone. Further development of this concept led to the establishment of a final treatment model. It was found that 1 week of therapy was the optimal period to interrupt the “vicious circle” of mechanisms driving disease progression and to initiate recovery [10].

Unfortunately, the results of later randomized placebo-controlled trials showed that the effectiveness of free radical scavengers was similar to placebo, and this treatment has been discontinued in many centres that had used it successfully – such as in the Netherlands, where the method originated [11, 12]. In the authors’ centre, however, it remains a first-line treatment for patients with acute forms of CRPS and continues to be used in many hospitals in Poland.

### **OPERATIVE TREATMENT OF DISTAL RADIAL FRACTURES WITH PERCUTANEOUS K-WIRE FIXATION**

Surgical treatment of distal radial fractures was introduced in the 1950s and consisted of closed fracture reduction followed by percutaneous fixation with 1 or 2 K-wires. To maintain the anatomical position of the bone fragments after reduction, K-wires were inserted percutaneously, protruding above the skin. A plaster splint or cast was applied to the wrist, and the protruding K-wires were embedded in the plaster for stability. A fracture fixed and immobilized in this manner had greater stability, a lower risk of displacement, and a greater chance of healing in correct alignment.

This method of treatment was popular in the 1970s and 1980s until other, more advanced surgical techniques were introduced – external fixation and open reduction with internal fixation using plates. External fixation did not gain wide popularity, but plate fixation gradually became the leading method in the treatment of distal radial fractures, slowly replacing percutaneous K-wire fixation. Scientific studies comparing these 2 techniques showed that plate fixation offers greater stability and allows for treatment without additional immobilization. Another advantage is that the open surgical approach permits a more precise, nearly anatomical reduction of fractures [13, 14].

This scientific evidence led to increased interest in the plating method, and K-wire fixation gradually fell into disuse. Manufacturers of modern implants also played a significant role, as their promotion of newer – and ostensibly better – treatment methods was very effective. As a result, even those surgeons who had good experience with K-wire fixation eventually abandoned this technique.

However, in the authors’ institution, the method has been creatively developed and is still used with very good results. A modification of the original technique (so-called “augmented” fixation) involves the use of more K-wires (usually 5–7) of greater diameter (1.4–2.0 mm), inserted in a mixed trans-styloid and intra-focal configuration (Fig. 1). This modification provides increased stability of the fixation, making it more resistant to secondary displacement of the bone fragments.

The use of this modified technique for distal radial fractures allows for the achievement of satisfactory clinical outcomes and relatively few complications. Results of a study conducted at the authors’ institution have shown that palmar locking plates offer no advantage over K-wire fixation for less severe fracture configurations. As these types of fractures are much more common than comminuted and high-energy injuries, the K-wire fixation technique is associated with substantial economic benefits. A noteworthy advantage of this method is the logical balance between clinical and cost-effectiveness, as K-wire fixation is much less expensive than the exclusive use of modern plates. When treating numerous patients, being guided by these principles translates directly into substantially lower expenditures for the department, without diminishing the quality of treatment [15]. Nevertheless, K-wire fixation is currently much less popular for distal radial fractures than plate fixation.



**FIGURE 1.** X-ray of distal radial fracture: (a) a-p view; (b) lateral view; (c) fixed with K-wires – a-p view; (d) fixed with K-wires – lateral view

## FUNCTIONAL, CONSERVATIVE TREATMENT OF HAND FRACTURES

Conservative treatment of hand fractures has been employed for a long time, ever since rational management of bone injuries was established. For many years, immobilisation of the hand in a plaster cast was used, which, in some fracture configurations, could lead to unfavourable outcomes such as: symptomatic malunion, finger deformity, stiffness, and dysfunction. The introduction of surgical treatment for hand fractures in the early 1970s – first with the use of K-wires, and later with screws and plates – generated great interest in these techniques and expanded the indications for surgical intervention.

As in the case of distal radial fractures, the influence of companies manufacturing bone implants has played a significant role in promoting the benefits of their use in the treatment of hand fractures, most of which had previously been treated conservatively. As a result, many fractures that were once managed non-operatively began to be treated surgically. Scientific publications have not necessarily confirmed the superiority of surgical treatment, but it has been considered more favourable than conservative management, especially in terms of radiological outcomes, indicating bone union in

an anatomical position [16, 17, 18]. However, functional results have not always correlated with radiographic findings, and a proportion of patients experienced various forms of hand dysfunction. Moreover, the time to recovery was sometimes significantly longer compared to conservative treatment.

In the absence of clear scientific evidence confirming the superiority of surgical over conservative treatment, most hand fractures (metacarpal and phalangeal), that are non- or only slightly displaced and of stable configuration, have for several years been treated functionally at the authors' institution, without any immobilisation (Fig. 2). Patients are instructed on how to perform exercises, specifically making full flexion and extension of all fingers drawn up in 1 block (with fingers held close together) – Figures 3 and 4. These exercises are to be repeated ten times per session, with 4 sessions required daily.

Outcomes of this treatment have been excellent: all patients achieved full finger movement and very good hand function at a 1-month follow-up. All fractures consolidated, as confirmed radiologically at 3 months. In no case was a change to operative treatment necessary [19]. The author of this modification of the old-fashioned method for treating stable fractures of the metacarpal bones and phalanges is currently attempting to popularise this protocol elsewhere.



**FIGURE 2.** X-ray of fracture of the proximal phalanx: (a) a-p view; (b) oblique view



**FIGURE 3.** Appearance of the hand 2 weeks after the fracture shown in Figure 2 (index finger involved)



**FIGURE 4.** Full index finger flexion 2 weeks after the fracture shown in Figure 2

In summary, it can be stated that the treatment methods presented in this article, which were (somewhat unjustly) consigned to the past, can still be used to the benefit of patients and the satisfaction of physicians. It appears that the judgments of EBM declaring their ineffectiveness may have been somewhat premature.

## REFERENCES

- Livingstone JA, Atkins RM. Intravenous regional guanethidine blockade in the treatment of post-traumatic complex regional pain syndrome type 1 (algodystrophy) of the hand. *J Bone Joint Surg Br* 2002;84(3):380-6.
- Ramamurthy S, Hoffman J. Intravenous regional guanethidine in the treatment of reflex sympathetic dystrophy/causalgia: a randomized, double-blind study. *Anesth Analg* 1995;81(4):718-23.
- Glynn CJ, Basedow RW, Walsh JA. Pain relief following post-ganglionic sympathetic blockade with I.V. guanethidine. *Br J Anesth* 1981;53(12):1297-302.
- Field J, Monk C, Atkins RM. Objective improvements in algodystrophy following regional intravenous guanethidine. *J Hand Surg Br* 1993;18(3):339-42.
- Jadad AR, Carroll D, Glynn CJ, McQuay HJ. Intravenous regional sympathetic blockade for pain relief in reflex sympathetic dystrophy: a systematic review and randomized, double-blind crossover study. *J Pain Symptom Manage* 1995;10(1):13-20.
- Goris RJ. Treatment of reflex sympathetic dystrophy with hydroxyl radical scavengers. *Unfallchirurg* 1985;88(7):330-2.
- Sudeck P. Über die akute entzündliche Knochenatrophie. *Arch Klin Chir* 1900;62:147-54.
- Goris RJ, van Dongen LM, Winters HA. Are toxic oxygen radicals involved in the pathogenesis of reflex sympathetic dystrophy? *Free Radic Res Commun* 1987;3(1-5):13-8.
- Perez MRSG, Zuurmond AWW, Bezemer DP, Kuik JD, van Loenen CA, de Lange JJ, et al. The treatment of complex regional pain syndrome type I with free radical scavengers: a randomized controlled study. *Pain* 2003;102(3):297-307.
- Zyluk A, Puchalski P. Treatment of early complex regional pain syndrome type 1 by a combination of mannitol and dexamethasone. *J Hand Surg Eur Vol* 2008;33(2):130-6.
- Perez RS, Pragt E, Geurts J, Zuurmond WW, Patijn J, van Kleef M. Treatment of patients with complex regional pain syndrome type I with mannitol: a prospective, randomized, placebo-controlled, double-blinded study. *J Pain* 2008;9(8):678-86.
- Perez RS, Zollinger PE, Dijkstra PU, Thomassen-Hilgersom IL, Zuurmond WW, Rosenbrand KC, et al. Evidence based guidelines for complex regional pain syndrome type 1. *BMC Neurol* 2010;10:20. doi: 10.1186/1471-2377-10-20.
- Zong SL, Kan SL, Su LX, Wang B. Meta-analysis for dorsally displaced distal radius fracture fixation: volar locking plate versus percutaneous Kirschner wires. *J Orthop Surg Res* 2015;10:108. doi: 10.1186/s13018-015-0252-2.
- Schyamalan G, Theokli C, Pearse Y, Tennent D. Volar locking plates versus Kirschner wires for distal radial fractures – a cost analysis study. *Injury* 2009;40(12):1279-81.
- Zyluk A, Janowski P, Szlosser Z, Puchalski P. Percutaneous K-wires vs palmar locking plate fixation for different types of distal radial fractures: a comparison of the outcomes of two methods to controll our guidelines. *Handchir Mikrochir Plast Chir* 2018;50(5):319-25.
- Wellborn PK, Allen AD, Draeger RW. Current outcomes and treatments of complex phalangeal and metacarpal fractures. *Hand Clin* 2023;39(3):251-63.
- Neumeister MW, Winters JN, Maduakolum E. Phalangeal and metacarpal fractures of the hand: preventing stiffness. *Plast Reconstr Surg Glob Open* 2021;9(10):e3871.
- Taghinia AH, Talbot SG. Phalangeal and metacarpal fractures. *Clin Plast Surg* 2019;46(3):415-23.
- Żyluk A. Outcomes of treating hand fractures without using immobilization. *Pomeranian J Life Sci* 2022;68(3):1-4. doi: 10.21164/pomjlifesci.825.