

Hyperbaric oxygen treatment in recurrent development of complex regional pain syndrome: A case report

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Abstract

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A broad spectrum of conditions including neuropathic pain, complex regional pain syndrome (CRPS) and fibromyalgia, have been implicated as causes of chronic pain. There is a need for new and effective treatments that patients can tolerate without significant adverse effects. One potential intervention is hyperbaric oxygen treatment (HBOT). The case reported here is unique in describing repeated HBOT in a patient who developed recurrent post-traumatic CRPS of the lower as well as the upper limbs. In the first event, two months after distortion and abruption of the external right ankle, the patient suffered leg pain, oedema formation, mild hyperaemia, limited mobility of the ankle and CRPS Type 1. In the second event, the same patient suffered fracture-dislocation of the distal radius 1.5 years after the first injury. After the plaster cast was removed the patient developed pain, warmth, colour changes, oedema formation and limited wrist mobility with CRPS Type 1. Pharmacological treatment as well as HBOT were used with significant improvement of functional outcome in both cases. Some studies suggest that patients with a history of CRPS are more likely to develop secondary CRPS compared to the rates reported in the literature among the general population. Patients with a history of CRPS should be counselled that they may be at risk for developing secondary CRPS if they undergo surgery or sustain trauma to another extremity.

Introduction

Chronic pain is one of the most common complaints in clinical practice. A broad spectrum of conditions including neuropathic pain, complex regional pain syndrome, migraine and fibromyalgia, have been implicated as causes of a chronic pain condition.^{1–4}

Complex regional pain syndrome (CRPS) is a chronic pain condition characterised by spontaneous and evoked regional pain, usually beginning in a distal extremity, that is disproportionate in magnitude or duration to the typical course of pain after similar tissue trauma.⁵ Multiple peripheral and central mechanisms are involved, with the

individual share of particular factors over time. Possible contributors include musculoskeletal, peripheral and central sensitisation, autonomic changes and sympatho-afferent coupling, alterations in receptor populations (e.g., upregulation of adrenoceptors and reduced cutaneous nerve fiber density), brain changes, genetic, psychological factors, inflammatory and immune alterations and central changes in autonomic drive, which seem to contribute to regional and systemic disturbances in sympathetic activity.^{5–7}

Management of pain, especially when it becomes chronic, is a challenging task requiring a multidisciplinary approach. Currently, most pharmacological, nonpharmacological and interventional modalities achieve only temporary or

modest improvements in pain symptoms and often produce intolerable adverse effects that interfere with the quality of life and lead to poor compliance. There is a need for new and effective chronic pain treatments that patients can tolerate without significant adverse effects. One such novel treatment is hyperbaric oxygen treatment (HBOT). There is a growing body of evidence to suggest that HBOT is a noninvasive modality with lasting efficacy and minimal side effects that can be used to treat chronic pain conditions.^{8–11}

The aim of this case report was to report the apparent effect of repeated HBOT in a patient with post-traumatic CRPS in the lower limb and subsequently the upper limb. The report was developed according to the CARE reporting guidelines.¹²

Case presentation

Written informed consent for publication of case details was obtained from the patient.

EVENT 1

This 65-year-old woman had a history of general osteoporosis, right knee arthrosis and lower limb varicosities. In July 2018, she suffered distortion and abrasion of the external right ankle due to slipping and falling to the ground. She was treated by plaster fixation for four weeks. Due to the phlebothrombosis of the deep venous system of this extremity, novel oral anticoagulant therapy was applied for ten weeks. Two months after the injury, she suffered pain in the leg and calf below the knee. Oedema formation, mild hyperaemia, limited mobility of the ankle and an antalgic walking pattern were described. She was diagnosed with CRPS Type 1 (CRPS not associated with direct nerve injury). Pharmacological treatment included analgesics (non-steroidal anti-inflammatory drugs) and anxiolytic therapy, vitamin D and calcium substitution. Physical therapy was applied for eight weeks. A visual analogue pain scale was rated 6/10 with limb loading by walking. Four months after the injury, in November 2018, HBOT was started. Twenty HBOT sessions were given at pressures 202.6–243.1 kPa (2.0–2.4 atmospheres absolute). Significant improvement of functional outcome after the treatment was achieved, such as the disappearance of symptoms, alleviation of colour changes and oedema reduction. The limb was fully loaded, with no pain at rest and during walking. The VAS score was rated 0/10 after the end of HBOT in December 2018.

On 19 March 2019, she was referred to HBOT again for a gradual recurrence of problems, such as dysesthesia and pain of the right leg and calf. No oedema or colour changes were present. Ultrasound examination showed a patent deep venous system. Pharmacological treatment included anxiolytic therapy, vitamin D, calcium substitution, and sodium-risedronate (bisphosphonates) 35 mg once a week. Physical therapy was applied for six weeks before the start of HBOT. The patient underwent another sixteen sessions

of HBOT 202.6–243.1 kPa finishing in April 2019. There were no complications and side effects during the HBOT. Improvement and pain reduction was reported by the patient. The VAS score was rated 3–4/10 after the end of HBOT compared to 5–6/10 rated at the beginning.

EVENT 2

In December 2019, the same patient suffered an injury of the left wrist after the tripping on the sidewalk and falling. A dislocated fracture of the distal radius (Smith's fracture) was shown on X-ray. Reposition under the local anaesthesia and plaster fixation for six weeks were performed. After the plaster fixation was removed the patient complained of pain, warmth, colour changes as well as oedema formation of the wrist. Limited mobility of the wrist (dorsal flexion up to thirty degrees, palmar flexion up to fifteen degrees) and fingers were described. An X-ray revealed good position of fragments and progressive healing changes. She was once again diagnosed with CRPS Type 1. Pharmacological treatment included analgesic (tramadol hydrochloride/paracetamol 37.5 mg/325 mg twice daily) and antidepressant therapy (dosulepin hydrochloride), as well as promethazine hydrochloride. HBOT was started in January 2020. Twenty-two sessions of HBOT 202.6–243.1 kPa were given, finishing in March 2020, due to the worsening of the epidemiological situation and coronavirus disease pandemic outbreak. Significant pain reduction and partial oedema reduction were achieved, but reduction of the wrist mobility persisted. Slightly better finger mobility was apparent. Before HBOT, the pain VAS score was rated 0/10 at rest, 6/10 during movement, and the function of the hand was rated 7–8/10 (higher is worse). After the end of HBOT, the pain VAS score was rated 0/10 at rest, 2–3/10 during movement and the functional VAS score was 4–5/10.

Discussion

This report describes the effects of repeated HBOT administration in a patient with recurrent post-traumatic CRPS on both the lower and upper limbs. At an interval of 18 months after the first injury, the same patient had a forearm injury to the upper limb with development of CRPS, which was successfully treated with HBOT.

It is known that patients with CRPS have a higher chance of recurrence with a subsequent injury. In a retrospective review the incidence of CRPS after subsequent surgery or injury in a previous unaffected extremity was determined and compared to an average incidence reported in the literature.¹³ Ninety-three patients had a diagnosis of primary CRPS. Nineteen patients (20.4%) developed CRPS in one or more additional extremities compared to the incidence of 23.4 per 100,000 (0.0234%) in the literature. Twenty patients had a documented secondary injury or surgery in a second extremity. Fifteen patients (75%) developed secondary CRPS compared to a CRPS incidence rate of 6.4% following distal radius fracture.¹³

The aim of another study was to evaluate the risk factors for the development of complex regional pain syndrome (CRPS) after surgical treatment of traumatic hand injuries. CRPS was diagnosed in 68 patients (26.2 %). The mean postoperative pain score was greater in patients with CRPS than in those without CRPS. The patients with a pain score of ≥ 5 in the first three days after surgery and the patients with crush injury were at high risk for CRPS development after surgical treatment of traumatic hand injuries.¹⁴

HBOT may be effective in the treatment of CRPS. A double-blind, randomised, placebo-controlled study was designed to assess whether HBOT was superior to placebo in treating patients with post-traumatic CRPS of the wrist. Seventy-one patients were randomised into a treatment group ($n = 37$) that received fifteen daily 90-minute HBOT sessions at 243.1 kPa (2.4 atmospheres absolute) or a control group ($n = 34$) that received fifteen daily 90-minute sessions in the hyperbaric chamber (also at 243.1 kPa) breathing normal air. The CRPS patients who received HBOT were shown to have significantly lower (improved) VAS scores, wrist extension and less wrist oedema compared to the control group both after the final treatment.¹⁵

While there is some supportive evidence of a positive effect of HBOT on CRPS, this chronic pain condition does not appear on any of the lists of approved indications of major professional societies such as the list of indications of the 10th ECHM Consensus Conference 2016.¹⁶ This treatment method is neglected in many recent review articles or systematic reviews (SR),^{17–19} where it is either not mentioned at all or excluded from the analysis, most often because it is not considered a ‘commonly used treatment method’.²⁰ The present case report serves as a ‘reminder’ to the hyperbaric, orthopedic or pain medicine communities, that this treatment option exists, albeit based on limited scientific evidence of the clinical efficacy.

Possible mechanisms of action are multiple in relation to the above-mentioned currently accepted pathophysiological causes of CRPS. A positive effect of HBOT in CRPS could be related to restoration of aerobic metabolism, correction of hypoxia, correction of acidosis, and modulation of nitric oxide (NO) activity and oxidative stress.²¹ Previous animal studies have highlighted the analgesic effect caused by HBOT in models of nociceptive, inflammatory and neuropathic pain.^{22,23} HBOT has been found to decrease mechanical hyperalgesia and inflammation in a rodent model. The antinociceptive effect was apparent immediately following HBOT and persisted up to 5 h post-treatment.²² In patients with fibromyalgia syndrome (FMS) there is some evidence that HBOT can change brain metabolism and glial function to rectify the FMS-associated abnormal brain activity.²⁴ Work by one group suggests that HBOT can induce neuroplasticity that leads to repair of chronically impaired brain function and improved quality of life in post-stroke patients and patients with prolonged post concussion syndrome.^{25–27} Data from models of Parkinson’s disease

show that HBOT may play a neuroprotective role because of its ability to reduce oxidative stress and neurodegeneration, and protect against neuronal apoptosis.²⁸ It was shown that HBOT induces significant anti-inflammatory effect in different conditions and pathologies^{29,30} and may attenuate pain by reducing production of glial cell inflammatory mediators.^{31,32}

Conclusions

HBOT is not a standard treatment for CRPS, but it is a promising intervention for both acute and chronic treatment of the disease. Because of symptoms that limit patients in their daily lives, early diagnosis and active treatment approaches immediately after the onset of CRPS are critical factors in improving a patient’s prognosis. Further studies are needed to improve our understanding of the mechanisms underlying the effects of HBOT and clarify its role in the treatment of this troubling disorder.

References

- 1 Elliott AM, Smith BH, Penny KI, Smith WC, Chambers WA. The epidemiology of chronic pain in the community. *Lancet*. 1999;354(9186):1248–52. doi: [10.1016/S0140-6736\(99\)03057-3](https://doi.org/10.1016/S0140-6736(99)03057-3). PMID: 10520633.
- 2 Merskey H, Bogduk N, editors. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. 2nd ed. Seattle: IASP Press; 1994. [cited 2020 July 1]. Available from: <https://s3.amazonaws.com/rdcms-iasp/files/production/public/Content/ContentFolders/Publications2/FreeBooks/Classification-of-Chronic-Pain.pdf>.
- 3 Tsang A, Von Korff M, Lee S, Alonso J, Karam E, Angermeyer MC, et al. Common chronic pain conditions in developed and developing countries: Gender and age differences and comorbidity with depression-anxiety disorders. *J. Pain*. 2008;9:883–91. doi: [10.1016/j.jpain.2008.05.005](https://doi.org/10.1016/j.jpain.2008.05.005). PMID: 18602869.
- 4 El-Shewy KM, Kunbaz A, Gad MM, Al-Husseini MJ, Saad AM, Sammour YM, et al. Hyperbaric oxygen and aerobic exercise in the long-term treatment of fibromyalgia: A narrative review. *Biomed Pharmacother*. 2019;109:629–38. doi: [10.1016/j.biopha.2018.10.157](https://doi.org/10.1016/j.biopha.2018.10.157). PMID: 30399600.
- 5 Bruehl S. Complex regional pain syndrome. *BMJ*. 2015;351:h2730. doi: [10.1136/bmj.h2730](https://doi.org/10.1136/bmj.h2730). PMID: 26224572.
- 6 Stanton-Hicks Md'A. CRPS: What's in a name? Taxonomy, epidemiology, neurologic, immune and autoimmune considerations. *Reg Anesth Pain Med*. 2019;44:376–87. doi: [10.1136/rapm-2018-100064](https://doi.org/10.1136/rapm-2018-100064). PMID: 30777902.
- 7 Knudsen LF, Terkelsen AJ, Drummond PD, Birklein F. Complex regional pain syndrome: A focus on the autonomic nervous system. *Clin Auton Res*. 2019;29:457–67. doi: [10.1007/s10286-019-00612-0](https://doi.org/10.1007/s10286-019-00612-0). PMID: 31104164.
- 8 Sutherland AM, Clarke HA, Katz J, Katznelson R. Hyperbaric oxygen therapy: A new treatment for chronic pain? *Pain Pract*. 2016;16:620–8. doi: [10.1111/papr.12312](https://doi.org/10.1111/papr.12312). PMID: 25988526.
- 9 Knobler R. The severity spectrum in persistent complex regional pain syndrome (CRPS), palliation with ongoing hyperbaric oxygen therapy (HBOT), and the role of serial photo-documentation. *Neurology*. 2016 [cited 2020 July 1];86(16 Suppl). Available from: https://n.neurology.org/content/86/16_Supplement/P6.271.

- 10 Yngelmo E, Gill P, Dhillon Y. Hyperbaric therapy for the treatment of acute arterial insufficiency due to reflex sympathetic dystrophy [Abstract]. *Undersea Hyperb Med.* 2013;40:555.
- 11 Sawyer R. Hyperbaric oxygen therapy does not alter peripheral cutaneous perception measures in complex regional pain syndrome – preliminary case series. *Pain Practice.* 2009;9:93–168.
- 12 Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D, et al. The CARE Guidelines: Consensus-based clinical case reporting guideline development. *Glob Adv Health Med.* 2013;2:38–43. doi: [10.7453/gahmj.2013.008](https://doi.org/10.7453/gahmj.2013.008). PMID: [24416692](https://pubmed.ncbi.nlm.nih.gov/24416692/). PMCID: [PMC3833570](https://pubmed.ncbi.nlm.nih.gov/PMC3833570/).
- 13 Satteson ES, Harbour PW, Koman LA, Smith BP, Li Z. The risk of pain syndrome affecting a previously non-painful limb following trauma or surgery in patients with a history of complex regional pain syndrome. *Scand J Pain.* 2017;14:84–8. doi: [10.1016/j.sjpain.2016.10.005](https://doi.org/10.1016/j.sjpain.2016.10.005). PMID: [28850441](https://pubmed.ncbi.nlm.nih.gov/28850441/).
- 14 Savaş S, Inal EE, Yavuz DD, Uslusoy F, Altuntaş SH, Aydin MA. Risk factors for complex regional pain syndrome in patients with surgically treated traumatic injuries attending hand therapy. *J Hand Ther.* 2018;31:250–4. doi: [10.1016/j.jht.2017.03.007](https://doi.org/10.1016/j.jht.2017.03.007). PMID: [28501479](https://pubmed.ncbi.nlm.nih.gov/28501479/).
- 15 Kiralp MZ, Yildiz S, Vural D, Keskin I, Ay H, Dursun H. Effectiveness of hyperbaric oxygen therapy in the treatment of complex regional pain syndrome. *J Int Med Res.* 2004;32:258–62. doi: [10.1177/147323000403200304](https://doi.org/10.1177/147323000403200304). PMID: [15174218](https://pubmed.ncbi.nlm.nih.gov/15174218/).
- 16 Mathieu D, Marroni A, Kot J. Correction: Tenth European Consensus Conference on Hyperbaric Medicine: Recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment. *Diving Hyperb Med.* 2017;47:131–2. doi: [10.28920/dhm47.2.131-132](https://doi.org/10.28920/dhm47.2.131-132). PMID: [28641327](https://pubmed.ncbi.nlm.nih.gov/28641327/). PMCID: [PMC6147755](https://pubmed.ncbi.nlm.nih.gov/PMC6147755/).
- 17 Shim H, Rose J, Halle S, Shekane P. Complex regional pain syndrome: A narrative review for the practising clinician. *Br J Anaesth.* 2019;123:e424–e433. doi: [10.1016/j.bja.2019.03.030](https://doi.org/10.1016/j.bja.2019.03.030). PMID: [31056241](https://pubmed.ncbi.nlm.nih.gov/31056241/). PMCID: [PMC6676230](https://pubmed.ncbi.nlm.nih.gov/PMC6676230/).
- 18 O'Connell NE, Wand BM, McAuley J, Marston L, Moseley GL. Interventions for treating pain and disability in adults with complex regional pain syndrome – an overview of systematic reviews. *Cochrane Database Syst Rev.* 2013;2013(4):CD009416. doi: [10.1002/14651858.CD009416.pub2](https://doi.org/10.1002/14651858.CD009416.pub2). PMID: [23633371](https://pubmed.ncbi.nlm.nih.gov/23633371/). PMCID: [PMC6469537](https://pubmed.ncbi.nlm.nih.gov/PMC6469537/).
- 19 Eldufani J, Elahmer N, Blaise G. A medical mystery of complex regional pain syndrome. *Heliyon.* 2020;6(2):e03329. doi: [10.1016/j.heliyon.2020.e03329](https://doi.org/10.1016/j.heliyon.2020.e03329). PMID: [32149194](https://pubmed.ncbi.nlm.nih.gov/32149194/). PMCID: [PMC7033333](https://pubmed.ncbi.nlm.nih.gov/PMC7033333/).
- 20 Tran DQH, Duong S, Bertini P, Finlayson RJ. Treatment of complex regional pain syndrome: A review of the evidence. *Can J Anaesth.* 2010;57:149–66. doi: [10.1007/s12630-009-9237-0](https://doi.org/10.1007/s12630-009-9237-0). PMID: [20054678](https://pubmed.ncbi.nlm.nih.gov/20054678/).
- 21 Katznelson R, Segal SC, Clarke H. Successful treatment of lower limb complex regional pain syndrome following three weeks of hyperbaric oxygen therapy. *Pain Res Manag.* 2016;2016:3458371. doi: [10.1155/2016/3458371](https://doi.org/10.1155/2016/3458371). PMID: [27445607](https://pubmed.ncbi.nlm.nih.gov/27445607/). PMCID: [PMC4904619](https://pubmed.ncbi.nlm.nih.gov/PMC4904619/).
- 22 Wilson HD, Wilson JR, Fuchs PN. Hyperbaric oxygen treatment decreases inflammation and mechanical hypersensitivity in an animal model of inflammatory pain. *Brain Res.* 2006;1098:126–8. doi: [10.1016/j.brainres.2006.04.088](https://doi.org/10.1016/j.brainres.2006.04.088). PMID: [16750177](https://pubmed.ncbi.nlm.nih.gov/16750177/).
- 23 Zhao BS, Meng LX, Ding YY, Cao YY. Hyperbaric oxygen treatment produces an antinociceptive response phase and inhibits astrocyte activation and inflammatory response in a rat model of neuropathic pain. *J Mol Neurosci.* 2014;53:251–61. doi: [10.1007/s12031-013-0213-3](https://doi.org/10.1007/s12031-013-0213-3). PMID: [24390961](https://pubmed.ncbi.nlm.nih.gov/24390961/).
- 24 Efrati S, Golan H, Bechor Y, Faran Y, Daphna-Tekoa S, Sekler G, et al. Hyperbaric oxygen therapy can diminish fibromyalgia syndrome – prospective clinical trial. *PLoS One.* 2015;10(5):e0127012. doi: [10.1371/journal.pone.0127012](https://doi.org/10.1371/journal.pone.0127012). PMID: [26010952](https://pubmed.ncbi.nlm.nih.gov/26010952/). PMCID: [PMC4444341](https://pubmed.ncbi.nlm.nih.gov/PMC4444341/).
- 25 Efrati S, Fishlev G, Bechor Y, Volkov O, Bergan J, Kliakhandler K, et al. Hyperbaric oxygen induces late neuroplasticity in post stroke patients – randomized, prospective trial. *PLoS One.* 2013;8(1):e53716. doi: [10.1371/journal.pone.0053716](https://doi.org/10.1371/journal.pone.0053716). PMID: [23335971](https://pubmed.ncbi.nlm.nih.gov/23335971/). PMCID: [PMC3546039](https://pubmed.ncbi.nlm.nih.gov/PMC3546039/).
- 26 Boussi-Gross R, Golan H, Fishlev G, Bechor Y, Volkov O, Bergan J, et al. Hyperbaric oxygen therapy can improve post concussion syndrome years after mild traumatic brain injury – randomized prospective trial. *PLoS One.* 2013;8(11):e79995. doi: [10.1371/journal.pone.0079995](https://doi.org/10.1371/journal.pone.0079995). PMID: [24260334](https://pubmed.ncbi.nlm.nih.gov/24260334/). PMCID: [PMC3829860](https://pubmed.ncbi.nlm.nih.gov/PMC3829860/).
- 27 Boussi-Gross R, Golan H, Volkov O, Bechor Y, Hoofien D, Schnaider Beerli M, et al. Improvement of memory impairments in poststroke patients by hyperbaric oxygen therapy. *Neuropsychology.* 2015;29(4):610–21. doi: [10.1037/neu0000149](https://doi.org/10.1037/neu0000149). PMID: [25384125](https://pubmed.ncbi.nlm.nih.gov/25384125/).
- 28 Atzeni F, Masala IF, Cirillo M, Boccassini L, Sorbara S, Alciati A. Hyperbaric oxygen therapy in fibromyalgia and the diseases involving the central nervous system. *Clin Exp Rheumatol.* 2020;38 Suppl 123:94–8. PMID: [32116209](https://pubmed.ncbi.nlm.nih.gov/32116209/).
- 29 Lee YS, Chio CC, Chang CP, Wang LC, Chiang PM, Niu KC, et al. Long course hyperbaric oxygen stimulates neurogenesis and attenuates inflammation after ischemic stroke. *Mediators Inflamm.* 2013;2013:512978. doi: [10.1155/2013/512978](https://doi.org/10.1155/2013/512978). PMID: [23533308](https://pubmed.ncbi.nlm.nih.gov/23533308/). PMCID: [PMC3595722](https://pubmed.ncbi.nlm.nih.gov/PMC3595722/).
- 30 Lin KC, Niu KC, Tsai KJ, Kuo JR, Wang LC, Chio CC, et al. Attenuating inflammation but stimulating both angiogenesis and neurogenesis using hyperbaric oxygen in rats with traumatic brain injury. *J Trauma Acute Care Surg.* 2012;72:650–9. doi: [10.1097/TA.0b013e31823c575f](https://doi.org/10.1097/TA.0b013e31823c575f). PMID: [22491549](https://pubmed.ncbi.nlm.nih.gov/22491549/).
- 31 Hui J, Zhang ZJ, Zhang X, Shen Y, Gao YJ. Repetitive hyperbaric oxygen treatment attenuates complete Freund's adjuvant-induced pain and reduces glia-mediated neuroinflammation in the spinal cord. *J Pain.* 2013;14:747–58. doi: [10.1016/j.jpain.2013.02.003](https://doi.org/10.1016/j.jpain.2013.02.003). PMID: [23680474](https://pubmed.ncbi.nlm.nih.gov/23680474/).
- 32 Tai PA, Chang CK, Niu KC, Lin MT, Chiu WT, Lin CM. Attenuating experimental spinal cord injury by hyperbaric oxygen: stimulating production of vasculoendothelial and glial cell line-derived neurotrophic growth factors and interleukin-10. *J Neurotrauma.* 2010;27:1121–7. doi: [10.1089/neu.2009.1162](https://doi.org/10.1089/neu.2009.1162). PMID: [20334467](https://pubmed.ncbi.nlm.nih.gov/20334467/).

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