

CASE REPORT

The Treatment of Perioperative Spinal Cord Injury With Hyperbaric Oxygen Therapy

A Case Report

Jamie R. F. Wilson, BM, BCh, FRCS (Neurosurgery),^a Simone Schiavo, MD,^b
William J. Middleton, MD, BSc, FRCPC,^b Eric M. Massicotte, MD, MSc, MBA, FRCSC,^a
Marcus V. De Moraes, MD,^b and Rita Katznelson, MD, FRCPC^b

Study Design. Case report (level IV evidence).

Objective. To describe a potential novel application of hyperbaric oxygen therapy (HBOT) in the successful treatment of a postoperative spinal cord injury.

Summary of Background Data. A 68-year-old man presented with an acute spinal cord injury (ASIA impairment scale D), on the background of degenerative lower thoracic and lumbar canal stenosis. He underwent emergent decompression and instrumented fusion (T9–L5), with an uncomplicated intraoperative course and no electrophysiological changes. Immediate postoperative assessment demonstrated profound bilateral limb weakness (1/5 on the Medical Research Council [MRC] grading scale, ASIA impairment scale B), without radiological abnormality.

Methods. Conventional medical management (hypertension, level 2 care) was instigated with the addition of Riluzole, with no effect after 30 hours. At 36 hours 100% oxygen at 2.8 atmospheres was applied for 90 minutes, and repeated after 8 hours, with a further three treatments over 48 hours.

Results. The patient demonstrated near-immediate improvement in lower limb function to anti-gravity (MRC grading 3/5) after one treatment. Motor improvement continued over the following treatments, and after 2 weeks the patient was

ambulatory. At 4 months, the patient demonstrated normal motor function with no sphincteric disturbance.

Conclusion. The application of HBOT contributed to the immediate and sustained improvement (ASIA B to ASIA E) in motor recovery after postoperative spinal cord injury. HBOT may represent a new avenue of therapy for spinal cord injury, and requires further prospective investigation.

Key words: American Spinal Injury Association impairment scale, hyperbaric oxygen, spinal cord injury, spine surgery.

Level of Evidence: 4

Spine 2020;45:E1127–E1131

Hyperbaric oxygen therapy (HBOT) is the intermittent administration of inhaled 100% oxygen in a hyperbaric chamber at a pressure higher than 1 atmosphere absolute (ATA), or sea level. Health Canada approved indications for HBOT include decompression illness, gas embolism, necrotizing infections but is also increasingly used for the healing of selected complex wounds and severe burns.¹ The literature on the use of HBOT after spinal surgery has mainly focused on the treatment of postoperative spinal infections.^{2–5} The success of the use of HBOT in the treatment of acute spinal cord ischemia following aortic surgery suggests potential for its use after spinal cord injury (SCI).⁶ We report the first case of a patient who demonstrates recovery of a perioperative SCI after treatment with HBOT.

CASE REPORT

A 68-year-old man underwent an expedited T12–L5 laminectomy and instrumented fusion T9–L5, after presenting with bilateral leg weakness and poor ambulation secondary to degenerative stenosis at the conus level and scoliosis (Medical Research Council [MRC] grading 4–5/5 both lower limbs; American Spinal Injury Association [ASIA] impairment scale: grade D).⁷ Operating time was 6 hours, the intraoperative mean arterial pressure (MAP) was kept above 85 mmHg at all times with no variability, and estimated blood loss was 2500 mL. No response for

From the ^aDivision of Neurosurgery and Spinal Program, University of Toronto and Toronto Western Hospital, Toronto, Ontario, Canada; and ^bHyperbaric Medicine Unit, Department of Anesthesia and Pain management, University of Toronto and Toronto General Hospital, Toronto, Ontario, Canada

Acknowledgment date: August 13, 2019. First revision date: October 21, 2019. Second revision date: January 30, 2020. Acceptance date: February 24, 2020.

The manuscript submitted does not contain information about medical device(s)/drug(s).

No funds were received in support of this work.

No relevant financial activities outside the submitted work.

Address correspondence and reprint requests to Rita Katznelson, MD, FRCPC, Hyperbaric Unit, Department of Anesthesia and Pain Management, Toronto General Hospital, UHN, 200 Elizabeth street, G PMB 106E, Toronto, ON, M5G2C4, Canada; E-mail: rita.katznelson@uhn.ca

DOI: 10.1097/BRS.00000000000003502

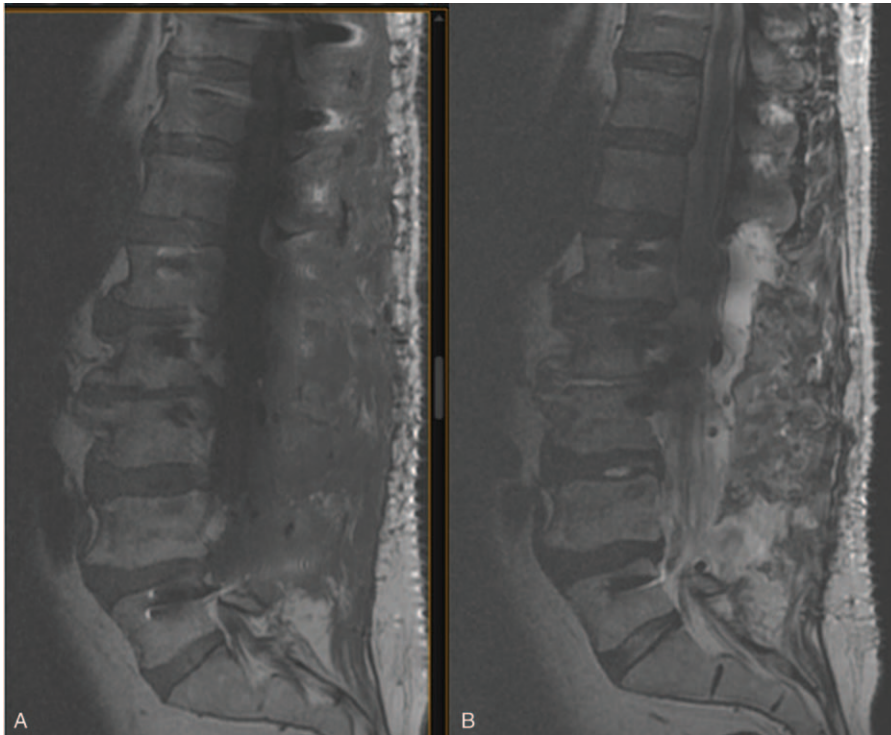


Figure 1. Magnetic resonance imaging T1 (A) and T2 (B) sagittal images performed immediately postoperatively demonstrated no compressive hematoma or cord signal change in the conus.

somatosensory evoked potentials and lower limb electromyograms could be obtained pre- or intraoperatively, with no intraoperative alarms.

Immediate postoperative examination demonstrated profound bilateral lower limb weakness (MRC 0–1/5; ASIA impairment scale B). An emergency Magnetic Resonance Imaging demonstrated no compressive hematoma, or any

signal abnormality within the cord or conus (see Figures 1 and 2). Medical management was instigated with a MAP target of more than or equal to 85 mmHg, Riluzole and admission to critical care,^{8,9} but no recovery was seen at 36 hours.

The first and second HBOT treatments were administered at 36 and 44 hours postoperatively (90 min at 2.8 ATA).

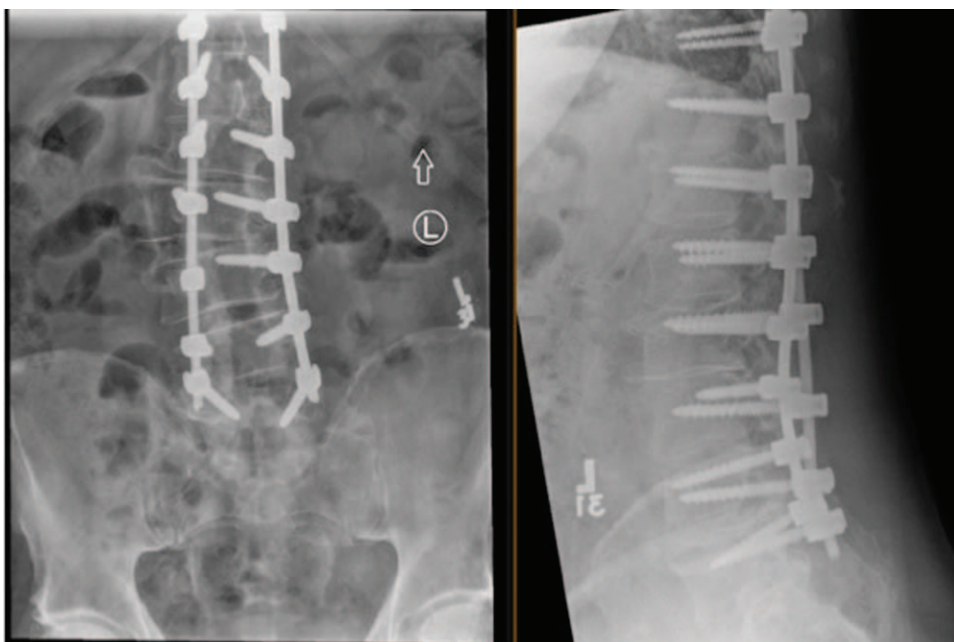


Figure 2. Postoperative x ray images showing satisfactorily positioned screws and two rod construct.

TABLE 1. Medical Research Council Grading (0–5) for Each Muscle Group in the Lower Limbs Before and After First Session of Hyperbaric Oxygen Therapy

HBOT No. 1	Right Leg		Left Leg	
Examinations	Pre-HBOT	Post-HBOT	Pre-HBOT	Post-HBOT
Hip flexion	2	3	0	1
Knee extension	1	3	0	1
Ankle dorsiflexion	1	3	0	1
Ankle plantar flexion	1	3	0	2
Dorsiflexion toe-EHL	1	3	1	2

EHL indicates extensor hallucis longus muscle; HBOT, hyperbaric oxygen therapy.

TABLE 2. Medical Research Council Grading (0–5) for Each Muscle Group in the Lower Limbs Before and After the Fourth (Penultimate) Session of Hyperbaric Oxygen Therapy

HBOT No. 4	Right Leg		Left Leg	
Examinations	Pre-HBOT	Post-HBOT	Pre-HBOT	Post-HBOT
Hip flexion	3	3	1	1
Knee extension	3	4	1	1
Ankle dorsiflexion	4	4	3	3
Ankle plantar flexion	4	4	3	3
Dorsiflexion toe-EHL	4	4	2	2

EHL indicates extensor hallucis longus muscle; HBOT, hyperbaric oxygen therapy.

Immediately following the first treatment there was a marked improvement of motor function (3/5) in the right lower limb (Table 1), with further improvement after the second. Two 90-minute sessions at 2.4 ATA were performed on day 2 with some motor improvement, but this plateaued after the fourth session (Table 2). A final treatment was performed the next day, with no complications throughout the treatment course. The patient continued to improve, became ambulatory 2 weeks post-surgery, and was discharged home after 7 weeks of rehabilitation. At 4 months, lower limbs had normal power (5/5), with no sphincter disturbance (ASIA impairment scale E).

DISCUSSION

HBOT is a non-invasive intervention with few side effects, and a growing body of evidence for the treatment of neurological injuries, particularly for early and delayed spinal cord ischemia.^{6,10–15} The therapeutic effects are thought to be from the supra-physiologic increase in the amount of dissolved unbound oxygen carried by the blood, which allows oxygenation of ischemic areas, and activates oxidant–antioxidant mechanisms via an endothelial nitric oxide pathway.^{16,17} It also reduces edema and protects the blood-brain-barrier through mechanisms involving modulation of M1 macrophage response, matrix metalloproteinase activity, and aquaporin channel expression.^{18–35}

Estimates of perioperative SCI are variable, but are reported as high as 23% to 32% in high-risk cases.^{36–39} Best evidence suggests a “major decline” can take up to 24 months to recover.³⁷ This case demonstrates a rapid and sustained return of lower limb function to ASIA E after 4 months. If the trajectory for a patient with a major decline in Lower Extremity Motor Score (LEMS) after spine surgery is to return to near-baseline function after 24 months,^{37,40} then this case represents a significant improvement in the time to recovery. The notion that the documented recovery may have occurred in the absence of HBOT can be counteracted by the fact that no motor recovery was seen up to the start of HBOT, and that the recovery was seen rapidly after therapy ended. Also, the speed and extent of recovery seen with this case is to a degree that is very different to the average recovery following major decline in LEMS after surgery.³⁷ The authors suggest that, in addition to aggressive medical management,⁴¹ HBOT has the potential to provide a strong impact on neurological recovery after perioperative injury.

CONCLUSION

The neurological motor recovery with HBOT described in this case is dramatically quicker and to a larger extent to previously reported major perioperative SCI. The pathobiology underlying this effect has a sound basis, and further investigation into the effect of HBOT after perioperative SCI is warranted.

➤ Key Points

- ❑ The use of hyperbaric oxygen therapy has not been described in the treatment of postoperative spinal cord injury.
- ❑ Hyperbaric oxygen therapy is well tolerated and can be safely applied to perioperative spine surgery patients.
- ❑ The use of hyperbaric oxygen therapy in this case appears to have significantly decreased the time to neurological recovery compared with previously reported duration of recovery from postoperative spinal cord injury.
- ❑ The application of hyperbaric oxygen therapy has a sound biological basis in spinal cord injury, and should continue to be a fervent avenue of clinical investigation for the future.

References

1. Weaver LK UaHMS. *Hyperbaric Oxygen Therapy Indications*. 13th ed; 2014.
2. Inanmaz ME, Kose KC, Isik C, et al. Can hyperbaric oxygen be used to prevent deep infections in neuro-muscular scoliosis surgery?. *BMC Surg* 2014;14:85.
3. Larsson A, Uusijärvi J, Lind F, et al. Hyperbaric oxygen in the treatment of postoperative infections in paediatric patients with neuromuscular spine deformity. *Eur Spine J* 2011;20:2217–22.
4. Liu J-T, Liao W-J, Chang C-S, et al. Management of deep infection after instrumentation on lumbar spinal surgery in a single institution. *Biomed Res Int* 2015;2015:842010.
5. Onen MR, Yuvruk E, Karagoz G, et al. Efficiency of hyperbaric oxygen therapy in iatrogenic spinal infections. *Spine (Phila Pa 1976)* 2015;40:1743–8.
6. Parotto M, Ouzounian M, Fedorko L, et al. Hyperbaric oxygen therapy for spinal cord ischaemia after complex aortic repair - a retrospective review. *Anaesthesiol Intensive Ther* 2018;50:103–9.
7. Roberts TT, Leonard GR, Cepela DJ. Classifications in brief: American Spinal Injury Association (ASIA) Impairment Scale. *Clin Orthop Relat Res* 2017;475:1499–504.
8. Hachem LD, Ahuja CS, Fehlings MG. Assessment and management of acute spinal cord injury: from point of injury to rehabilitation. *J Spinal Cord Med* 2017;40:665–75.
9. Ahuja CS, Nori S, Tetreault L, et al. Traumatic spinal cord injury-repair and regeneration. *Neurosurgery* 2017;80:S9–22.
10. Kohshi K, Abe H, Mizoguchi Y, et al. Successful treatment of cervical spinal epidural abscess by combined hyperbaric oxygenation. *Mt Sinai J Med* 2005;72:381–4.
11. Wajima Z, Aida S. Does hyperbaric oxygen have positive effect on neurological recovery in spinal-epidural haematoma? A case report. *Br J Anaesth* 2011;107:1006–8.
12. Lee K, Strozky D, Rahman C, et al. Acute spinal cord ischemia: treatment with intravenous and intra-arterial thrombolysis, hyperbaric oxygen and hypothermia. *Cerebrovasc Dis* 2010;29:95–8.
13. Morishita A, Tomioka H, Katahira S, et al. Delayed visceral and spinal cord malperfusion after axillo-bifemoral bypass for complicated acute type b aortic dissection. *Ann Vasc Dis* 2014;7:331–4.
14. Puttaswamy V, Bennett M, Frawley JE. Hyperbaric oxygenation treatment of acute paraplegia after resection of a thoracoabdominal aortic aneurysm. *J Vasc Surg* 1999;30:1158–61.
15. Yamashiro S, Kuniyoshi Y, Miyagi K, et al. Acute postoperative paraplegia complicating with emergency graft replacement of the ascending aorta for the type a dissection. *Ann Thorac Cardiovasc Surg* 2003;9:330–3.
16. Patel NP, Huang JH. Hyperbaric oxygen therapy of spinal cord injury. *Med Gas Res* 2017;7:133–43.
17. Venetsanou K, Fildissis G, Tokta R, et al. The role of nitric oxide in cellular response to hyperbaric conditions. *Eur J Appl Physiol* 2012;112:677–87.
18. Wang Y, Li C, Gao C, et al. Effects of hyperbaric oxygen therapy on RAGE and MCP-1 expression in rats with spinal cord injury. *Mol Med Rep* 2016;14:5619–25.
19. Geng CK, Cao HH, Ying X, et al. The effects of hyperbaric oxygen on macrophage polarization after rat spinal cord injury. *Brain Res* 2015;1606:68–76.
20. Satake K, Matsuyama Y, Kamiya M, et al. Nitric oxide via macrophage iNOS induces apoptosis following traumatic spinal cord injury. *Mol Brain Res* 2000;85:114–22.
21. Yu Y, Matsuyama Y, Yanase M, et al. Effects of hyperbaric oxygen on GDNF expression and apoptosis in spinal cord injury. *Neuro-Report* 2004;15:2369–73.
22. Shams Z, Khalatbary AR, Ahmadvand H, et al. Neuroprotective effects of hyperbaric oxygen (HBO) therapy on neuronal death induced by sciatic nerve transection in rat. *BMC Neurol* 2017;17:220.
23. Nie H, Xiong L, Lao N, et al. Hyperbaric oxygen preconditioning induces tolerance against spinal cord ischemia by upregulation of antioxidant enzymes in rabbits. *J Cereb Blood Flow Metab* 2005;26:666–74.
24. Francis A, Baynosa R. Ischaemia-reperfusion injury and hyperbaric oxygen pathways: a review of cellular mechanisms. *Diving Hyperb Med* 2017;47:110–7.
25. Hentia C, Rizzato A, Camporesi E, et al. An overview of protective strategies against ischemia/reperfusion injury: the role of hyperbaric oxygen preconditioning. *Brain Behav* 2018;8:e00959.
26. Lamkanfi M, Dixit VM. Inflammasomes: guardians of cytosolic sanctity. *Immunol Rev* 2009;227:95–105.
27. Liu X, Zhou Y, Wang Z, et al. Effect of VEGF and CX43 on the promotion of neurological recovery by hyperbaric oxygen treatment in spinal cord-injured rats. *Spine J* 2014;14:119–27.
28. Tai P-A, Chang C-K, Niu K-C, et al. 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.
29. Yang J, Liu X, Zhou Y, et al. Hyperbaric oxygen alleviates experimental (spinal cord) injury by downregulating HMGB1/NF- κ B expression. *Spine (Phila Pa 1976)* 2013;38:E1641–8.
30. Li Y, Wang Y, Zhang S, et al. Hyperbaric oxygen therapy improves local microenvironment after spinal cord injury. *Neural Regen Res* 2014;9:2182–8.
31. Xu J, Huang G, Zhang K, et al. Nrf2 activation in astrocytes contributes to spinal cord ischemic tolerance induced by hyperbaric oxygen preconditioning. *J Neurotrauma* 2014;31:1343–53.
32. Yang J, Wang G, Gao C, et al. Effects of hyperbaric oxygen on MMP-2 and MMP-9 expression and spinal cord edema after spinal cord injury. *Life Sci* 2013;93:1033–8.
33. Agrawal S, Lau L, Yong V. MMPs in the central nervous system: where the good guys go bad. *Semin Cell Dev Biol* 2008;19:42–51.
34. Noble LJ, Donovan F, Igarashi T, et al. Matrix metalloproteinases limit functional recovery after spinal cord injury by modulation of early vascular events. *J Neurosci* 2002;22:7526–35.
35. Sun Y, Liu D, Su P, et al. Changes in autophagy in rats after spinal cord injury and the effect of hyperbaric oxygen on autophagy. *Neurosci Lett* 2016;618:139–45.
36. Fehlings MG, Kato S, Lenke LG, et al. Incidence and risk factors of postoperative neurologic decline after complex adult spinal deformity surgery: results of the Scolio-RISK-1 study. *Spine J* 2018;18:1733–40.
37. Kato S, Fehlings MG, Lewis SJ, et al. An analysis of the incidence and outcomes of major versus minor neurological decline after complex adult spinal deformity surgery: a subanalysis of Scolio-RISK-1 Study. *Spine (Phila Pa 1976)* 2018;43:905–12.
38. Kim SS, Cho BC, Kim JH, et al. Complications of posterior vertebral resection for spinal deformity. *Asian Spine J* 2012;6:257–65.

39. Smith JS, Klineberg E, Lafage V, et al. Prospective multicenter assessment of perioperative and minimum 2-year postoperative complication rates associated with adult spinal deformity surgery. *J Neurosurg Spine* 2016;25:1–14.
40. Lenke LG, Fehlings MG, Shaffrey CI, et al. Neurologic outcomes of complex adult spinal deformity surgery: results of the prospective, multicenter Scolio-RISK-1 Study. *Spine (Phila Pa 1976)* 2016;41:204–12.
41. Dakson A, Brandman D, Thibault-Halman G, et al. Optimization of the mean arterial pressure and timing of surgical decompression in traumatic spinal cord injury: a retrospective study. *Spinal Cord* 2017;55:1033–8.