

Healing under pressure: hyperbaric oxygen and myocutaneous flap repair for extreme persistent perineal sinus after proctectomy for inflammatory bowel disease

X. H. S. Chan*, C. E. Koh*†, M. Glover‡, P. Bryson§¶, S. P. L. Travis** and N. J. Mortensen*

*Department of Colorectal Surgery, Oxford University Hospitals NHS Trust, Oxford, UK, †SOuRCe (Surgical Outcomes Research Centre), Royal Prince Alfred Hospital, Sydney, Australia, ‡Hyperbaric Medicine Unit, St Richard's Hospital, Chichester, UK, §Diving Services, Abermed, Forest Grove House, Aberdeen, UK, ¶Formally of the Diving Diseases Research Centre, Tamar Science Park, Plymouth, UK and **Translational Gastroenterology Unit, Oxford University Hospitals NHS Trust, Oxford, UK

Received 12 August 2013; accepted 15 September 2013; Accepted Article online 22 November 2013

Abstract

Aim Persistent perineal sinus (PPS) following proctectomy for inflammatory bowel disease affects about 50% of patients. Up to 33% of cases of PPS remain unhealed at 12 months and the most refractory cases are unhealed at 24 months despite optimal conventional therapy. Reports of hyperbaric oxygen therapy (HBOT) for chronic wounds and Crohn's perianal disease led us to explore perioperative HBOT with rectus abdominis myocutaneous (RAM) flap repair in a highly selected group of patients with extreme PPS who had failed all other interventions.

Method Patients with extreme PPS received preoperative HBOT (a 90-min session at 2.2–2.4 atmospheres, five times per week for 5–6 weeks, for a total of up to 30 sessions), before abdominoperineal PPS excision and perineal reconstruction with vertical or transverse RAM flap repair within 2–4 weeks of completing HBOT. Postoperative HBOT (10 further 90-min sessions) was administered within 2 weeks where practicable.

Results Between 2007 and 2011, four patients with extreme PPS underwent RAM flap repair with preoperative HBOT; two also received postoperative HBOT.

The median (range) duration of PPS before HBOT was 88.5 (23–156) months. All patients had previously failed multiple (5 to > 35) surgical procedures. Complete healing occurred in all patients at a median (range) follow-up of 2.5 (2–3) months. There were no further hospital admissions for PPS at a median (range) follow-up of 35 (8–64) months.

Conclusion Hyperbaric oxygen therapy combined with PPS excision and perineal reconstruction with a RAM flap led to complete perineal healing in four patients with extreme PPS and appears a safe and effective extension to the therapeutic pathway for exceptionally treatment-refractory PPS.

Keywords IBD, surgery, gastroenterology, PPS

What does this paper add to the literature?

We define the treatment of refractory persistent perineal sinus (PPS) and show how preoperative hyperbaric oxygen therapy combined with rectus abdominis myocutaneous flap repair may offer a safe and effective treatment option for patients with extreme PPS occurring after proctectomy for inflammatory bowel disease.

Introduction

Persistent perineal sinus (PPS) following proctectomy for inflammatory bowel disease (IBD) is common [1–3]. Defined as a chronic perineal wound that remains unhealed at 6 months [4], its incidence ranges from 11% to 57% [1–3,5,6] and it occurs more commonly

after proctectomy for IBD, particularly Crohn's disease, than after proctectomy for anorectal carcinoma [1,6–8]. Up to 33% of cases of PPS are not healed at 12 months [1], after which time the chance of spontaneous healing diminishes. In the most refractory of cases the perineal wound remains unhealed after 24 months, despite optimal medical and surgical management ('extreme PPS').

Despite the many therapeutic options [9–15], the management of PPS continues to be difficult in patients with IBD who have extreme PPS. The use of hyperbaric oxygen therapy (HBOT) to promote the healing of

Correspondence to: Prof. Neil J. Mortensen, Department of Colorectal Surgery, Oxford University Hospitals NHS Trust, Churchill Hospital, Oxford OX3 7LJ, UK.
E-mail: neil.mortensen@nds.ox.ac.uk

chronic wounds, particularly diabetic foot ulcers, is well established [16,17]. Its adaptation to patients with Crohn's perianal disease refractory to medical or surgical treatments has had some success [18,19]. It has been hypothesized that the increased tissue oxygen tension provided by HBOT would break the cycle of tissue hypoxia and inflammation in IBD [20] that perpetuates PPS and contributes to the failure of attempts at plastic reconstruction. This paper reports our experience with a new therapeutic strategy that uses HBOT before, and where possible after, PPS excision and rectus abdominis myocutaneous (RAM) flap reconstruction in IBD patients with refractory PPS.

Method

Between January 2007 and December 2011, four patients with extreme PPS following proctectomy for IBD underwent preoperative HBOT (25–30 daily sessions, each at 2.2–2.4 atmospheres for 90 min, five times per week for 5–6 weeks) followed by abdominoperineal excision within 2–4 weeks of the PPS combined with a vertical or transverse RAM flap. Further postoperative HBOT (10 daily sessions at 2.2–2.4 atmospheres for 90 min, five times per week for 2 weeks) was given when logistically possible. The patients had had a PPS for more than 2 years despite medical treatment and simple surgery, including debridement and drainage. No patient had evidence of sepsis or active Crohn's disease. The treatment strategy was developed with reference to previous reports of HBOT used in the management of the chronic wounds of patients with perianal Crohn's disease [18,19,21]. HBOT was administered by the Royal Hospital Haslar (Gosport, Hampshire; one patient), St Richard's Hospital (Chichester, West Sussex; two patients) and the Hyperbaric Medical Centre (Plymouth, Devon; one patient). All RAM flaps were performed by the surgeon NJM.

Preoperatively, sepsis and nutritional deficiencies were corrected. Medical comorbidities, such as type II diabetes mellitus, were optimized. Histopathology was reviewed to confirm the underlying diagnosis. The only patient with known Crohn's disease received a therapeutic trial of infliximab but this was suspended owing to an adverse reaction and a lack of clinical benefit. The medical records of patients were reviewed and complete healing was defined as complete epithelialization of the wound with cessation of discharge.

Results

Patient characteristics are listed in Table 1. Patients 1 and 2 had undergone proctocolectomy for medically refrac-

tory IBD (for Crohn's disease in patient 1 and for ulcerative colitis in patient 2). Patient 3 had undergone a three-stage restorative proctocolectomy with ileoanal pouch formation. Pelvic sepsis and pouch-perineal fistulation led initially to an attempt at pouch revision and eventually excision. In patient 4, an initial subtotal colectomy was complicated by dehiscence of the rectal stump, leading to necrotizing fasciitis of the abdominal wall. After a subsequent restorative proctectomy the pouch was finally removed owing to poor function and pouchitis.

All four patients had previously undergone five to 35 operations, including examination under anaesthesia (EUA) with debridement and/or curettage, and attempted perineal excision of the chronic sinus with primary closure or with vacuum-assisted closure (VAC). Patients 1 and 4 had also undergone failed combined abdominoperineal excision of the PPS with a pedicled omental flap and local flap closure. The median (range) duration of PPS before embarking on HBOT was 88.5 (23–156) months. Patients 1 and 3 received 30 and 25 preoperative HBOT sessions, respectively. Postoperative HBOT was possible in only two of the patients, with each receiving 10 sessions.

Adverse events occurred in one patient, who developed mild transient aural barotrauma during preoperative HBOT, which resolved spontaneously. This patient completed the course of preoperative HBOT. Postoperative complications occurred in two patients; these included a postoperative myocardial infarction in one and minor flap loss requiring local surgical debridement in both. Both were consequently unable to have postoperative HBOT. Complete wound healing was achieved in all four patients at a median (range) of 2.5 (2–3) months following surgery and none required further hospital admission for PPS at a median (range) of 35 (8–64) months.

Discussion

In this small series of patients with PPS treated by various means, HBOT followed by local surgery was uniformly successful. The patients had had PPS for a median of 7 years despite numerous therapeutic attempts by medical or surgical means. The usual surgical treatment for PPS is excision of the sinus [22,23], with or without a myocutaneous flap. The RAM flap is the procedure most commonly used for perineal reconstruction. Unlike gracilis [13] or gluteal perforator [14] flaps, it fills the pelvis well and provides a skin paddle for perineal wound closure, giving healing rates of up to 90% in PPS occurring after proctectomy for anorectal carcinoma [24]. There is considerably less experience with RAM flaps in patients having PPS after proctectomy for IBD, with

Table 1 Patient characteristics, treatment and outcome.

Patient no.	Age (gender)	Comorbidity	Reason for proctectomy	Duration of PPS (months)	Previous treatments for PPS	Management strategy/ Interval between HBOT and surgery (weeks)	Outcomes/Time from postoperative HBOT (months)
1	41 years (male)	None	Medically refractory Crohn's colitis	156	Antibiotics (when required) Infliximab > 35 EUA ± debridement ± abscess drainage ± local wound closure One abdominoperineal excision of PPS + pedicled omental flap (failed)	30 preoperative HBOT sessions (2) VRAM flap repair 10 postoperative HBOT sessions (2)	Complete healing (2) No hospital admissions for PPS (64)
2	58 years (male)	Type II diabetes, hypertriglyceridaemia	Medically refractory UC Nonrestorative proctocolectomy	132	> 10 EUA ± debridement ± drainage of abscess cavity ± local excision of PPS + VAC dressings	25 preoperative HBOT sessions (2) TRAM flap repair No postoperative HBOT because of myocardial infarction	Complete healing (3 – from surgery) No hospital admissions for PPS (46 – from surgery)
3	42 years (female)	None	Medically refractory UC Three-stage restorative proctocolectomy Pouch-perineal fistulae leading to pouch failure Pouch revision Recurrent fistulae 12 months later Initially defunctioned but persistent discharge leading to pouch excision	23	Antibiotics (when required) > 5 EUA ± debridement ± abscess drainage VAC dressings	30 preoperative HBOT sessions (2) VRAM flap repair 10 postoperative HBOT sessions (1)	Complete healing (2) No hospital admissions for PPS (24)
4	53 years (male)	Type II diabetes	Medically refractory indeterminate colitis Subtotal colectomy + closed mucous fistula with necrotizing fasciitis after subcutaneous stump blowout Restorative proctectomy	45	> 8 EUA ± debridement ± abscess drainage One abdominoperineal excision of PPS + pedicled omental flap (failed)	30 preoperative HBOT sessions (4) VRAM flap repair No postoperative HBOT sessions because of prolonged hospital stay postsurgery and complete	Complete healing (3) No hospital admissions for PPS (8)

Table 1 (Continued).

Patient no.	Age (gender)	Comorbidity	Reason for proctectomy	Duration of PPS (months)	Previous treatments for PPS	Management strategy/ Interval between HBOT and surgery (weeks)	Outcomes/Time from postoperative HBOT (months)
			Recurrent pouchitis and pouch dysfunction Initially defunctioned but persistent discharge leading to pouch excision		PPS	wound healing during that time	

EUA, examination under anaesthesia; HBOT, hyperbaric oxygen therapy; PPS, persistent perineal sinus; UC, ulcerative colitis; VAC, vacuum-assisted closure; VRAM, vertical rectus abdominis myocutaneous flap; TRAM, transverse abdominis myocutaneous flap.

variable results in case reports [15]. To our knowledge there are no data on its effectiveness in extreme PPS. Omentoplasty has been reported to be successful in over 80% of patients after proctectomy for Crohn’s disease [12] but the failure of this technique in two patients in the present series supported our preference for RAM flaps.

Hyperbaric oxygen therapy is a well-established treatment for chronic wounds, particularly if ischaemic [25]. There are several small studies demonstrating its success in promoting healing in medically refractory perineal Crohn’s disease [18,19,26–28]. It relieves hypoxia by increasing central and peripheral tissue oxygen tension. This is thought to break the vicious cycle of oxidative stress, inflammation, tissue oedema and impaired oxygen extraction that perpetuates nonhealing [20]. HBOT may also reduce inflammation through decreasing the production of potent pro-inflammatory cytokines, such as interleukin (IL)-1, IL-6 and tumour necrosis factor-alpha (TNF- α) [27], and increasing the mobilization of stem cells [29].

Persistent perineal sinus is a form of chronic wound, and hence the combination of HBOT with surgical excision of the sinus and filling of the defect with a RAM flap is logical. The successful integration of HBOT with surgery in the management of refractory PPS has previously been described in a case report of a patient with Crohn’s disease [21]. Postoperative HBOT, where practicable, can augment preoperative HBOT, but its value was not assessed in all four patients in the present study, although healing still took place in the two who did not have it.

Hyperbaric oxygen therapy is not without risk. Although serious adverse events are rare, aural barotrauma [25] and reversible worsening of myopia [28] have been reported. Psychological intolerance may also occur [18].

We acknowledge that this is a small, uncontrolled study. Nevertheless, given the long duration of chronic PPS and the success in all four patients, the management plan described indicates that this approach should be considered when a PPS fails to heal after many months to years.

In summary, HBOT, in conjunction with excision of the PPS with a RAM flap perineal reconstruction, resulted in complete perineal healing at a median of 3 years in four patients with a PPS of median duration of over 7 years.

Author contributions

XHSC & CEK collected and analysed the data, and drafted the paper. MG & PB advised on and carried

out the hyperbaric oxygen treatment. SPLT conceptualized and designed the study. NJM performed all RAM flaps, conceptualized and designed the study. MG, PB, SPLT & NJM authors provided critical review for intellectual content. All authors gave final approval of the version to be published.

References

- Lohsiriwat V. Persistent perineal sinus: incidence, pathogenesis, risk factors, and management. *Surg Today* 2009; **39**: 189–93.
- Prudhomme M, Dehni N, Dozois RR, Tiret E, Parc R. Causes and outcomes of pouch excision after restorative proctocolectomy. *Br J Surg* 2006; **93**: 82–6.
- Karoui M, Cohen R, Nicholls J. Results of surgical removal of the pouch after failed restorative proctocolectomy. *Dis Colon Rectum* 2004; **47**: 869–75.
- Watts J, de Dombal F, Goligher J. Long-term complications and prognosis following major surgery for ulcerative colitis. *Br J Surg* 1966; **53**: 1014–23.
- Marks CG, Ritchie JK, Todd IP, Wadsworth J. Primary suture of the perineal wound following rectal excision for inflammatory bowel disease. *Br J Surg* 1978; **65**: 560–4.
- Ferrari B, DenBesten L. The prevention and treatment of the persistent perineal sinus. *World J Surg* 1980; **4**: 167–72.
- Bauer J, Gelernt I, Salk B, Kreef I. Proctectomy for inflammatory bowel disease. *Am J Surg* 1986; **151**: 157–62.
- Corman M, Veidenheimer M, Collier J, Ross V. Perineal wound healing after proctatectomy for inflammatory bowel disease. *Dis Colon Rectum* 1978; **21**: 155–9.
- Kirkegaard P, Madsen P. Perineal sinus after removal of the rectum. Occlusion with fibrin adhesive. *Am J Surg* 1983; **145**: 791–4.
- McLeod R, Palmer J, Cohen Z. Management of chronic perineal sinuses by wide excision and split-thickness skin grafting. *Can J Surg* 1985; **28**: 315–6.
- Bascom T, Bascom JU. Persistent perineal sinus after proctectomy for Crohn's disease; simplified repair using skin flap. *Am J Surg* 2002; **184**: 85; author reply.
- Yamamoto T, Mylonakio E, Keighley M. Omentoplasty for persistent perineal sinus after proctectomy for Crohn's disease. *Am J Surg* 2001; **57**: 185–8.
- Ryan J. Gracilis muscle flap for the persistent perineal sinus of inflammatory bowel disease. *Am J Surg* 1984; **148**: 64–70.
- Shaw A, Futrell J. Cure of the chronic perineal sinus with gluteus maximus flap. *Surg Gynecol Obstet* 1978; **147**: 417–20.
- Collie M, Potter M, Bartolo D. Myocutaneous flaps promote perineal healing in inflammatory bowel disease. *Br J Surg* 2005; **92**: 740–1.
- Abidia A, Laden G, Kuhan G *et al.* The role of hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind randomised-controlled trial. *Eur J Vasc Endovasc Surg* 2003; **25**: 513–8.
- Kalani M, Jorneskog G, Naderi N, Lind F, Brismar K. Hyperbaric oxygen (HBO) therapy in treatment of diabetic foot ulcers. Long-term follow-up. *J Diabetes Complications* 2002; **16**: 153–8.
- Colombel J, Mathieu D, Bouault J *et al.* Hyperbaric oxygenation in severe perineal Crohn's disease. *Dis Colon Rectum* 1995; **38**: 609–14.
- Lavy A, Weisz G, Adir Y, Ramon Y, Melamed Y, Eidelman S. Hyperbaric oxygen for perianal Crohn's disease. *J Clin Gastroenterol* 1994; **19**: 202–5.
- Rosignol D. Hyperbaric oxygen treatment for inflammatory bowel disease: a systematic review and analysis. *Med Gas Res* 2012; **2**: 6.
- Nelson EW Jr, Bright DE, Villar LF. Closure of refractory perineal Crohn's lesion. Integration of hyperbaric oxygen into case management. *Dig Dis Sci* 1990; **35**: 1561–5.
- MacLeod R, Palmer J, Cohen Z. Management of chronic perineal sinuses by wide excision and split-thickness skin grafting. *Can J Surg* 1985; **28**: 315–8.
- Browder W, Carey A, Ryan R. Previously undescribed treatment for persistent peritoneal-perineal fistula following proctectomy. *Ann Plast Surg* 1987; **19**: 563–5.
- Brough W, Schofield P. The value of the rectus abdominis myocutaneous flap in the treatment of complex perineal fistula. *Dis Colon Rectum* 1991; **34**: 148–50.
- Roedel-Wiedmann I, Bennett M, Kranke P. Systematic review of hyperbaric oxygen in the management of chronic wounds. *Br J Surg* 2005; **92**: 458–61.
- Takehima F, Makiyama K, Doi T. Hyperbaric oxygen as adjunct therapy for Crohn's intractable enteric ulcer. *Am J Gastroenterol* 1999; **94**: 3374–5.
- Weisz G, Lavy A, Adir Y *et al.* Modification of in vivo and in vitro TNF-alpha, IL-1, and IL-6 secretion by circulating monocytes during hyperbaric oxygen treatment in patients with perianal Crohn's disease. *J Clin Immunol* 1997; **17**: 154–9.
- Brady CE III, Cooley BJ, Davis JC. Healing of severe perineal and cutaneous Crohn's disease with hyperbaric oxygen. *Gastroenterology* 1989; **97**: 756–60.
- Thom S, Bhopale V, Velazquez O, Goldstein L, Thom L, Buerk D. Stem cell mobilization by hyperbaric oxygen. *Am J Physiol Heart Circ Physiol* 2006; **290**: H1378–86.