

【 症例報告 】

低栄養状態における創傷治癒に高気圧酸素療法とプロスタグランディンE1との併用療法が奏効した1例

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高気圧酸素療法は浮腫の軽減, 虚血再灌流障害の防御, そして創傷治癒を増強するということから数十年の間多くの疾患に用いられてきた。低栄養状態の外科手術症例においては縫合不全の危険性が高くなるが, 今回我々は総蛋白 4.5 g/dl (参考値 6.5-8.2), アルブミン 2.0 g/dl (3.7-5.2), ヘモグロビン 8.4 g/dl (11.3-15.2) ヘモグロビン A1c 7.5% (4.3-5.8) と 極度の低栄養状態および糖尿病合併の胃癌症例 (Stage IV) の胃全摘術後 (D1) の管理においてプロスタグランディンE1 (0.5 µg/kg/h) 併用高気圧酸素療法 (2 Absolute Atmosphere) を試みた。術後4日目の透視にて縫合不全の所見なく, 術後7日目に食事を開始する事ができた。プロスタグランディンE1併用高気圧酸素療法は低栄養状態の外科手術症例の術後管理において有益な方法であることが示唆された。

キーワード 高気圧酸素, 低栄養状態, 創傷治癒, 胃全摘術, プロスタグランディンE1

A Case that the Combination Therapy of Hyperbaric Oxygen and Prostaglandin E1 effects on Wound Healing in Malnutrition

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Hyperbaric oxygen (HBO) therapy has been used for many severe human illness for several decades based on the postulated benefits of reduction of edema, protection from reperfusion injury, and enhanced wound healing¹⁾. The risk of wound dehiscence is increased in surgical patient in malnutrition. To our knowledge, we present the first recorded case of HBO therapy adjunct to administrating prostaglandin E1 for postoperative care after total gastrectomy for gastric cancer in severe malnutrition.

keywords HBO, malnutrition, wound healing, total gastrectomy, prostaglandin E1

CASE REPORT

A 62-year-old woman with gastric cancer was referred to us complaining of abdominal discomfort, weight loss (more than 15% of her usual body weight), anorexia and malaise during the last six months. She had a previous history of melena and a past medical history of insulin dependent diabetes mellitus (DM) being treated with insulin for 40 years. On physical examination

a tender mass was palpable in the epigastric region and a distended abdomen with ascites was found. In laboratory data, total protein was 4.5 g/dl (reference range 6.5-8.2), albumin 2.0 g/dl (3.7-5.2), hemoglobin 8.4 g/dl (11.3-15.2) and hemoglobin A1c 7.5% (4.3-5.8). Other hepatorenal function tests were within normal reference range. Computed tomography (CT) showed a massive ascites and the wall thickness of the stomach with



Fig. 1 CT demonstrating a massive ascites and the wall thickness of the stomach with invasion to the pancreas

invasion to the pancreas (Fig. 1). Barium upper gastrointestinal examination revealed nondistensible stomach due to diffusely infiltrating carcinoma (Fig. 2). Clinical tumor stage was Stage IV by the TNM classification.

The patient was a nurse who fully understood predictable poor outcome of the operation. However, she desired to be treated with the operation for ingesting orally. After all we decided to treat her by the operation for quality of life. Conventional Roux-en-Y esophagojejunostomy after total gastrectomy (D1) was performed. During 4 days after the operation HBO therapy (2 Absolute Atmosphere) combined with infusion of prostaglandin E1 ($0.5 \mu\text{g}/\text{kg}/\text{h}$) were added to routine postoperative care. Postoperative contrast study with 76% Gastrografin revealed no anastomotic leakage at the 4th postoperative day (Fig. 3). Then, orally feeding was started without any complication at the 7th postoperative day.

DISCUSSION

The inverse relationship between nutritional status and wound healing potential is well recognized. Both prolonged and short-term types

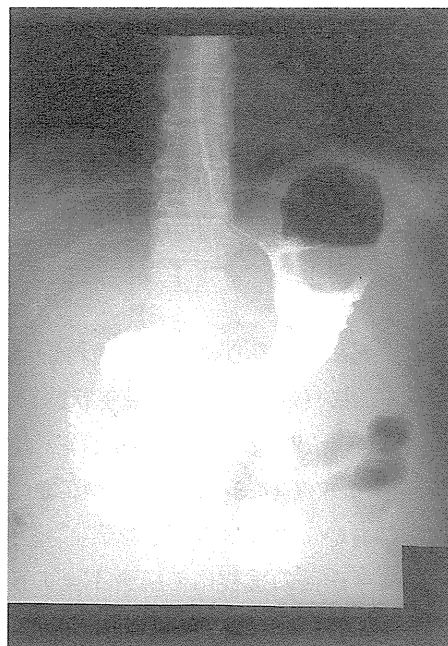


Fig. 2 Barium upper gastrointestinal examination showing nondistensible stomach due to diffusely infiltrating carcinoma

of malnutrition diminish anastomotic healing²⁾. A history of greater than 10% or certainly 15% weight loss and an albumin value of less than 3 gm. per 100 ml. is considered as a high-risk group in the abdominal surgery. However, albumin infusion usually is not an effective therapy because the albumin will degrade quickly and infusion dose not address the underlying causes of adverse operative outcome³⁾. In wounds, intercapillary distances are large and oxygen consumption is relatively low. Hypoalbuminemia induce edema of tissue consequent to extending intercapillary distance, which may be one of the reasons of anastomotic leakage in hypoalbuminemia. Because the driving force of diffusion is partial pressure, a higher PO₂ is needed to force oxygen into injured and healing tissues especially in malnutrition.

HBO at 2.0 to 3.0 Absolute Atmosphere increases peripheral tissue oxygen delivery, despite

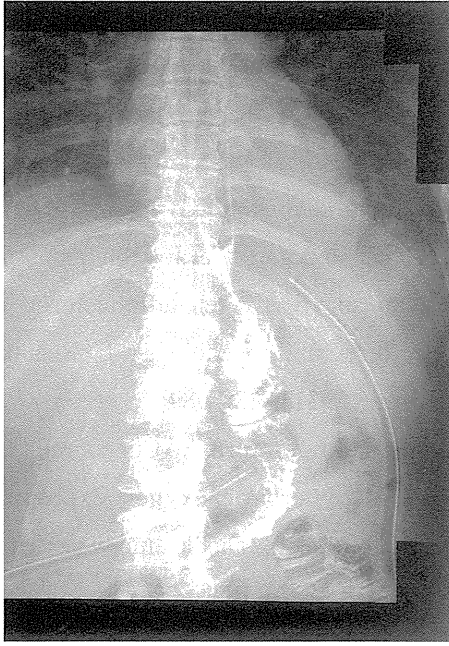


Fig. 3 Postoperative contrast study revealing no anastomotic leakage

vasoconstrictive reductions in peripheral blood flow⁴. This elevation in tissue PO₂ enhances fibroblast proliferation, collagen synthesis, and angiogenesis^{5,6}, which result in acceleration of tissue repair and wound healing. Furthermore, intermittent HBO therapy significantly reduced muscle edema and necrosis in consisting of a dog hindlimb compartment syndrome⁷. HBO therapy also reduced post-ischemic edema in a rat model of ischemia-reperfusion injury⁸, indicating the ability of protection for post-ischemic edema of anastomotic region. More consistent improvement in outcome has been observed in a prospective trial of HBO in diabetic patient with chronic ulcers⁹. Although these effects of HBO have potential for therapeutic benefit, the precise mechanism is unclear. Zamboni and coworkers reported that HBO inhibited neutrophil adherence and postischemic vasoconstriction in ischemic rat tissue¹⁰. Recently Luongo and coworkers reported

that HBO therapy reduced peritoneal leukocytosis and exudate, and decreased plasma and peritoneal nitric oxide metabolite concentrations and reduced plasma tumor necrosis factor (TNF) - α in animals shocked model by zymozan¹¹. They can explain induction of vasoconstriction and inhibition of bacterial translocation in HBO therapy. In our case, by using combination of HBO therapy and administration of Prostaglandin E1 to maintain a high PO₂ in the injured tissue and to decrease peripheral vascular resistance, the patient with hypoalbuminemia, anemia, and weight loss had a good clinical course without anastomotic leakage and wound dehiscence. Those results may be according to the postulated benefits of reduction of edema, protection from reperfusion injury, anti-infective effect and enhanced wound healing.

Despite the fact that an operation is not generally advised to a patient in severe malnutrition, a good outcome in our case may allow us to recommend the combination therapy as the postoperative treatment in such a severe case.

In conclusion, the combination of HBO and Prostaglandin E1 may be one of the most effective therapies of postoperative care for surgical patients in severe malnutrition. In the future, we plan prospective studies of this combination therapy in patients with colonic perforation, strangulated ileus and wound dehiscence.

REFERENCES

1. Tibbles PM, Edelsberg JS : Hyperbaric oxygen therapy. *N Engl J Med.* 334. 1642-1648. 1996
2. Ward MW, Danzi M, Lewin MR, et al: The effects of subclinical malnutrition and refeeding on the healing of experimental colonic anastomoses. *Br J Surg.* 69. 308-310. 1982
3. Rothschild MA, Oratz M, Schreiber SS: Serum

- albumin. *Hepatology*. 8. 385-401. 1988
4. Dooly JW, Mehm, WJ : Noninvasive assesment of the vasoconstrictive effects of hyperoxygenation. *J Hypertens Med*. 4. 177.1990
 5. Hunt TK, Pai MP : The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. *Surg Gynecol Obstet*. 135 : 561-567. 1972
 6. Kinghton DR, Silver IA, Hunt TK : Regulation of wound-healing angiogenesis - effect of oxygen gradients and inspired oxygen concentration. *Surgery*. 90. 262-270. 1981
 7. Bird AD, Telfer ABM : Effect of hyperbaric oxygen on limb circulation. *Lancet*. 1. 355. 1965
 8. Nylander G, Lewis D, Noddstrom H, Lasson J : Reduction of the post ischemic edema with hyperbaric oxygen. *Plast Reconstr Surg*. 76. 596-603. 1985
 9. Doctor N, Pandya S, Supe A : Hyperbaric oxygen therapy in diabetic foot. *J Postgrad Med*. 38. 112-114. 1992
 10. Zamboni WA, Roth AC, Russel RC, Neniroff PM, Cassas L, Smoot EC: The effect of acute hyperbaric oxygen therapy on axial pattern skin flap survival when administered during and after total ischemia. *J Reconst Microsurg*. 5. 343-347. 1989
 11. Luongo C, Imperatore F, Cuzzocrea S, et al: Effects of hyperbaric oxygen exposure on a zymosan- induced shock model. *Crit Care Med*. 26. 1972-1976. 1998