

Therapeutic experience of hyperbaric oxygenation in ulcerative colitis refractory to medical treatment (Case report)

Tıbbi tedaviye refrakter ülseratif kolitte hiperbarik oksijenin terapötik kullanımı

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ÖZET: Tıbbi tedaviye yanıt vermeyen aktif ülseratif pankolitli bir hastada hiperbarik oksijenin etkinliği araştırıldı. Hasta ülseratif kolit nedeniyle 5 yıldır tedavi altında idi. Oral mesalazin tedavisi altında iken ağır ülseratif kolit kliniği ile hastaneye yatırıldı. Hem kolonoskopik hem de histopatolojik incelemeler sonucu ağır aktif ülseratif koliti olduğu görüldü. Günde 4 g. oral mesalazin ve mesalamin rektal enamaya ek olarak günde 60 mg i.v. prednizolon ve total parenteral nutrisyon ile 7 günlük tedaviye rağmen hastalığında hiçbir düzelme olmadı. Bu aşamada, günde 120 dk. süre ile 30 gün boyunca, 2 mutlak atmosfer basıncı altında % 100 oksijen inhalasyonundan oluşan hiperbarik oksijen tedavisine başlandı. Tedavi, kanamanın 11 gün içerisinde durmasını sağladı. Üçüncü haftada yapılan endoskopik muayenede grade II ve altıncı haftada da grade I endoskopik bulgular saptandı. Abdominal yakınmalarında anlamlı düzeltilmeler de gözlemlendi. Tıbbi tedaviye refrakter ağır ülseratif kolitli bir hastada tıbbi tedaviye hiperbarik oksijenin eklenmesinin remisyonu hızlandırdığı gözlemlendi. Bu bulgunun anlamlılığını ortaya koymak için fazla hasta sayılı uzun dönem çalışmalara gerek vardır.

Anahtar Kelimeler : Hiperbarik oksijen tedavisi, refrakter, ülseratif kolit.

ULCERATIVE colitis is an inflammatory disease of the colon that primarily affects young adults in the third decade and patients after 50 years of age, in the course of which remissions and exacerbations are common. Prognosis of the disease is closely related to the localisation of the lesions, duration and severity of the activation and the cultural and socioeconomic level of the patient. The purpose of the treatment is to maintain remission. Favorable responses are possible and remission rates are higher in the patients with distal or left-sided disease than those with pancolitis, and the

SUMMARY: The efficacy of hyperbaric oxygenation in a patient with active ulcerative pancolitis who did not respond to medical treatment was evaluated.

The patient had been under treatment for 5 years for her ulcerative colitis. She was admitted to hospital in a clinical state of severe ulcerative colitis while she had been on oral mesalazine treatment. She was found to have severe active pancolitis with both colonoscopic and histopathologic examinations. Her disease did not improve despite treatment with oral mesalazine 4 g. daily plus mesalamin rectal enema in addition to i.v. prednisolon 60 mg. and total parenteral nutrition for 7 days. Thereafter hyperbaric oxygenation therapy was initiated, consisting of 100 % oxygen inhalation at 2 absolute atmospheric pressures, 120 minutes daily for 30 days.

The treatment was successful in cessanting of active bleeding within 11 days. Endoscopic examination in the 3rd week revealed grade II, and in the 6th week grade I endoscopic findings. Significant improvement was obtained in her abdominal discomfort.

Addition of hyperbaric oxygenation therapy to medical treatment was seen to induced remission in a patient with severe ulcerative colitis refractory to medical treatment. Long term studies with large number of patients are needed to elucidate the significance of this finding.

Key words: Hyperbaric oxygen therapy, refractory, ulcerative colitis.

clinical presentation may vary from mild to severe forms (1).

In progressive cases the disease may result with surgical colectomy due to severe complications such as massive bleeding, toxic megacolon, dysplasia and risk of colonic carcinoma (2). In moderate and severe forms successful results were reported with sulphasalazine, aminosalicylates and corticosteroids and remission can be induced with these treatment (3). Immunosuppressive treatment was also reported to be effective in cases refractory to medical treatment, but they have important side effects (4). New therapeutic modalities (short chain

fatty acids, 5-lipoxygenase inhibitors, eicosapentaenoic acid, specific 5-lipoxygenase inhibitor A-64077, selective thromboxane synthesis inhibitors, gamma globulins, monoclonal anti-CD4 antibody etc.) are still under investigation.

Hyperbaric oxygenation (HBO) has been in medical usage since 1775 in the treatment of various diseases. HBO have been used in the field of gastroenterology in the treatment of peptic ulcer, inflammatory bowel disease, cirrhosis of the liver and radiation colitis and favorable results have been reported (5,6,7).

CASE REPORT

We present here a case of a 39-year-old female who was admitted to the Department of Gastroenterology, Gülhane Medical Academy, Haydarpaşa Training Hospital in August 1994 with the complaints of fever, abdominal crampy pain, weakness and bloody diarrhea 10-12 times a day with passage of mucus as well.

The patient has been under treatment since 1988 with the diagnosis of chronic relapsing ulcerative pancolitis. She was treated with sulphasalazine and corticosteroids both initially and during relapses. She has been on maintenance sulphasalazine treatment during remissions until 1993 when mesalazine (1 g. daily) was started as maintenance therapy. She has been on this treatment and in remission since then. The exacerbation that started in July 1994, progressed gradually with fever (39 °C) and bloody diarrhea of 10-12 times a day. Abdominal crampy pain and passage of mucus were added to the clinical picture along with weakness and tachycardia due to remarkable anemia. Clinical severity of the attack was considered as "severe" according to the clinical grading system defined by Truelove and Witts (8).

Colonoscopic examination demonstrated extensive erythema and edema with loss of submucosal vascular pattern and ulcerative and bleeding lesions in the whole colon.

Multiple large bowel specimens obtained by endoscopic biopsy were fixed in 96% alcohol. On light microscopy the histopathologic findings were those of active ulcerative colitis with crypt abscesses and ulcerations as well as extensive damage in crypts.

The case was considered as a severe form of ulcerative pancolitis and was put on oral mesalazine (4 g. daily) and mesalazine enema with additional prednisolon (60 mg daily) along with total parenteral

nutrition. A treatment course of 7 days failed to improve the clinical situation of the patient except for a little decrease in her fever. Diagnostic work up for the evaluation of conditions that may lead to refractoriness to the medical treatment (amebiasis, urinary infection etc.) or complications (toxic megacolon, perforation etc.) was negative.

On the 15th day of admission, before surgery consultation was sought, HBO therapy consisting of 100% oxygen inhalation at 2 atmospheric pressures 120 minutes daily was initiated without the cessation of medical treatment. The HBO therapy was administered in a one-man chamber for 30 days without any serious side effects. On the twenty day of HBO treatment, number of defecations decreased considerably as well as better control of the fever of the patient. Eleven days after the initiation of HBO treatment bloody diarrhea stopped completely. In the 3rd week of the treatment a definite improvement of the other complaints of the patient occurred and endoscopy revealed a near normal appearance of the large bowel mucosa with mild hyperemia and edema. Medical treatment was continued with tapering and cessation of steroids and with mesalazine 1 gr. daily. At the end of the 6th week, endoscopy was repeated and revealed a mucosa in remission. The patient has been on mesalazine 1 gr. daily since then and being followed up as the case of ulcerative colitis in remission.

DISCUSSION

Ulcerative colitis is classified into three forms according to the course of the disease as acute and severe or fulminant form, chronic relapsing form and chronic continuous form.

In 90 % of the cases with proctitis or proctosigmoiditis, prognosis is favorable and chronic treatment is not needed. In patients with moderate and severe disease decision to initiate steroid treatment is important due to its potential side effects (1). Truelove and Jewell have reported remission in 39 of 46 severe ulcerative colitis cases who were treated with IV prednisolon 60 mg daily and hyperalimentation (9). Remission rates are 88% in patients without extensive disease and 46.8% in those with pancolitis. Similar results have been obtained with ACTH and pulse steroid treatments (8). Immunosuppressive therapy is an alternative in cases refractory to corticosteroid treatment. Cyclosporin, 6-mercaptopurin and azothioprin have similar treatment efficacy and have important side-effects such as pancreatitis,

allergic reactions, myelosuppression and hepatitis (4). Immunosuppressive treatment is recommended for those patients who have chronic continuous disease or chronic steroid toxicity and who do not have a high risk for colonic carcinoma. There is not a widely accepted treatment scheme for the long-term usage of these drugs.

Mortality rates are affected by life-threatening complications and necessity of surgical procedures due to these complications in cases refractory to medical treatment (2).

Limited reports have been encountered in the literature on the subject of HBO treatment in inflammatory bowel disease. It has been reported that disease activity index decreased significantly in the first and second weeks with the addition of HBO treatment in perianal Crohn's Disease cases refractory to medical treatment and that perianal fistula in one case healed completely with this treatment (10,11). We have not encountered any report of HBO therapy in the treatment of ulcerative colitis in the literature available.

We have initiated HBO therapy on the 15th day of medical treatment in our case, who was a case of acute fulminant form, in whom remission could not

have been induced with 5-ASA (oral + rectal enema), corticosteroids and hyperalimentation treatment. Rectal bleeding stopped completely on the 11th day and both clinical, endoscopic and histopathologic remissions were obtained on the third week.

Increase of tissue oxygenation is known to have an important role in wound healing and tissue regeneration (10). In addition, HBO therapy is known to inhibit prostaglandin synthesis. During HBO therapy bacteriostatic and bactericidal effects occur both direct and indirect routes due to an increase in tissue oxygen pressure, as well as the inhibition of bacterial toxins and enhancement of collagen production and fibroblastic activity (10,11). Dramatic response have also been reported to occur with HBO therapy in a case of radiation colitis (7).

In conclusion, hyperbaric oxygen therapy can be chosen as an adjuvant treatment to other treatments which have potential side effects, in case with ulcerative colitis refractory to medical treatment since it does not have important side effects and is easily reproducible. These results should be evaluated and confirmed in future controlled studies with large number of patients.

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