Crohn's disease and hyperbaric oxygen therapy[1]

Doença de Crohn e oxigenoterapia hiperbárica

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ABSTRACT
PURPOSE: Evaluate the application of Hyperbaric Oxygen Therapy (HBO) in patients with Crohn's disease (CD) refractory to pharmacologic therapy, who developed abdominal, anorectal or skin complications.
METHODS: Fourteen selected patients with refractory CD and treated at the School of Medicine of Ribeirao Preto, University of Sao Paulo (FMRP-USP) and at the Center of Hyperbaric Medicine, São Paulo Hospital (CEMEHI) were submitted to HBO.
RESULTS: Of the 14 patients evaluated, 11 had a satisfactory response.
CONCLUSION: HBO has shown benefits in patients with CD refractory to pharmacologic therapy.
Key words: Crohn Disease. Hyperbaric Oxygenation. Complications.

RESUMO
OBJETIVOS: Avaliar a aplicação da Oxigenoterapia Hiperbárica (HBO) nos pacientes com doença de Crohn (CD), refratários a terapia farmacológica, que evoluíram com complicações abdominais, orificiais ou dermatológicas.
MÉTODOS: Catorze pacientes selecionados no Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo e no Centro de Medicina Hiperbárica do Hospital São Paulo de Ribeirão Preto eram portadores de Doença de Crohn refratária ao tratamento farmacológico e foram submetidos a sessões de HBO.
RESULTADOS: Dos 14 pacientes avaliados, 11 apresentaram resposta satisfatória.
CONCLUSÃO: A HBO tem demonstrado benefício nos pacientes com Doença de Crohn refratários ao tratamento farmacológico.
Descritores: Doença de Crohn. Oxigenação Hiperbárica. Complicações.

Introduction

Crohn's disease (CD) is an idiopathic, chronic, transmural, inflammatory disorder that can affect the whole gastrointestinal tract[1]. Studies demonstrate a dysfunctional relationship between genetic, immunological and environmental factors resulting in an imbalance between proinflammatory and anti-inflammatory mediators[2-4]. Its incidence has increased in recent decades, especially in developed countries; and this has stimulated the interest in novel pharmacological and surgical therapies.

The "Biological therapy" is the most advanced weapon against the disease and it targets the TNF-alpha. TNF is a naturally occurring cytokine involved in inflammatory and immune responses. Several studies have demonstrated the benefits of these medications as they provide a longer-lasting remission, corticosteroids independence and prevention of complications such as fistulas and stenosis[5-8].

With the advent of new drugs for CD there has been a remarkable clinical improvement as these medications seek to control the inflammatory cascade[9-13]. However, even with the

anti-TNF therapy associated or not to other immunosuppressive drugs, there are still challenging cases refractory to medical and surgical treatment and tissue destruction is the ultimate result[14,15].

Poor healing of the mucosa, fistulae persistence, infectious processes and progressive stenosis are some of the complications that can cause nutritional depletion and immunosuppression of the patients. These factors lead to prolonged hospitalization, systemic infections and significant increase in morbidity and mortality[16-19].

Drug optimization tends to be ineffective and surgical intervention may be necessary[20]. There is a higher risk of complication in patients with CD and it is known that correct healing in the areas of resection is impaired by bacterial colonization[21].

Several authors advocate the use of Hyperbaric Oxygen Therapy (HBO) as an adjuvant option in patients with refractory disease and the results are favorable[22-24]. Is consists in expose the patient in a chamber with 100% oxygen with higher pressure (2ATA). HBO promotes increments in plasmatic partial pressures of O_2, thus enhancing tissue levels of oxygenation. It´s know that HBO promotes healing in chronic wounds[24].

The purpose of this study is to report the experience of the authors with the utilization of HBO as adjuvant therapy in selected cases.

Methods

Fourteen patients prospectively selected were followed at the Division of Coloproctology in FMRP-USP and in the CEMEHI with chronic abdominal wounds (enteric-cutaneous fistula), perineal disease (fistulas or chronic perineal wounds) or pyoderma gangrenosum were considered refractory to pharmacological therapy.

The number of sessions ranged from 10-50 according to patient's evolution. We used a Sechrist monoplace chamber pressurized to 2.4 ATA. The sessions lasted 2 hours and were performed daily.

Results

Of the 14 patients studied, 6 had abdominal injuries due to enteric-cutaneous fistula, 10 had perineal disease and 2 presented with pyoderma gangrenosum. Eleven patients (78,5%) had a satisfactory improvement, healing and good local control of inflammation. Three patients (21,5%) maintained injuries and required surgical approaches (Table 1).

In the present study 11 of the 14 patients had a complete or partial improvement of their cicatrization. The following images show these benefits (Figures 1, 2 and 3).

TABLE 1 - Patients and results.

Patients	Abdominal Injury	Perineal Injury	Pyoderma Gangrenosum	Number of Sessions	Satisfactory Result
LGM, 29 years	YES	YES	NO	20	YES
MAG, 45 years	YES	NO	NO	20	YES
SLV, 20 years	NO	YES	NO	20	NO
FFVM, 41 years	NO	YES	NO	32	YES
CPD, 41 years	NO	YES	NO	20	YES
RBR, 41 years	YES	NO	YES	40	YES
TCS, 32 years	NO	YES	NO	40	YES
JNAC, 52 years	NO	YES	NO	20	YES
LCPJ, 41 years	NO	YES	NO	40	YES
ACT, 35 years	YES	NO	NO	20	YES
JG, 38 years	NO	YES	NO	30	YES
MAS, 42 years	NO	YES	NO	18	NO
JC,	YES	NO	NO	20	NO
VHLL, 49 years	YES	YES	YES	50	YES

FIGURE 1 - LGM, 29 years – abdominal (before and after) and perineal (before and after) disease. Before and after 20 sessions of HBO.

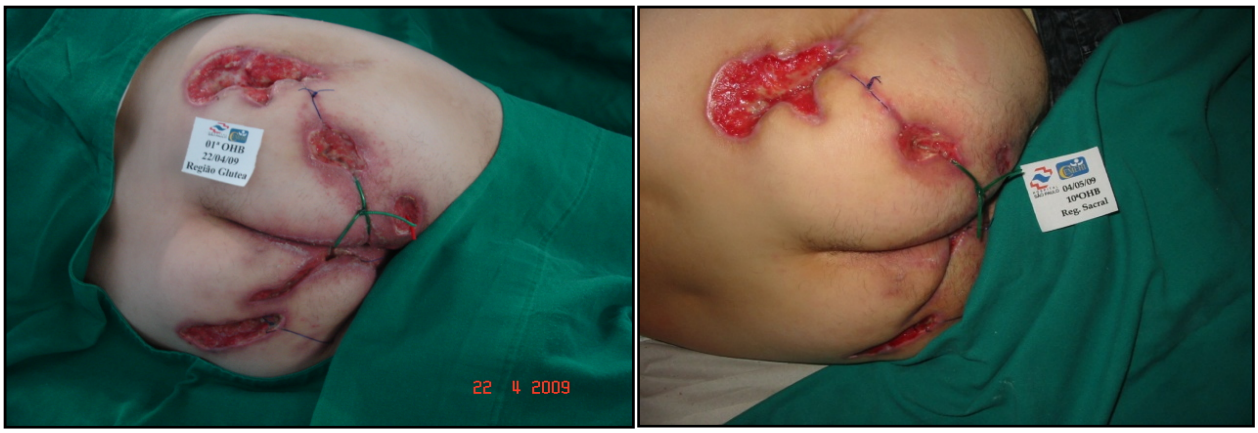

FIGURE 2 - LCPJ, 41 years – complex anorectal fistulae. Before and after sessions of HBO.

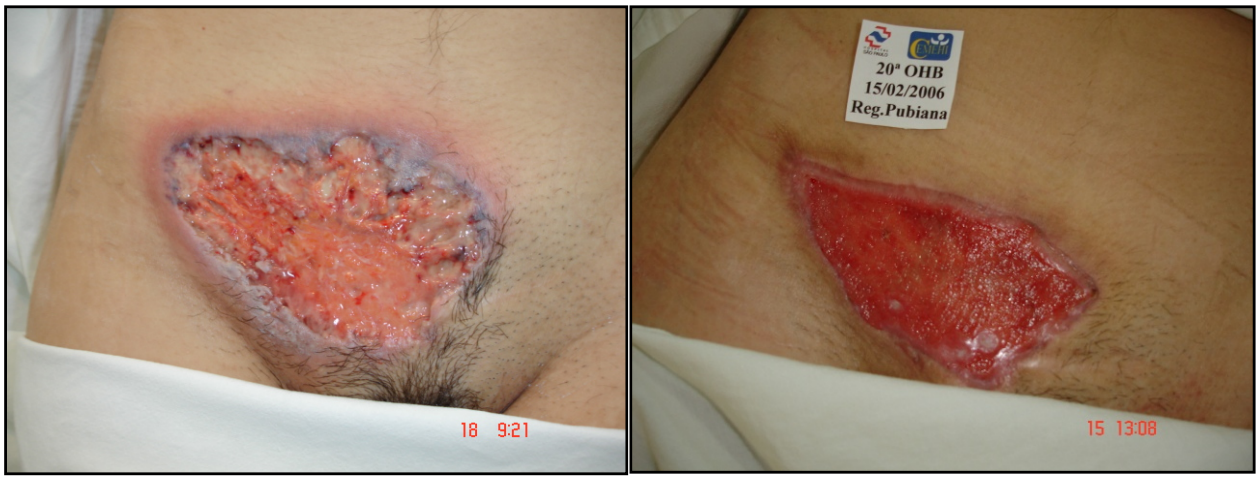

FIGURE 3 - RBR, 41 years – pyoderma gangrenosum. Before and after 20 sessions of HBO.

Discussion

Even with all pharmacological advances in the treatment of CD, many patients still present a relapsing course. Some cases are impressively aggressive and mutilating. This situation usually requires surgical intervention and other measures to improve wound healing[20].

Utilization of HBO in patients with CD has increased in recent years. HBO promotes increments in plasmatic partial pressures of O_2, thus enhancing tissue levels of oxygenation. Tissue hyperoxia increases the healing processes as it leads to vasoconstriction and decreased edema and also stimulates angiogenesis and proliferation of fibroblasts and collagen. There are also some reports of increased bacteriostatic and bactericidal effects[17-23].

HBO acts directly in the inflammatory cascade and the effect of such therapy can be explained by reduced activity of nitric oxide synthase and inhibition of inflammatory cytokines. It is effective in suppressing the activity of COX-2 and the stimuli for the THF-alpha production. Vascular endothelial growth factor (VGEF) is significantly increased with HBO[25].

Conclusions

The understanding of the pathophysiology of CD has increased in recent years as our genetic and molecular knowledge progresses, resulting in more effective therapies. Nevertheless, the response is not uniform among patients and progression to complications such as extensive perineal disease may be inevitable. HBO was initially indicated only for complex perineal disease. Our report, as many other in the literature, expands the traditional HBO applications and shows its efficacy in controlling both systemic and local inflammatory activity. The benefits become evident as the healing process advances.

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