



International Journal of Alternative and Complementary Medicine

Review Article

HYPERBARIC OXYGEN THERAPY AS A COMPLEMENTARY OR ALTERNATIVE THERAPY FOR CHRONIC ORAL AND GASTROINTESTINAL DISORDERS: A NARRATIVE REVIEW

Ali Mohamed Ali Ismail

Lecturer, Department of Physical Therapy for Cardiovascular/ Respiratory Disorder and Geriatrics, Faculty of Physical Therapy, Cairo University, Giza, Egypt

Abstract

Failure of traditional conservative pharmacological agents in the treatment of chronic oral and gastrointestinal tract disorders (GITD) increased the use of complementary and alternative therapies (CAT) to make use of the strong anti-fibrotic and anti-inflammatory effects of CAT. The purpose of this review is to focus on the role of hyperbaric oxygen therapy (HBOT) in the treatment of chronic oral and GIITD. Being one of CAT, HBOT can be utilized as a main and/or an adjunctive therapeutic modality in the treatment of GITD. In addition to anti-fibrotic and anti-inflammatory effects induced by CAT, HBOT adds more great benefits as neovascularization increase, bacterial growth inhibition, promotion of intestinal mucosal healing, enhancement of delayed gastric emptying in dyspeptic patients, increase of the intestinal motility, and hypoxia improvement by supplying more oxygen especially for fibrosed and/or radiation-induced tissue injuries. Awareness of HBOT – as a complementary treatment for chronic oral and GITDS – is highly needed to develop more future research in this field.

Keywords: Hyperbaric oxygen therapy, complementary and alternative therapy, oral cavity, gastrointestinal diseases.



Article Info

Received: 04-09-2020

Revised: 17-11-2020

Accepted: 25-11-2020

*Corresponding Author

Ali Mohamed Ali Ismail,

PhD, Department of Physical Therapy for Cardiovascular/Respiratory Disorder and geriatric, Faculty of Physical Therapy, Cairo University, Giza, Egypt.

Tel: 20-01005154209.

E-mail: ali.mohamed@pt.cu.edu.eg

INTRODUCTION

The utilization of complementary and alternative therapies (CAT) as a form of health care is increased with a high continuous form. Frequently, traditional physicians are not aware of CAT especially with increased rated potential interactions between the CAT and the traditional medical therapy forms [1]. Hyperbaric oxygen therapy (HBOT) as one of CAT [2] can be utilized in the treatment of chronic gastrointestinal tract diseases (GITD) [3] especially with the evidence-based strong antifibrotic and/or anti-inflammatory effects of CAT in chronic GITD treatment [1].

HBOT is the administration of intermittent or continuous oxygen (O₂) at supra-atmospheric pressures usually > 1.4 atmospheric pressure [4]. With the concurrent consideration of large HBOT indications that concern different specialties [5], enhancing the basic HBOT knowledge has a great impact on the individual interests, clinical experience, future work, scientific researches, clinical practice [6], and better inter-professional cooperation between health care professions and medicine. All of these benefits lead to better patient care [7].

This narrative review aims to enhance the basic knowledge of hyperbaric oxygen and its role – as a complementary or an alternative therapy - in chronic disorders of the oral and gastrointestinal tract (GIT).

HBOT Overview

HBOT includes short-term, near 100 % inhaled and diffused oxygen (O₂) reached systemically via airways and blood, achieved by allowing the patient to breathe high concentrated O₂ with pressure more than one absolute atmosphere (ATA) [8].

According to the patient's status, HBOT introduced to the patients through hoods, masks, and chambers. In chambers, patients are allowed to sit or lie in mono-placed (takes one patient only) or multi-placed (take 5-25 patients) controlled O₂ leveled chambers. HBOT chambers are well equipped to accommodate hospital beds and medical assistants, allow ongoing therapies, involving intravenous (IV) fluids and/or IV medications, and the physiologic monitoring through specifically engineered port pathways for wires and tubing [10].

One or two HBOT sessions are needed in the acute conditions and may extend to over 30 sessions in chronic ones with individualized session time varied from 45 minutes to five hours but the maximal safe

duration for a session is 120 minutes. To avoid a boringly long time during the sessions, a television is provided to the patients inside the HBOT chambers [9].

Because many acute or chronic severe medical conditions do not respond to traditional or conventional therapies, HBOT is indicated as an adjunctive or in sometimes the main therapy in traumatic, inflammatory, infectious, ischemic natured conditions [11] with increased evidence of HBOT-associated clinical and cost-effective utility [12]. HBOT mechanism of action is based on increasing the O₂ supply to the destructed tissues – especially ones induced by radiotherapy - to enhance the blood supply, wound healing, fibrosis, inflammation, generation of new vascular beds (angiogenesis) [13].

Approved HBOT indications are air or gas embolism, gas gangrene, poisoning of carbon monoxide (CO), acute traumatic ischemia, compartment syndrome, severe anemia, arterial occlusion or insufficiency, wound healing and compromised flaps and grafts, refractory osteomyelitis, necrotizing soft-tissue infections, acute thermal burn injury, intracranial abscess, bony and soft tissue-induced radiation injury, idiopathic sudden sensorineural hearing loss, and diving decompression sickness [14].

HBOT is contraindicated in pneumothorax and pulmonary bullae as in chronic obstructive pulmonary disease (COPD) [10] and may relatively be contraindicated in pregnancy, previous ear and thoracic surgeries, and claustrophobia (phobia of tightly closed space) [15]. Common side effects are reported during the use of HBOT as potential O₂ toxicity and middle-ear barotrauma. Reported less common side effects tend to cease after the end of the session as convulsions, seizures, hypoglycemia [10], progressive myopia (pupil nearsightedness which is a very rare side effect), and pulmonary dyspnea [16].

1- HBOT FOR DISORDERS OF THE ORAL CAVITY

Oral submucous fibrosis

Oral submucous fibrosis (OSMF) is a chronic progressive disease characterized by local scarring, fibrosis, and precancerous lesions of any part of the oral cavity [17] starting with stomatitis with vesicle formation [15] then progress to the inflammation of the lamina propria and degeneration of the underlying muscles [17]. The associated fibrosis, ischemia, hypoxia, ulceration, and thereby increased expression of hypoxia-induced factor-one-alpha

(HIF-1 α) increase the transformation chance to malignancy [18]. Patients complain from taste disorders, limited mobility of the tongue, dry and burning mouth sensation, pain, altered tone, dysphagia, inability to eat [17], and restricted mouth opening [19].

There is no specific or single treatment for relieving signs and symptoms of OSMF [20] but the interaction is needed between the drugs, intraoral appliances, pre and post-operative physical therapy, and osteopathy [21]. Physical therapy for OSMF attempts to affect tissue remodeling through movement, routine exercises, various splints or other tools to enhance the opening of the mouth, focused heat like microwave diathermy [19] and ultrasound, and soft tissue mobilization [20].

Recently, the Novel treatment of HBOT for OSMF improves cellular regulatory effect, induces lymphocyte apoptosis or/and diminishes lymphocytic proliferation [15], limits the fibroblastic activity and increases its apoptosis, declines the production of inflammatory cytokines and reactive oxygen species, enriches the tissue with O₂, enhances the angiogenesis and antioxidant capacity [17], re-oxygenates the hypoxic OSMF microenvironment, prevent the OSF malignant transformation, and increases mouth opening by preventing the progressive fibrosis [22].

Salivary gland dysfunction

The patients who undergo regular head and neck radiation therapy may experience serious damage to salivary glands [23]. Salivary gland dysfunction results in xerostomia (dry mouth sensation) and/or hyposalivation (objective low saliva flow) [24]. Such changes lead to difficulties in speech, taste, deglutination, mastication, swallowing, oral discomfort with soreness and burning, dental discomfort and caries may progress to osteoradionecrosis, and increased probability of oral cavity infection and bad breath (halitosis) [25] due to disruption to the normal species of the oral flora [26].

The HBOT can be an effective alternative treatment modality for late-term complications (including hyposalivation) acquired after the application of radiotherapy following cancer resection [27].

Approximately 97 % of O₂ is normally transported bound to hemoglobin (Hb), and only a small portion of it is transported in solute. The idea of using HBOT is its ability to increase the O₂ from 3 ml/L at normal ATA up to 60 ml/L at 3 ATA of pure oxygen carried

in solute. Since O₂ is in solution, it enters obstructed areas that not reached by red blood cells (RBCs) and can even facilitate oxygenation of tissues with impaired Hb oxygen carriage. HBOT can thus be useful in restoring natural homeostasis in hypoxic tissues by inducing angiogenesis, increasing O₂ tension [28], collagen synthesis, and stem cell recruitment [23].

Restoration of vascular supply to salivary gland dysfunction induced by radiotherapy enables tissue regeneration, restoration of normal saliva flow [23], and thereby improves the quality of life of patients by controlling the complications induced by hyposalivation that mentioned above [29].

Periodontal disease

Many risk factors - including, for example, diabetes mellitus (DM), smoking, and low salivary flow - lead to inflammation of gingival and periodontal tissue. This inflammation is induced by the bacteria within dental plaque with further progression to a gradual missing of attachment apparatus fixing the teeth with a negative impact on the oral functions [30]. The treatment includes antibiotics, antiseptics, and other various approaches which are allowed for a short period [31] especially if there is a recurrence in many patients as in diabetics with low associated-immunity, impaired tissue healing and continuous bleeding [32].

HBOT has a hopeful effect on chronic periodontal and gingival inflammation due to HBOT decreases 99% of the gram-negative anaerobic bacteria, periodontal microorganisms, and gingival hemorrhage. Also, it increases the healing of periodontal tissue and O₂ pressure in gingival pockets [31].

In recent experimental research on diabetic rats with periodontitis showed that the combined consumption of sea cucumber gel (3% concentration) and HBOT (at 2.4 ATA for 3x30 minutes with five-minute rest intervals for seven days) decreased the expression of inflammatory cytokines as interleukin-1 β (IL-1 β), interleukin-10 (IL-10), and reactive oxygen expression. HBOT not only increased the secretions of anti-inflammatory, anti-tumor immunity, and antioxidant factors but also improved secretion of ligands as the 70 kilodalton heat shock proteins (Hsp70s) that fix or repair the insulin receptors that experience high free radical oxidative damage [33].

In smokers or diabetics with delayed wound healing around surgically fixed dental implants, HBOT

relieved the associated pain, swelling, and inflammation. Also, HBOT enhanced wound healing by the increased formation of new collagen fibers, capillaries, and epithelial tissue [34].

2- HBOT FOR GIT DISORDERS

Functional dyspepsia

Functional dyspepsia (FD) is a chronic and recurrent symptomatic gastrointestinal manifestations without underlying organic disease. The symptoms of FD include early satiation, epigastric pain and burning, and bothersome postprandial fullness. The pathophysiology of FD may be explained as impaired gastric accommodation to a meal, delay of gastric emptying, and visceral hypersensitivity [35].

The combined course of Gengjian decoction with an HBOT course for 28 days can increase gastric motility, enhance the clinical symptoms of FD, and has a definite hopeful effect on female perimenopausal FD [36].

HBOT may increase the compression of intestinal gas, declines the colonic dilatation, improves the mucosal circulation, and thereby improves the intestinal movement due to the increased absorption of the intestinal gas. The improved gut motility may be enhanced because HBOT improves both the peristaltic movement and severe constipation, resulting in the absence of bloating and appetite recovery. Improved intestinal movement by HBOT may remove the delayed whole-gut transit and bloat, promote gastric emptying, and induce the hunger feeling [37].

Inflammatory bowel disease

Inflammatory bowel disease (IBD) is two primary forms: Crohn's disease (CD) and ulcerative colitis (UC). While CD affects the mucosal and superficial submucosal layers of the rectum and the large intestine, UC affects any part of the GIT [38]. IBD is a chronic inflammation of GIT with relapses and remissions of symptomatic abdominal painful cramps, rectal bleeding, diarrhea, malnutrition, and weight loss [39]. Recent literature indicates that IBD's pathophysiology includes immune dysregulation, genetic vulnerability, dysfunction of the intestinal barrier, and microbial flora alterations [40]. Although there is no pharmacological treatment for IBD, the used drugs are efficient to relieve the symptoms and delay relapses but with many undesired side effects forcing many patients to seek to adjunctive therapies [38].

HBOT is a treatment choice for IBD patients which is fairly safe and potentially successful. Breathing under pressure 100 % O₂ raises plasma and tissue oxygen levels, thereby improve hypoxia, and improves blood O₂ content to enter the inflamed intestines or chronic nonhealing fistulas. HBOT modifies the signaling pathways involved in tissue response to hypoxia and wound repair, especially the pathways of hypoxia-inducible factor (HIF) and heme oxygenase (HO). More specifically, HBOT inhibits the development of pro-inflammatory cytokines and chemokines IL-1, IL-6, and tumor necrosis factor- α (TNF- α) which are responsible for the metabolic stress induced by active inflammation. These pathways and inflammatory cytokines contribute significantly to the local microenvironmental markers responsible for IBD development, and there is considerable interest in targeting these pathways for IBD therapy [41].

One of HBOT's suggested mechanisms of action is to facilitate intestinal mucosal healing in cases of UC by increasing the numbers of stem cells in the colonic mucosa. To help in the repair process, HBOT enhances the differentiation of colonic stem cells, resident in colonic mucosal crypts, and the movement of bone marrow stem cells to the colonic mucosa. Also, HBOT is reported to stimulate UC healing by increased fibroblast proliferation [42].

Chronic idiopathic intestinal pseudo-obstruction

Chronic idiopathic intestinal pseudo-obstruction (CIPO) is defined as a severe failure of the intestinal tract to propel its contents. Despite a clinical picture mimics the mechanical obstruction affecting pediatrics (15%) and adults (20%), there is no organic occluding lesion to the gut. Intestinal failure increases the disability of individuals to control their normal oral nutrition and body weight [43] with recurrent exacerbations of abdominal distension and/or bloating, nausea and/or vomiting, and abdominal pain [44]. Pathophysiology is unknown but the defective propulsion as a result of GIT innervation and/or smooth muscle atrophy evokes the symptoms [45]. Bacterial overgrowth of the small intestine may lead to diarrhea and steatorrhea [44]. CIIP treatment involves nutritional, pharmacological, and surgical unsatisfactory approaches and the long-term result is generally poor [43].

By inhibiting the bacterial overgrowth, HBOT can treat the symptoms and the complications of CIIP.

Bacterial overgrowth has been suggested to exacerbate episodes of CIIP by a vicious circle starting with intestinal stasis, overgrowth of Gramnegative aerobic and anaerobic bacteria, increased intestinal secretion and dilated intestine stimulates local hypoxia which ends again with bacterial overgrowth. The strong inhibitory effect of HBO on bacterial overgrowth may be explained by increased phagocytosis through restored free radicals of neutrophils to kill the common bacteria, positive direct effect on several bacterial strains and bacterial flora, accelerated dissolution of the abnormally accumulated gas by replacing it with O₂ that enhanced the alleviation of obstructive symptoms. Also, HBO has a possible positive effect on edema and necrosis removal from the intestinal tissue by improving the local hypoxia [45].

Pneumatosis intestinalis

Pneumatosis intestinalis (PI) is the radiological presence of gas in the bowel wall. PI may be asymptomatic or a life-threatening condition. Severe PI may show loss of appetite, diarrhea, obstruction, flatulence, and abdominal pain [46]. It can be related to iatrogenic causes or a wide range of diseases ranging from intestinal ischemia to accidental findings in an otherwise healthy patient [47].

Antibiotics, bowel rest, surgery, and HBOT are treatment options. HBOT can be highly effective and safe in symptomatic PI if there is no need for urgent surgery. HBOT raises the arterial O₂ tension, which pushes O₂ into the hydrogen-containing cysts by spreading O₂ from areas of high tension in the artery to low tension in the hydrogen-containing cyst. In turn, accumulated O₂ in the cysts raises the partial pressure of hydrogen in the cysts, which enforces hydrogen to diffuse from the high-pressure cyst to the low-hydrogen bloodstream. Cyst resolution follows as O₂ leaves the cyst through reabsorption to be utilized in cellular metabolism. Consequently, increased HBOT-induced tissue oxygenation may encourage phagocytic activity and directly target the gas-producing organisms through anaerobic impairment [48].

Radiation-induced chronic GIT inflammation

Radiation therapy is a vital treatment modality in various abdominal and pelvic malignancies. Chronic side effects are reported due to radiation induced-injury of the mucosal lining of the large and small

bowel with sophisticated pathophysiological processes range from inflammation to oxidative damage. According to the lesion site, patients may suffer from nausea, vomiting, abdominal cramping pain, rectal bleeding, and watery diarrhea [49]. HBOT counteracts this otherwise hard-to-treat complication of radiation therapy.

HBOT is a useful alternative treatment modality for a delayed wound healing induced by the completion of serial surgical dilations to the esophageal lumen to treat a chronic radiation-induced esophagitis complicated as fibrosed stricture after palliative thoracic radiation. Fifty HBO treatments increased the tolerance to the regular diet without any swallowing difficulties or odynophagia. Enhanced tissue healing under HBOT conditions may be due to the raised tissue perfusion with O₂, altered inflammatory pathways via inhibition of cytokines, the promotional release of growth factor, and angiogenesis. In addition to the previous mechanism, HBOT stimulates re-epithelialization and collagen formation, preserves the marginal perfused tissue, and inhibits toxin production and bacterial growth in chronic induced-radiation proctitis (rectal mucositis) and enteritis [50].

CONCLUSION

Hyperbaric oxygen - as a strong complementary therapy - can treat disorders of the oral cavity and GIT which not respond to pharmaceutical drugs via many physiological responses. It can improve oral function and stop the malignant transformation of OSMF by HBOT-induced anti-hypoxic effects. In radiotherapy-induced dysfunction of salivary glands, HBOT can inhibit mouth dryness and restore the normal salivation due to restoration of the vascular supply. With its strong anti-inflammatory and healing properties, HBOT can treat chronic periodontitis, IBD, and radiation-induced GIT inflammations. In FD, HBOT can improve the delayed gastric emptying and gastric pain. Due to the suggested bactericidal effect, HBOT can improve the intestinal gases, gastric motility, appetite in CIIP. More future researches are needed on the role of HBOT - as one of the complementary therapies - in the treatment of chronic disorders of the oral cavity and GITD.

ACKNOWLEDGMENT

None.

CONFLICT OF INTEREST

The author declares that there is not conflict of interest.

REFERENCES

1. Haas L, McClain C, Varilek G. Complementary and alternative medicine and gastrointestinal diseases. *Curr Opin Gastroenterol* 2000;16:188-196.
2. Liptak GS. Complementary and alternative therapies for cerebral palsy. *Ment Retard Dev Disabil Res Rev* 2005;11:156-163.
3. Chiarioni G, Pesce M, Fantin A, Sarnelli G. Complementary and alternative treatment in functional dyspepsia. *United European Gastroenterol J* 2018;6:5-12.
4. Ahmad FM, Sankhla CS. Hyperbaric oxygen therapy in neurological diseases. *Neurol India* 2019; 67:655.
5. El Oumri AA, Badi H, Khaloufi S. Hyperbaric oxygen therapy: Focus. *Open J Emerg Med* 2018;6:15-20.
6. Henrykowska G, Buczyński A, Lewicka M, Zawadzka M. The Knowledge of a selected group of medical students on hyperbaric oxygen therapy. *Pol Hyperb Res* 2018;62:75-83.
7. Sytsma TT, Haller EP, Youdas JW, Krause DA, Hellyer NJ, Pawlina W, et al. Long-term effect of a short interprofessional education interaction between medical and physical therapy students. *Anat Sci Edu* 2015;8:317-323.
8. Löndahl M, Boulton AJ. Hyperbaric oxygen therapy: Useless or useful? A battle. *Diabetes Metab Res Rev* 2020;e3233.
9. Jeter JP, Wong EB. Hyperbaric oxygen therapy in dermatology. *Cutis* 2020;105:24-27.
10. Kirby JP, Snyder J, Schuerer DJ, Peters JS, Bochicchio GV. Essentials of hyperbaric oxygen therapy: 2019 review. *Missouri Med* 2019;116:176.
11. Wandawa G, Mustaqimah DN, Sidik S, Saraswati H, Putri FA, Auerkari EI. Efficacy of hyperbaric oxygen therapy as an adjunctive therapy of chronic periodontitis. *J Int Dent Med Res* 2017;10:72.
12. Mcmillan G, Glover M. The clinical and economic potential of hyperbaric oxygen therapy in the treatment of diabetic ulceration and other conditions. *Int J Low Extrem Wounds* 2007;6:130-138.
13. Koo JH, Song SH, Oh HS, Oh SH. Comparison of the short-term effects of hyperbaric oxygen therapy and complex decongestive therapy on breast cancer-related lymphedema: A pilot study. *Med J* 2020;99:e19564.
14. Hexdall E, Brave R, Kraft K, Siewers J. Diving deep into hyperbaric oxygen therapy. *Nurs J* 2019;46:28-36.
15. Kumar MA, Radhika B, Gollamudi N, Reddy SP, Yaga US. Hyperbaric oxygen therapy—a novel treatment modality in oral submucous fibrosis: a review. *J Clin Diagn Res* 2015;9.
16. Eve DJ, Steele MR, Sanberg PR, Borlongan CV. Hyperbaric oxygen therapy as a potential treatment for post-traumatic stress disorder associated with traumatic brain injury. *Neuropsychiatr Dis Treat* 2016;12:2689.
17. Shih YH, Wang TH, Shieh TM, Tseng YH. Oral submucous fibrosis: a review on etiopathogenesis, diagnosis, and therapy. *Int J Mol Sci* 2019;20:2940.
18. Tilakaratne WM, Iqbal Z, Teh MT, Ariyawardana A, Pitiyage G, Cruchley A, et al. Upregulation of HIF-1 α in malignant transformation of oral submucous fibrosis. *J Oral Path Med* 2008;37:372-377.
19. Arakeri G, Rai KK, Boraks G, Patil SG, ALjabab AS, Merckx MAW et al. Current protocols in the management of oral submucous fibrosis: an update. *J Oral Path Med* 2017;46:418-423.
20. Tyagi H, Lakhanpal M, Dhillon M, Baduni A, Goel A, Banga A. Efficacy of therapeutic ultrasound with soft tissue mobilization in patients of oral submucous fibrosis. *JIAOMR* 2018;30:349.
21. ARORA A. Treatment modalities in oral submucous fibrosis: a review. *J Adv Med Dent Sci Res* 2019;7:11-15.
22. Sharma M, Radhakrishnan R. Limited mouth opening in oral submucous fibrosis: reasons, ramifications, and remedies. *J Oral Path Med* 2017;46:424-430.
23. Hadley T, Song C, Wells L, Lehnhardt J, Rogers MW, Anderson J, et al. Does hyperbaric oxygen therapy have the potential to improve salivary gland function

- in irradiated head and neck cancer patients?. *Med Gas Res* 2013;3:15.
24. Ismail AMA, EZZ EL-din HM, Abdelaal MEM. Impact of transcutaneous electrical nerve stimulation (TENS) on hyposalivation in type 2 diabetics. *Biosci Res* 2019;16: 690-694.
 25. Lovelace TL, Fox NF, Sood AJ, Nguyen SA, Day TA. Management of radiotherapy-induced salivary hypofunction and consequent xerostomia in patients with oral or head and neck cancer: meta-analysis and literature review. *Oral Surg Oral Med Oral Path Oral Radiol* 2014;117:595-607.
 26. Meng L, Liu J, Peng B, Fan M, Nie M, Chen Z, et al. The persistence of *Streptococcus mutans* in nasopharyngeal carcinoma patients after radiotherapy. *Caries Res* 2005;39:484-9.
 27. Uslu GH, Çebi G, Çobanoğlu B. Hyperbaric oxygen therapy in the treatment of complications of irradiation in laryngeal cancer. *Contemp Oncol* 2018;22:202.
 28. Sønstevold T, Johannessen AC, Reed RK, Salvesen GS, Stuhr L. Hyperbaric oxygen treatment did not significantly affect radiation injury in the mandibular area of rats. *Oral Surg Oral Med Oral Path Oral Radiol* 2018;125:112-119.
 29. Gerlach NL, Barkhuysen R, Kaanders JHAM, Janssens GORJ, Sterk W, Merckx MAW. The effect of hyperbaric oxygen therapy on quality of life in oral and oropharyngeal cancer patients treated with radiotherapy. *Int J Oral Max Surg* 2008;37:255-259.
 30. Al Habashneh R, Mashal MA, Khader Y, Qudah R. Clinical and biological effects of adjunctive photodynamic therapy in refractory periodontitis. *Lasers Med Sci* 2019;10:139.
 31. Robo I, Heta S, Karkanaqe L, Ostreni V. HBOT application at cases of gingival inflammation. *J Dent Oral Sci* 2019;1:1-16.
 32. Badr DE, Alenazi MH, Alowein MA, Alodhay MM, Alahaideb MM, Alamri AA, et al. Association between diabetes and periodontal disease: a literature review. *EC Dent Sci* 2019;18:2467-2474.
 33. Mulawarmanti D, Parisihni K. The Effect of sticopus hermanii-hyperbaric oxygen therapy to inflammatory response of diabetic periodontitis. *IOP Conf Ser Earth Environ Sci* 2019;217:012060.
 34. Liao J, Wu MJ, Mu YD, Li P, Go J. Impact of hyperbaric oxygen on tissue healing around dental implants in beagles. *Med Sci Mon Int Med J Exp Clin Res* 2018;24:8150.
 35. Oh JH, Kwon JG, Jung HK, Tae CH, Song KH, Kang SJ, et al., Clinical practice guidelines for functional dyspepsia in Korea. *J Neurogastroenterol Motil* 2020;26:29.
 36. Dong Y, Xing L, Zhu A. Observation of Gengjian decoction combined with hyperbaric oxygen therapy on functional dyspepsia during perimenopausal period. *Hebei J Trad Chin Med* 2012;1:46.
 37. Masuda A, Nakano T, Uehara H, Kuroki K, Tei C. Hyperbaric oxygen for anorexia nervosa. *Int Med* 2001;40:635-637.
 38. Eckert KG, Abbasi-Neureither I, Köppel M, Huber G. Structured physical activity interventions as a complementary therapy for patients with inflammatory bowel disease—a scoping review and practical implications. *BMC Gastroenterol* 2019;19:115.
 39. Duff W, Haskey N, Potter G, Alcorn J, Hunter P, Fowler S. Non-pharmacological therapies for inflammatory bowel disease: Recommendations for self-care and physician guidance. *World J Gastroenterol* 2018;24:3055.
 40. Rossignol DA. Hyperbaric oxygen treatment for inflammatory bowel disease: a systematic review and analysis. *Med Gas Res* 2012;2:6.
 41. Dulai PS, Gleeson MW, Taylor D, Holubar SD, Buckley JC, Siegel CA. Systematic review: The safety and efficacy of hyperbaric oxygen therapy for inflammatory bowel disease. *Aliment Pharm Ther* 2014;39:1266-1275.
 42. Bekheit M, Baddour N, Katri K, Taher Y, El Tobgy K, Mousa E. Hyperbaric oxygen therapy stimulates colonic stem cells and induces mucosal healing in patients with refractory ulcerative colitis: a prospective case series, *BMJ Open Gastroenterol* 2016;3:e000082.
 43. Antonucci A, Fronzoni L, Cogliandro L, Cogliandro RF, Caputo C, De Giorgio R, et al. Chronic intestinal pseudo-obstruction. *World J Gastroenterol* 2008;14:2953.

44. De Giorgio R, Sarnelli G, Corinaldesi R, Stanghellini V. Advances in our understanding of the pathology of chronic intestinal pseudo-obstruction. *Gut* 2004;53:1549-1552.
45. Yokota T, Suda T, Tsukioka S, Takahashi T, Honma T, Seki K, et al. The striking effect of hyperbaric oxygenation therapy in the management of chronic idiopathic intestinal pseudo-obstruction. *Am J Gastroenterol* 2000;95:285-288.
46. Di Pietropaolo M, Trinci M, Giangregorio C, Galluzzo M, Miele V. Pneumatosis cystoides intestinalis: case report and review of literature. *Clin J Gastroenterol* 2020;13:31-36.
47. Umaphathi BA, Friel CM, Stukenborg GJ, Hedrick TL. Estimating the risk of bowel ischemia requiring surgery in patients with tomographic evidence of pneumatosis intestinalis. *Am J Surg* 2016;212:762-768.
48. Feuerstein JD, White N, Berzin TM. Pneumatosis intestinalis with a focus on hyperbaric oxygen therapy. *Mayo Clin Proc* 2014;89:697-703.
49. Singh G, Sharma D, Rathi A, Singh K. Curcumin for radiation induced enteritis: A review article. *Int J Med Paediatr Oncol* 2017;3:1-2.
50. Yuan JH, Song LM, Liu Y, Li MW, Lin Q, Wang R, et al. The Effects of hyperbaric oxygen therapy on pelvic radiation induced gastrointestinal complications (rectal bleeding, diarrhea, and pain): a meta-analysis. *Front Oncol* 2020;10:390.