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HBOT's effect on Cancer Patients after Radiation Therapy

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Abstract
It is widely accepted that radiotherapy that is often used for patients with cancer causes many side-effects in patients. In many cases, these adverse outcomes are closely connected to such patients' particular problems – the location targeted for treatment, other complications, age, and other factors. Therefore, the treatment of these side effects comes as the next step in a patient's healing process (Daruwalla & Christophi, 2006). One of the researched and utilized ways of managing the consequences of radiation is hyperbaric oxygen therapy (HBOT). According to Moen and Stuhr (2012), HBOT's primary purpose is to deal with hypoxia, the condition in which tissues are deprived of oxygen supply. This statement suggests that the oxygen-supplying therapy can help patients with a variety of radiation-induced problems. This review investigates the findings regarding the effectiveness of HBOT on patients who underwent radiotherapy for cancer treatment. The examination covers 12 different studies and focuses on positive and negative outcomes and the potential influence of HBOT on other therapies.

Literature Review

First of all, one should remark that the exploration of the HBOT's effects on cancer patients is not a recent addition to cancer-related research. In fact, some of the articles mentioned below review the information collected as early as in the 1980s. Thus, it is possible to assume that many researchers have assessed the various impacts that HBOT can have on different complications. Nevertheless, some areas of research attract more than others, which is discussed further.

The first general topic that is reviewed in medical literature is the overall effect that HBOT has on patients undergoing on finishing radiotherapy. According to Stępień, Ostrowski, and Matyja (2016), HBOT can have two significant roles in being coupled with radiotherapy treatments. First of all, HBOT may enhance the impact of radiotherapy on cancer cells, acting as a radiosensitizer and leading to patients having a more productive experience than they would have otherwise (Stępień et al., 2016). The second potential purpose of HBOT is to reduce the negative outcomes of radiotherapy, by "[improving] local tumor control" and "[reducing] delayed radiation injury" (Stępień et al., 2016, p. 101). The authors pay attention to the first potential use of HBOT as a radiosensitizer, stating that its research is not as comprehensive as that of HBOT's survival improvement. They also provide

findings which suggest that HBOT is more effective in preventing outcomes of radiotherapy rather than its positive impact (Stępień et al., 2016). Moen and Stuhr (2012) recommend HBOT to follow radiotherapy for patients to reduce the persistence of complications. Thus, one may concentrate on exploring this purpose of HBOT.

A significant part of all gathered studies examines the influence of HBOT on complications related to the anorectal and pelvic regions. Pelvic radiation therapy may result in a broad variety of side effects, including radiation proctitis with such symptoms as diarrhea, rectal bleeding, and rectal pain (Jones, Evans, Bristow, & Levin, 2006). It can also fail to suppress the recurrence of anal carcinomas which may reappear or stay on a patient's body after treatment (Bem, Bem, & Singh, 2000). Radiation-induced toxicity is another harmful consequence of such therapy since some patients may develop vaginal ulcers, fistulas, cystitis, and other skin injuries in the treated regions (Safra et al., 2008). Overall, many studies show that HBOT is considered as an approach to combating the increased morbidity of radiation for cancers in the pelvic region.

The majority of the mentioned above researchers find that HBOT is highly effective in reducing or eliminating the issues that arise after radiation therapy. Mayer et al., (2001) conclude that genitourinary and gastrointestinal problems can be resolved with HBOT. Their study examines the outcomes of sixteen patients with prostate cancer and reveals that bleeding stopped completely in all five patients with proctitis and in "six out of eight patients with cystitis" (Mayer et al., 2001, p. 151). Therefore, the majority of participants had a positive experience with HBOT. Oscarsson, Arnell, Lodding, Ricksten, and Seeman-Lodding (2013) conduct a prospective cohort study on the treatment of cystitis and proctitis induced by radiotherapy and find that HBOT helped more than 75% of all participants. The therapy is found to be useful in individual cases of cystitis or proctitis as well as their combination (Oscarsson et al., 2013). Interestingly, the scholars note that the improvements were sustained during the later follow-ups, and patients did not encounter any major side effects of HBOT.

HBOT can treat many of the mentioned above complications caused by radiation proctitis. Jones et al. (2006) use the LENT-SOMA scale to determine not only whether the symptoms disappear in some patients but also if they become less or more harsh in others. As can be seen in Table 1, many participants experienced positive effects of HBOT. Out of nine patients with rectal bleeding, four individuals had a complete resolution of rectal bleeding. Rectal pain decreased or ceased to exist in three out of five participants. Finally, diarrhea improved in three patients and disappeared in one patient out of five. Overall, only two persons did not have any changes in their health after treatment. One patient's bleeding worsened, but it is unclear whether it was an effect of their other therapies (Jones et al., 2006). To sum up, the therapy is regarded as highly effective based on the conclusions of this study.

Table 1 Treatment Outcomes Following Hyperbaric Therapy

Symptoms/functions	No. of patients (*n*)	Complete resolution (*n*)	Lent/Soma down grading (*n*)	No response (*n*)	Progression (*n*)
Bleeding	9	4	3	1	1
Pain/discomfort	5	3	1	1	
Diarrhea	5	1	3	1	

(Jones et al., 2006, p, 93).

Radiation-induced toxicity raises other issues apart from proctitis in both men and women. Safra et al. (2008) collect information about the effect of HBOT on female problems, namely vaginal fistulas, ulcers, skin injuries, as well as combined cystitis and proctitis. Similar to other discussed

studies, the scholars find that the patients Common Toxicity Criteria (CTC) scores improved substantially after treatment. Bleeding and dysuria stopped in the majority of patients, while hematuria and scar complications resolved in all patients with these problems (Safra et al., 2008). Furthermore, none of the patients reported any side effects of the therapy. Thus, while CTC scores before HBOT ranged from 2 to 4, after undergoing treatments, all patients had scores from 0 to 2 – a major improvement for all involved persons.

Delayed and nonhealing injuries constitute another complication of radiation therapy. Bem et al. (2000) demonstrate the positive effects of HBOT on patients with complications in the anorectal region. They focus on wounds that could not be healed with other conventional methods and find that HBOT helped both examined patients with their refractory wounds. Fink, Chetty, Lehm, Marsden, and Hacker (2006) discover that difficult to treat delayed injuries can be treated with HBOT. Out of 14 patients who underwent radiotherapy for gynecological cancers, ten had an improvement in symptoms (Fink et al., 2006). Again, HBOT is recommended in both studies as a way to deal with rare and seemingly untreatable conditions.

However, HBOT is not limited to the treatment of radiology outcomes in the pelvic region. Daruwalla and Christophi (2006) come to a conclusion that HBOT does not increase malignancy growth, but possibly has general cancer-inhibitory effects aside from other positive influences. Wilkinson and Doolette (2004) explore the implementation of HBOT for patients with necrotizing soft tissue infection (NSTI) and find that it increases survival rates and lowers the danger of limb loss. Teguh et al. (2009) analyze the impact that HBOT can have on patients who underwent radiotherapy for nasopharyngeal and oropharyngeal cancer. They conclude that HBOT brought positive results, reducing the patients' pain and dryness in the mouth, and improving their swallowing, saliva stickiness, and the overall quality of life (Teguh et al., 2009). For example, the impact of HBOT on patients' pain in the mouth in comparison to that of patients not treated with HBOT can be seen in Figure 1.

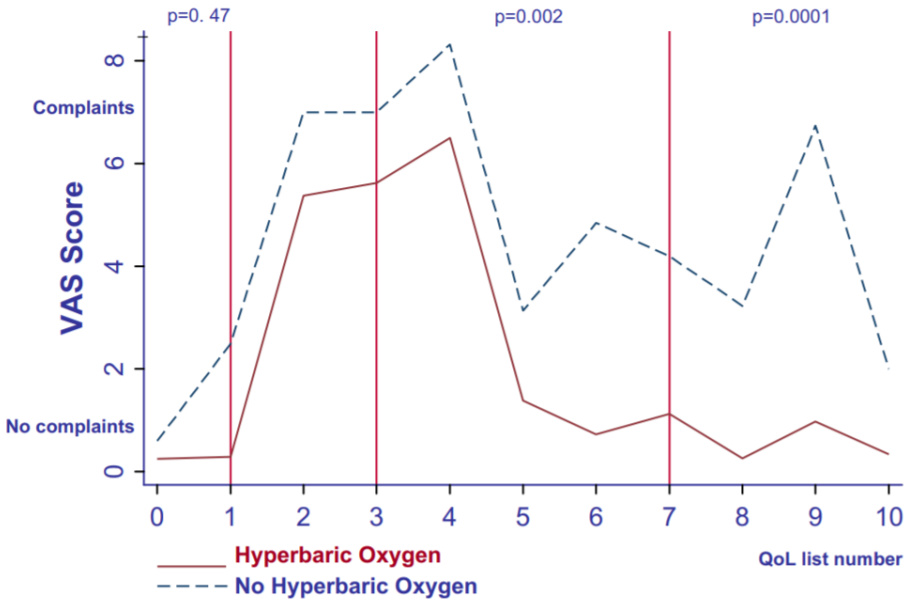

Figure 1 A visual analog scale of the pain in mouth question (Teguh et al., 2009, p. 715).

Some studies do not come to the conclusions supported by the major portion of available research. Returning to the topic of pelvic area complications, Glover et al. (2016) find that HBOT failed to improve patients' gastrointestinal symptoms such as rectal bleeding in comparison

to the control group. Sultan et al. (2017) also reported on the ineffectiveness of HBOT for treating osteoradionecrosis of the jaw. As a result, they recommended against routine use of the therapy. Both studies note that their findings are different from those of other authors and call for more research to be conducted. It should be remarked that the two studies have a different approach to coming to this conclusion. Glover et al. (2016) perform a double-blind, controlled, randomized study of patients from one hospital. On the other hand, Sultan et al. (2017) conduct a thorough review of studies published in the period from 1980 to 2016. Therefore, the scholars find inconsistent results, which leads them to disregard HBOT as a reliable approach.

Conclusion

Overall, the overwhelming number of studies about the effect of HBOT suggests that the topic continues to be relevant for cancer research. The impact of radiotherapy on patients is complex since this treatment can lead to a variety of complications, some of which are challenging to resolve. Many studies suggest HBOT as one of the most effective approaches to dealing with such issues. Two main purposes of HBOT are mentioned, the first one is it being a radiosensitizer, a therapy that enhances the effectiveness of radiation. The second one is the most investigated out of the two. Here, HBOT is an approach to relieving adverse outcomes of radiation. HBOT is found to help patients with the issues that radiotherapy brings since radiation suppresses the body's ability to transfer oxygen, and HBOT supplies the tissues with the needed ingredients for restoration.

In particular, the investigation of HBOT's positive influence on pelvic area problems is in-depth, supplying one with vital knowledge about the consequences for patients with such conditions as radiation proctitis, cystitis, rectal bleeding, and pain. Here, the majority of scholars find that HBOT is extremely helpful, lowering patients' level of toxicity, eliminating some of the problems, and significantly reducing others. Some of the researchers suggest that non healing wounds and delayed injuries can also be improved with the help of HBOT. The majority of findings support the helpful nature of this therapy, although some articles present contradictory conclusions. The current state of the literature on the subject shows that HBOT's reliability should be questioned thoroughly in order to further the investigation.

References

1. Bem, J., Bem, S., & Singh, A. (2000). Use of hyperbaric oxygen chamber in the management of radiation-related complications of the anorectal region. *Diseases of the Colon & Rectum*, *43*(10), 1435-1438.
2. Daruwalla, J., &Christophi, C. (2006). Hyperbaric oxygen therapy for malignancy: A review. *World Journal of Surgery*, *30*(12), 2112-2131.
3. Fink, D., Chetty, N., Lehm, J. P., Marsden, D. E., & Hacker, N. F. (2006). Hyperbaric oxygen therapy for delayed radiation injuries in gynecological cancers. *International Journal of Gynecological Cancer*, *16*(2), 638-642.
4. Glover, M., Smerdon, G. R., Andreyev, H. J., Benton, B. E., Bothma, P., Firth, O., ... Martin, S. (2016). Hyperbaric oxygen for patients with chronic bowel dysfunction after pelvic radiotherapy (HOT2): A randomised, double-blind, sham-controlled phase 3 trial. *The Lancet Oncology*, *17*(2), 224-233.
5. Jones, K., Evans, A. W., Bristow, R. G., & Levin, W. (2006). Treatment of radiation proctitis with hyperbaric oxygen. *Radiotherapy and Oncology*, *78*(1), 91-94.
6. Mayer, R., Klemen, H., Quehenberger, F., Sankin, O., Mayer, E., Hackl, A., & Smolle-Juettner, F. M. (2001). Hyperbaric oxygen–an effective tool to treat radiation

morbidity in prostate cancer. *Radiotherapy and Oncology*, *61*(2), 151-156.

7. Moen, I., &Stuhr, L. E. (2012). Hyperbaric oxygen therapy and cancer—A review. *Targeted Oncology*, *7*(4), 233-242.
8. Oscarsson, N., Arnell, P., Lodding, P., Ricksten, S. E., & Seeman-Lodding, H. (2013). Hyperbaric oxygen treatment in radiation-induced cystitis and proctitis: a prospective cohort study on patient-perceived quality of recovery. *International Journal of Radiation Oncology, Biology, and Physics*, *87*(4), 670-675.
9. Safra, T., Gutman, G., Fishlev, G., Soyfer, V., Gall, N., Lessing, J. B., ... Grisaru, D. (2008). Improved quality of life with hyperbaric oxygen therapy in patients with persistent pelvic radiation-induced toxicity. *Clinical Oncology*, *20*(4), 284-287.
10. Stępień, K., Ostrowski, R. P., &Matyja, E. (2016). Hyperbaric oxygen as an adjunctive therapy in treatment of malignancies, including brain tumours. *Medical Oncology*, *33*, 101.
11. Sultan, A., Hanna, G. J., Margalit, D. N., Chau, N., Goguen, L. A., Marty, F. M., ... Tishler, R. B. (2017). The use of hyperbaric oxygen for the prevention and management of osteoradionecrosis of the jaw: A Dana-Farber/Brigham and Women's Cancer Center multidisciplinary guideline. *The Oncologist*, *22*(3), 343-350.
12. Teguh, D. N., Levendag, P. C., Noever, I., Voet, P., van der Est, H., van Rooij, P., ... Schmitz, P. I. (2009). Early hyperbaric oxygen therapy for reducing radiotherapy side effects: Early results of a randomized trial in oropharyngeal and nasopharyngeal cancer. *International Journal of Radiation Oncology, Biology, and Physics*, *75*(3), 711-716.
13. Wilkinson, D., &Doolette, D. (2004). Hyperbaric oxygen treatment and survival from necrotizing soft tissue infection. *Archives of Surgery*, *139*(12), 1339-1345.