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Review

Photobiomodulation and Cancer: What Is the Truth?

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Abstract

Background: Photobiomodulation (PBM) therapy is a rapidly growing approach to stimulate healing, reduce pain, increase athletic performance, and improve general wellness. ***Objective:*** Applying PBM therapy over the site of a tumor has been considered to be a contraindication. However, since another growing use of PBM therapy is to mitigate the side effects of cancer therapy, this short review seeks to critically examine the evidence of whether PBM therapy is beneficial or harmful in cancer patients. ***Materials and methods:*** PubMed and Google Scholar were searched. ***Results:*** Although there are a few articles suggesting that PBM therapy can be detrimental in animal models of tumors, there are also many articles that suggest the opposite and that light can directly damage the tumor, can potentiate other cancer therapies, and can stimulate the host immune system. Moreover, there are two clinical trials showing increased survival in cancer patients who received PBM therapy. ***Conclusions:*** PBM therapy may have benefits in cancer patients and should be further investigated.

Keywords: photobiomodulation, low-level laser therapy, cancer, cancer therapy side effects, contraindication, antitumor immune response

Introduction

Photobiomodulation (PBM) is the use of red or near-infrared (NIR) light to heal, restore, and stimulate multiple physiological processes and to repair damage caused by injury or disease. PBM started out as what used to be known as ''low-level laser therapy, LLLT'' in the late 1960s and was clinically applied for wound healing and the relief of pain and inflammation in a wide range of orthopedic conditions. For many years, it was thought that there was something ''special'' about lasers and the monochromatic and coherent nature of the light in the laser beam. But, in the 1990s, light emitting diodes (LEDs) were introduced and rapidly gained popularity due to their much lower cost and the absence of safety concerns that were associated with lasers, which previously had led to requirements for ''laser safety training courses.''

It is now widely accepted that the noncoherent light from LEDs behaves the same as coherent laser light for most medical applications. In addition, the ability to deliver reasonable power densities (up to 100 mW/cm^2) over relatively large areas of the body and to mix different wavelengths together (for instance, red and NIR) are major advantages of LED arrays. An important consideration that applies to many areas of PBM is that of the ''biphasic dose–response'' or Arndt–Schulz curve.[1,2] This principle states that there are optimum parameters (energy density or power density) that provide a benefit to the particular disease, and if these parameters are substantially exceeded, the benefits disappear and can even lead to damaging effects if the dose is extremely high. This phenomenon is also called ''hormesis'' and has been comprehensively reviewed by Calabrese and Mattson[3] and Calabrese and Baldwin.[4]

PBM and Cancer

Because PBM was shown to stimulate the growth of cancer cells in cell culture studies,[5] and can also increase the aggressiveness of some cancer cells,[6] some commentators have asserted that PBM may be contraindicated in clinical use in patients with cancer.[7] However, not all experimental studies have found the same results. In contrast, it was realized that PBM was highly effective in the mitigation of numerous distressing side effects that occur as a result of a range of different kinds of cancer therapy.[8,9]

Figure 1 presents a graphical summary of the different kinds of cancer-therapy side effects that could possibly be treated by PBM. These side effects can be so severe that they often lead to the suspension or discontinuation of the cancer therapy with consequent risk to the patient. Perhaps the single most effective indication for PBM (among all known diseases

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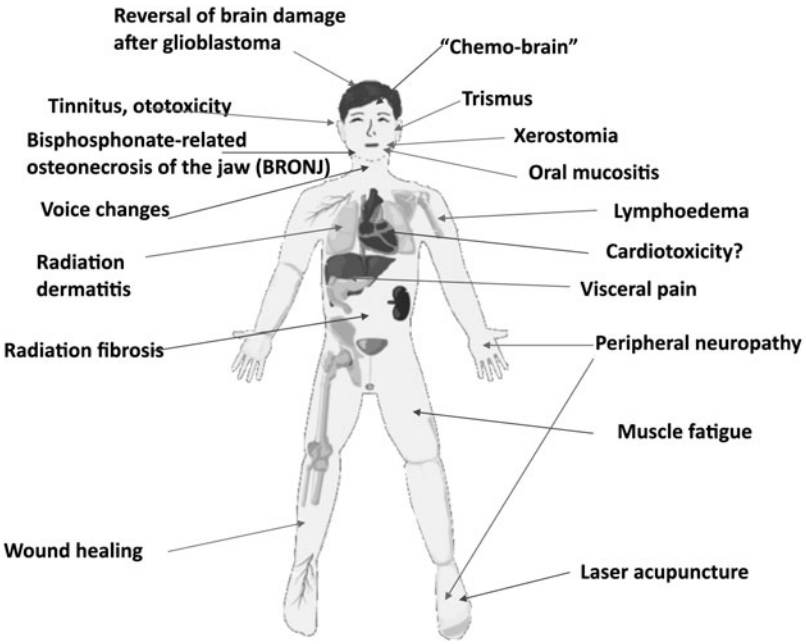

FIG. 1. Cancer therapy side effects possibly treated by PBM. PBM, photobiomodulation.

and conditions) is that of oral mucositis.[10] Oral mucositis is a common side effect of many kinds of chemotherapy and of radiotherapy for head and neck cancer.[11] Other side effects that are under investigation by PBM treatment are chemotherapy-induced peripheral neuropathy,[12] radiation dermatitis associated with breast cancer therapy,[13] and lymphedema as a result of breast cancer surgery.[14]

Some years ago, when PBM was routinely carried out with laser beams directly applied to the affected tissue region, its use for the mitigation of cancer-therapy side effects was employed with the caveat that the laser should not be used directly over the site of the tumor. However, now that large-area LED arrays and even whole-body light bed systems are becoming more common, the question of whether these devices are safe for a patient with cancer needs to be addressed as pointed out by Sonis et al.[15] Moreover, individuals who are using PBM for general health improvement or for increase in athletic performance[16] are asking the question: what if I have an undiagnosed malignant or premalignant lesion?

Can PBM Stimulate Cancer?

Despite the existence of numerous studies that have shown that PBM can increase the growth rate of cancer cells in cell culture,[17] the number of studies that suggest that PBM can actually exacerbate or stimulate cancer growth in animal tumor models *in vivo* are relatively few. One study by Frigo et al. compared the effects of PBM (660 nm, 2.5 W/cm^2) delivered once a day for 3 days either at a low dose or a high dose in subcutaneous melanoma in mice.[18] The low dose (150 J/cm^2) reduced the tumor size (not statistically significant), while the high dose (1050 J/cm^2) significantly increased the tumor size. However, this study suffered from some problems such as the claim that a C57BL/6 tumor (B16F10) was grown in a nonsyngeneic mouse strain (BALB/c).

Another study from Rhee et al. looked at PBM (650 nm, 100 mW/cm^2) as a single dose to an orthotopic mouse model of anaplastic thyroid cancer.[19] However, these investigators used an immunodeficient nude mouse model, which does not accurately reflect most human patients. The tumor growth was faster in the PBM groups; HIF-1a and p-Akt were increased, while TGF-b1 expression was decreased.

The third study looked at PBM in the Syrian hamster cheek pouch model of chemical carcinogenesis caused by application of dimethylbenzanthracene (DMBA).[20] Researchers applied PBM (660 nm, 424 mW/cm^2) every other day for 4 weeks starting at end of the cancer induction period (8 weeks of DMBA). More tumors in the PBM group were histologically graded as ''poorly differentiated,'' and presumably would have a worse prognosis.

Can PBM Directly or Indirectly Attack Cancer?

When we consider the possibility that PBM can have a beneficial effect on cancer, it is important to realize that there are three possible ways by which this may happen (Fig. 2). The first involves the direct effect of the light on the tumor

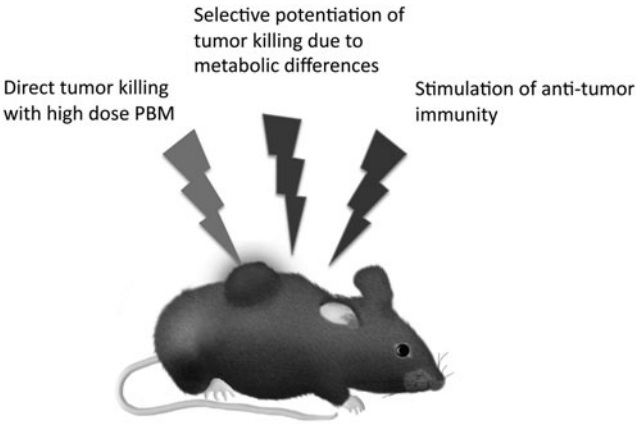

FIG. 2. Possible mechanisms by which PBM could be applied against cancer.