

Recent Development of Laser Photo-Chemotherapy (LPC) for Bone Tumors



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Mini Review

Photodynamic therapies (PDT) have become increasingly popular in the adjuvant treatment of different tumor entities [1]. Chemotherapeutic agents, such as cisplatin may be used in combination with laser-induced thermal therapy (LITT) in an improvement to PDT, known as laser photo chemotherapy (LPC) [1,2]. Based on recent reports on the application of laser photo chemotherapy (LPC) on malignant bone cells under chemotherapeutic conditions with cisplatin or zoledronic acid, the authors feel compelled to describe in this mini-review some relevant aspects of such combined therapy as a potential therapeutic strategy for osteosarcoma [3].

Chemotherapy is regularly used for treating Ewing sarcoma and osteosarcoma, but it isn't often used for other bone cancers, like chordomas and chondrosarcomas, because they aren't very sensitive to chemo [4]. However, it can be useful for some special types of chondrosarcoma, like the dedifferentiated and mesenchymal lineag [3,4]. Anti-cancer agents are sometimes used for bone cancer that has spread through the bloodstream to the lungs and/or other organs [5]. The drugs mainly used for this condition include: Doxorubicin (Adriamycin®), Cisplatin, Carboplatin, Etoposide (VP-16), Ifosfamide (Ifex®), Cyclophosphamide (Cytosan®), Methotrexate and Vincristine (Oncovin®) [3,5]. In this regard, a number of investigators have shown that some of the above anti-cancer agents are likely candidates for light and or heat activation in cancer cells, as laser photo chemotherapy (LPC) has been consistently used for treatment of retinoblastoma since 1996 [3,6-8].

The propensity for survivors of heritable retinoblastoma to develop second primary osteosarcomas at substantially greater frequency than either the general population or survivors of nonheritable retinoblastoma is well known [9,10]. There is some molecular genetic evidence that the development of these two disparate tumor types involves specific somatic loss of constitutional heterozygosity for the region of human chromosome 13 that includes the RB1 locus [11]. In regards

to chemotherapy a number of investigators have shown that anthracyclines and cis-platinum are likely candidates for light or heat activation in cancer cells [1,2,12]. In this sense, Heyman et al. [3] have recently reported a significant decrease of cell bioviability and histomorphological alterations suggestive of higher apoptical activity in osteosarcoma cell lines (Saos-2) treated by cisplatin and zoledronic acid followed by diode laser irradiation, when compared with non-irradiated cells. Therefore, LPC outcomes for retinoblastoma may suggest that a conceptual approach towards osteosarcoma treatment may be possible based on recent clinical studies on combined therapy [12,13-18].

Photo chemotherapy with lasers is an alternative therapy which consists of using a monochromatic light delivered via external irradiation or via interstitial fiber optics to enhance the "killing" threshold in tumors containing light and/or heat-sensitive anticancer agents [12]. The development of photoactivatable pro-drugs of platinum-based antitumor agents is aimed at increasing the selectivity and thereby lowering toxicity of this important class of antitumor drugs [19-21]. Hence, laser photo chemotherapy explores three distinct mechanisms of antitumor action: direct anti-cancer effect

- i. Additionally: thermal
- ii. Light sensitizer
- iii. Effects [1,2,22].

These drugs may be injected intravenously at concentrations lower than normal chemotherapeutic levels, or at higher intratumor doses reducing systemic toxicity while enhancing local tumoricidal effects by laser photoactivation in situ [2,23,24]. Anthracyclines have also been identified that have greater photosensitization potential than daunomyucin [25]. With all the supporting evidence of translational and clinical protocols laser photo chemotherapy has established itself as an alternative treatment for retinoblastoma [18,26,27]. Most of

these studies were conducted in children where there has been a few standardized clinical protocols, in particular for unilateral retinoblastoma [27,28]. One of these studies by Ventura et al. [29] was sophisticated enough to direct intra-arterial chemotherapy for combined laser photo activation in an advanced unilateral case in an 8-year old girl with no other options for treatment [29].

In sum, bone tumors are rare neoplasm that causes significant morbidity and mortality that despite important medical advances in the past 20 years produced few significant changes in function or survival for patients affected with these diseases. Based on the successful establishment as an alternative treatment for retinoblastoma LPC may become an alternative option for this devastating disease.

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