SPECIAL LECTURE SESSION

Role of 830 nm Low Reactive Level Laser on the Growth of an Implanted Glioma in Mice

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Abstract. The effect of low reactive level laser therapy (LLLT; 830 nm, 60 mW, continuous wave) was studied using the model of a glioma implanted in mice. Two different models were used. In the first model, therapies were applied post the first day of glioma implantation; in the second model, post the fourteenth day of glioma implantation. Using the first model, therapies were designed as follows. 1) control group (no therapy), 2) direct LLLT (15 seconds twice per day; on the skin covering the implanted glioma), 3) indirect LLLT (15 seconds twice per day; on abdominal skin area rather than the site of the implanted glioma), 4) indirect LLLT (30 seconds twice per day), 5) anti-cancer drug (ACNU) group, 6) mouse β-interferon (Mu-β-IFN) group, 7) direct LLLT plus Mu-β-IFN group, 8) ACNU plus Mu-β-IFN group, 9) indirect LLLT (15 seconds twice per day) plus ACNU plus Mu-β-IFN group. Using the second model, therapies were designed as follows. 1) control group (no therapy), 2) indirect LLLT (15 seconds twice per day), 3) indirect LLLT (15 seconds twice per day) plus Mu-β-IFN group, 4) Mu-β-IFN plus ACNU group. Our results indicated that, applied on the first day after glioma implantation, both direct and indirect LLLT were effective in inhibiting the tumor growth. In addition, it appeared that the effect of LLLT might be dose-dependent. Finally, the group of direct LLLT plus Mu-β-IFN was most effective in limiting the tumor growth and the incidence of growth as compared with the other groups. However, when applied to the model fourteen days after glioma implantation, indirect LLLT contributed to tumor growth. LLLT (830 nm, 60 mW) may therefore be one of the biological responsive modifier's via skin tissue. Also, the active role of the LLLT in vivo model might depend on the biological interaction between the tumor bearing host and the tumor. (Keio J Med 42 (4): 177–179, December 1993)

Key words: glioma, laser surgery

Introduction

Low reactive level laser therapy (LLLT) has been used in many clinical studies in the past. However, the acting mechanisms of LLLT have not yet been satisfactorily clarified. As has been reported in some journals, LLLT may induce pain relief through the function of the opioids nerve and the activating of macrophages and T-lymphocytes in both vivo and vitro. We thought that the results reported in various journals might indicate the possibility of using LLLT to moderate the immune system through the skin. We studied the effect of LLLT (830 nm, 60 mW) in tumor bearing hosts using a glioma implanted in mice as compared with the effect of other therapies.

Materials and Methods

Animal and tumor model

C57 Black Mice, male, aged 3 weeks were used in this study. Glioma cell line (203 GL) induced by methylcolanthrene in mice was used. The implanted glioma was created by removing a small section (8 mm³) of a tumor from one mouse and injecting it subcutaneously into the dorsal area of another. Two different models were used. In the first model, therapies were applied post the first day of tumor implantation. In the second, therapies were applied post the fourteenth day of tumor implantation.

Experimental designs

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Using the model of post the first day of an implanted glioma, the following therapies were designed: 1) Control group (no therapy, N = 10), 2) direct LLLT group (15 seconds twice per day: On the skin covering the implanted glioma, N = 11), 3) indirect LLLT group (15 seconds twice per day: On the abdominal skin area rather than the site of the implanted glioma, N = 10), 4) indirect LLLT group (30 seconds twice per day, N = 5), 5) anticancer drug (ACNU) group (N = 10), 6) mouse-β-interferon (Mu-β-IFN) group (N = 10), 7) direct LLLT (15 seconds twice per day) plus Mu-β-IFN group (N = 11), 8) Mu-β-IFN plus ACNU group (N = 10), 9) indirect LLLT (15 seconds twice per day) plus Mu-β-IFN plus ACNU group (N = 7).

Using the model of post the fourteenth day of an implanted glioma, the following therapies were designed: 1) Control group (no therapy, N = 5), 2) indirect LLLT (15 seconds twice per day) group (N = 7), 3) indirect LLLT (15 seconds twice per day) plus Mu-β-IFN group (N = 8), 4) Mu-β-IFN plus ACNU group (N = 7).

Usage of laser and drugs: The laser instrument is a semiconductor laser (Gallium Aluminium Arsenide: GaAlAs, 830 nm, 60 mW, spot size: <0.3 cm, continuous wave). Each model was irradiated every day for a period of 32 days. ACNU, 0.07 mg dose, was subcutaneously into the mice once a week. Mu-β-IFN, $5 \times 10^4$ U, was subcutaneously injected into the mice everyday for a period of 32 days.

Estimation of the effect of therapies: The effectiveness of therapies was estimated by both the incidence and the growth volume of the implanted tumor over a 32 day period according to the following formula:

$$V(\text{mg}) = \frac{\text{short diameter}^2 + \text{long diameter}}{2}$$

Results

Results of each therapy in the model of post the first day of glioma implantation

The average percentages of tumor volume in each group over the volume of each control group after a 32 day period of therapies was presented in Fig 1. Direct and indirect LLLT inhibited the volume growth of tumor. So too did other single therapies (ACNU and Mu-β-IFN). Indirect LLLT plus Mu-β-IFN group was most successful in inhibiting the volume growth of tumor, and even in the incidence of tumor (Fig 2).

Results of each therapy in the model of post the fourteenth day of glioma implantation

The average percentages of tumor volume in each group over the volume of control group after a 32 day period of therapies was presented in Fig 3. The indirect LLLT contributed to the increased volume of tumor in this model. However, Mu-β-IFN offset the volume of tumor increased by indirect LLLT. Mu-β-IFN plus ACNU therapy reduced a small amount of tumor growth in this model.
The relation between LLLT and immunological response has been considered in several journals. Dima et al. report that photodynamic therapy increased the activity of lymphocytes in non-irradiated regions. In our study the effects of both direct and indirect LLLT inhibited the growth after glioma implantation, indicating that it might induce anti-tumoral effects via skin tissue. These results allow us to speculate that LLLT might contribute to a photoimmunological system. However, when applied to the model fourteenth day post glioma implantation, indirect LLLT contributed to the growth of the tumor. These results raise the question as to why the same therapy should limit the tumor growth when applied post first day of glioma implantation, and yet produce adverse results when applied post fourteenth day of glioma implantation. The active role of the LLLT (830 nm) in vivo model might depend on the biological interaction including the immune system between the tumor bearing host and the tumor. Further experimenta- tion will be necessary to investigate the results from the viewpoint of the immunological interaction. However, our results are intriguing when compared with the effect of ultraviolet irradiation on the development of the cancer growth in the primary host.

References