

THE INFLUENCE OF PHOTSENSITIVE PEPTIDOMIMETICS ON WEIGHT INDICES OF IMMUNE ORGANS OF EXPERIMENTAL ANIMALS WITH TRANSPLANTABLE LEWIS LUNG CARCINOMA

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The use of photodynamic therapy of drugs capable of selective accumulation in the tumor or in affected cells, in particular photosensitive peptidomimetics, increases its effectiveness in various treatment schemes.

Aim. Determination of weight indices (WI) of thymus and spleen in animals with carcinoma after photodynamic therapy with peptidomimetics: LMB002 and LMB033.

Methods. Studies of WI of immune organs were carried out in mice of the C57 Black line on the 28th day after transplantation of Lewis lung carcinoma. The therapeutic effect was studied using photosensitive peptidomimetics: LMB002 and LMB033. The natural antibiotic gramicidin C was used as a control.

Results. Comparison of the WI of the spleen of intact animals and animals with tumors showed a twofold ($P < 0.05$) increase in animals with tumors. As for the WI of the thymus, a tendency to its increase was observed in animals with tumors, compared to intact ones, but no significant difference was found. The following results were obtained: a decrease in the WI of the spleen in animals with tumors and the introduction of placebo and an increase in the WI of the spleen in animals treated with gramicidin C; an increase in spleen WI and a slight decrease in thymus WI under the influence of LMB002, an increase in spleen WI under the influence of LMB033, while the thymus WI did not change.

Conclusions. It was established that the WI of the spleen during therapy with photosensitive peptidomimetics LMB033 and LMB002 increased in all groups of experimental animals compared to intact ones. The most significant effect on the spleen index was observed for the schemes of double administration of LMB033 and double phototherapy. No significant changes in the weight index of the thymus during therapy with photosensitive peptidomimetics LMB033 and LMB002 were found.

Key words: peptidomimetics, photodynamic therapy, cell culture, Lewis lung carcinoma.

Today, photodynamic therapy (PDT) is a highly effective method for cancer treatment. PDT induces acute inflammation, expression of heat shock proteins, tumor invasion, and infiltration by leukocytes, and can enhance the presentation of tumor antigens to T cells [1, 2].

To increase the effectiveness of non-invasive treatment methods, photo-controlled peptidomimetics are used, which are prescribed in a non-cytotoxic concentration

range. Peptidomimetics are capable of selective accumulation in a tumor or affected cells [3, 4]. They are usually administered in an inactive, less toxic isomeric form, which is subsequently activated under the influence of light with a high level of spatiotemporal precision at the desired site of action. Thus, after reaching the target of the action, light-induced thermal inactivation of peptidomimetics contributes to their wide application, as safe medicines [5, 6].

Materials and Methods

Studies were conducted on a transplantable model of LLC in mice of the C57 Black line [7]. Inoculation of tumor cells was carried out in the femoral muscle in a concentration of 0.8×10^6 cells of the primary LLC culture, which was grown in an *invitro* system in a culture medium DMEM (Sigma, USA) containing 10% FBS (Sigma, USA) in standard CO₂ incubator conditions at 37 °C and 100% humidity. After reaching a complete monolayer, cells were washed from the culture medium, counted, dissolved in physiological buffer, and inoculated into experimental animals.

To determine the weight index (WI) of the spleen and thymus in animals with tumors and animals with tumors and therapy, mice were weighed, after euthanasia, the immune organs were removed, weighed, and according to the given formula, the weight indices of the immune organs were determined.

$$I_{\text{spleen}} (\%) = \frac{\text{spleen weight}}{\text{the weight of the animal}} \times 100$$

$$I_{\text{thymus}} (\%) = \frac{\text{thymus weight}}{\text{the weight of the animal}} \times 100$$

The obtained data were averaged by groups of experimental animals and presented in the form of histograms.

The drugs for phototherapy were photo-controlled peptidomimetics: LMB002 and LMB033. The natural antibiotic gramicidin C was used as a control.

7 groups of animals were used in the study ($n = 5$).

I group — intact control group of animals;

II group — a group of animals with a transplanted tumor (control without treatment), these animals were kept in a dimmed light/dark regime during the experimental period;

III group — a group of animals injected with Gramicidin C (GS), two procedures (intratumoral injection of GS, no irradiation), an interval of two days between procedures;

IV group — a group of animals that were injected with the peptidomimetic LMB033(closed form), according to the scheme: two intratumoral injections of the compound, no radiation, and an interval between injections of two days.

V group — a group of animals injected with the peptidomimetic LMB002(closed form), according to the scheme: two intratumoral injections of the compound, no radiation, and

an interval of two days between injections.

VI group — a group of animals administered peptidomimetic LMB033 (closed form), according to the scheme: two intratumoral injections of the compound, with double irradiation, the interval between injections is two days.

VII group — a group of animals that were administered peptidomimetic LMB002 (closed form), according to the scheme: two intratumoral injections of the compound, with double irradiation, the interval between injections is two days.

Results and Discussions

Comparison of the weight index of the spleen of intact animals and animals with tumors showed a 2-fold ($p < 0.05$) increase in animals with tumors (Fig.).

As for the WI of the thymus, a tendency to increase was observed in animals with tumors compared to intact ones, but no significant difference was recorded. The increase in splenic WI in tumor-bearing animals is a consequence of immunosuppression and inflammation.

Weight indicators of the spleen and thymus differed from those in the untreated control group: in animals with transplanted Lewis lung carcinoma, a decrease in the WI of the spleen was observed by the administration of a placebo, and in animals treated with gramicidin C — an increase in the WI of the spleen and a decrease in the thymus.

Therapy with peptidomimetics according to the scheme of double administration of LMB033 in the absence of irradiation did not lead to changes in the weight index of the spleen and thymus compared to the control; therapy with a double injection of the peptidomimetic LMB033 and irradiation led to an increase in the weight index of the spleen in the VI group of animals relative to the group of untreated animals, while the weight index of the thymus did not change.

An increase in the weight index of the spleen and a decrease in the weight index of the thymus in comparison with the control was observed, with the double administration of the peptidomimetic LMB002 to the animals and the absence of irradiation. The weight indices of the spleen and thymus in the group of animals treated with peptidomimetic therapy and exposed to radiation differ from the control: WI of the spleen increases and WI of the thymus decreases.

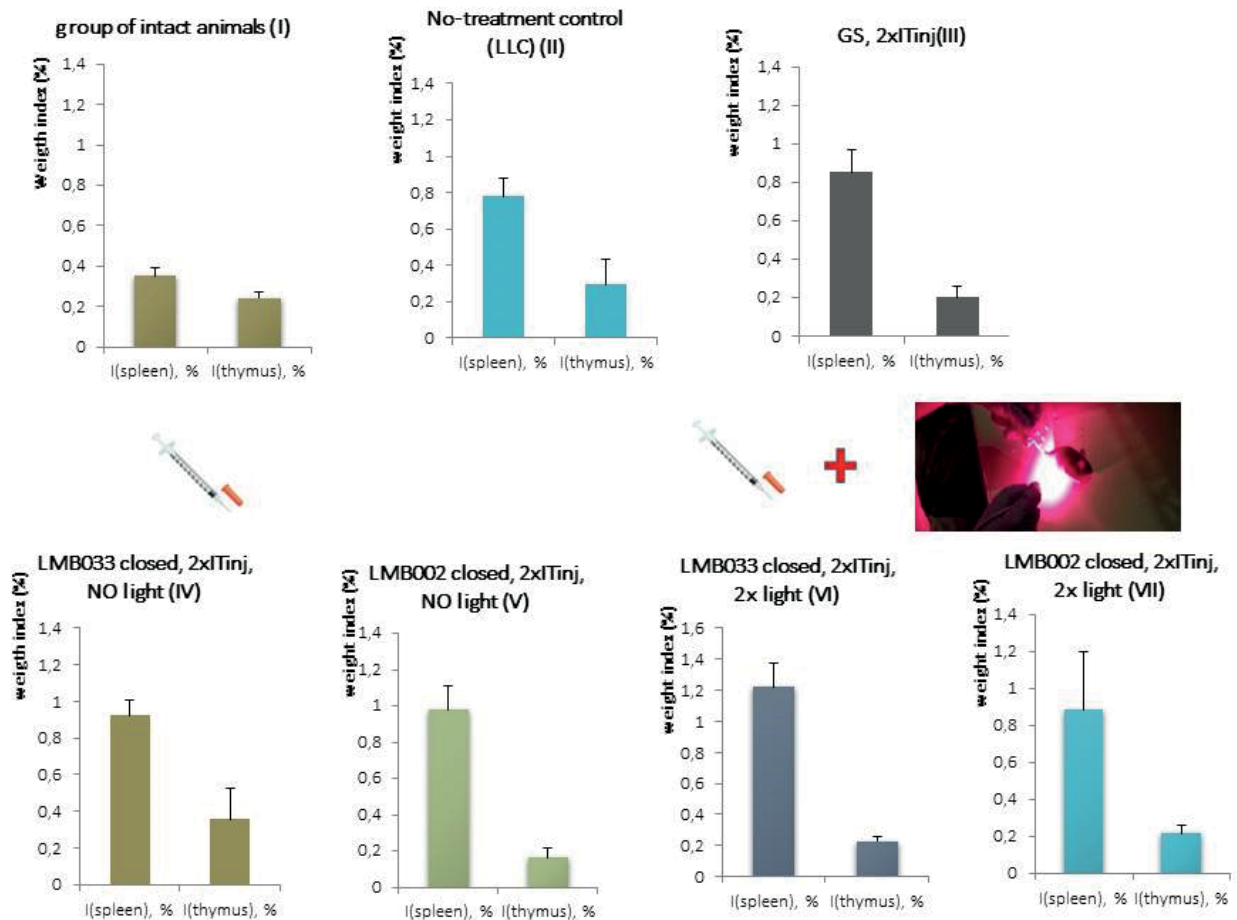


Fig. Weight index of the spleen and thymus of C57 Black mice under the influence of controlled photopeptidomimetics

Conclusions

It was established that the WI of the spleen during therapy with photosensitive peptidomimetics LMB033 and LMB002 increased in all groups of experimental animals compared to intact ones. The most significant effect on the spleen index was observed for the schemes of double administration of LMB033 and double phototherapy. No significant changes in the weight index of the thymus during therapy with photosensitive peptidomimetics LMB033 and LMB002 were found.

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