COMPARATIVE STUDY OF THE ACTION SPECTRUM OF ANTITUMOR PREPARATIONS FROM THE ALKYLATING AGENT GROUP ON TRANSPLANTABLE TUMORS IN MICE

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We have previously reported [1] on our results of comparative study of the action spectrum of antitumor preparations on transplantable tumors in rats and hamsters. The present article deals with the study of the action spectrum of several preparations on transplantable tumors of mice, and establishes the sensitivity of the most frequently used tumors to the potency of separate preparations, mainly from the alkylating agent group.

METHODS

The experiments were carried out on 10 strains of transplantable mouse tumors: sarcoma 180, sarcoma 37, sarcoma 298, lymphosarcoma LIO-1, Ehrlich's carcinoma, hepatoma 22, the flat-celled cancer of the fore-stomach OZH-5, mammary carcinoma (MC), Garding-Passi's melanoma and Claudmann's melanoma (S-91) [2].*

The antitumor preparations studied were embichin, asaline, asazol, ThioTepa, E-39, benzodet, myleran, colchamine, serotonin, chlorambucil, dopan, sarcolysin, and endoxan. All these preparation except for colchamine and serotonin belong to the group of alkylating agents.

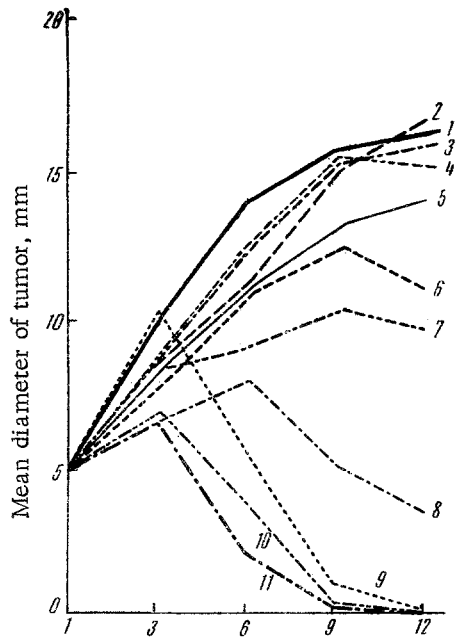
The effect of the preparations was tried simultaneously in one experiment. Treatment began five to seven days after transplantation, when it was felt that the tumor nodules were growing well. The experiments with lymphosarcoma LIO-1 were exceptional; in these the preparations were added after 48 h, and in the melanomas treatment was begun on the 18-22nd day. The effect of all preparations was evaluated with test of maximally tolerated doses. The duration of treatment was 12 days. In 24-48 h after the administration of the last preparation the animals were killed. The percent of inhibition of tumor growth, in weight, calculated at the end of the experiment by the formula $[(Mk-Mo)/Mk]\cdot 100$ and the change in mean diameter of the tumor during the experiment were the criteria of antitumor activity.

RESULTS

According to the data from the comparative studies the most sensitive tumor to the alkylating agents was sarcoma 298. The compounds under study inhibited its growth from 98% to 0. The most potent were sarcolysin, dopan, endoxan, ThioTepa and chlorambucil. At the same time, embichin, asaline, asazol, myleran and colchamine had almost no inhibitory effect on the growth of sarcoma 298. Thus, sarcoma 298 clearly differentiates the strength of preparations with alkylating action. In the figure are presented the changes in values for mean tumor diameter during treatment, which attests to the high sensitivity of the tumor to the effective strength of the various compounds.

Claudmann's melanoma possessed a somewhat lesser sensitivity, ThioTepa, sarcolysin, dopan, endoxan and benzodet having a strong effect. Such preparations as embichin, myleran and colchamine had almost no inhibitory effect on its growth. Using the Claudmann's melanoma, we easily differentiated preparations which possessed weak and strong activity. Use of sarcoma 180 and sarcoma 37 also gave a differentiation of the preparations being studied.

*Literature Cited [2] is omitted in the original Russian —Publisher's note.



Changes in mean diameter of sarcoma 298 at different periods of treatment with different preparations: 1) control; 2) colchamine; 3) embichin; 4) asazol; 5) myleran; 6) benzodet; 7) E-39; 8) chlorambucil; 9) dopan; 10) sarcolysin; 11) endoxan.

The preparations inhibited the growth of sarcoma 180 from 81% to 0, and sarcoma 37 from 84% to 15%. Sarcoma 180 appeared most sensitive to endoxan and sarcoma 37 to benzodet. Both tumors were resistant to embichin, asaline, asazol, myleran, and colchamine. The remain preparations produced moderate or insignificant inhibition of sarcoma growth.

In relation to the Garding-Passi melanoma the most active compound was serotonin (a nonalkylating agent). The action of the remaining compounds was moderate or insignificant. Moderate or weak inhibition was noted with use of mammary carcinoma. A clear differentiation of the antitumor activity of the preparations could not be made with both tumors.

The most resistant tumor was the Ehrlich's tumor, all compounds producing inhibition from 44 to 8%. The prestomach tumor OZH-5, lymphosarcoma LIO-1 and hepatoma 22 were relatively resistant to all preparations and, using them, a rather poor differentiation of preparation activity could be made.

The investigation we have carried out shows that preparations have nonidentical antitumor action spectrums: the broadest effect is produced by endoxan, chlorambucil, ThioTepa and benzodet (inhibition to 50% and greater in growth of 6-7 out of 10 tumors), a less pronounced effect by sarcolysin, dopan and serotonin (effect in five out of ten tumors), borderline by asaline (effect in two melanomas) and E-39 (action against sarcoma 298), and in none of the mouse tumors used was there any practical effect from embichin, asazol, myleran or colchamine.

LITERATURE CITED

1. G. H. Algire, J. nat. Cancer. Inst., 1944, Vol. 5, p. 151.