Effects of Direct Electric Current in Tumors Treatment.

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Abstract: Direct electric current (DEC) was supplied to Ehrlich solid tumor, based on three therapeutic schemes. In the first one the anode was inserted in the center of the tumor and the cathode was placed subcutaneously. DEC dose used was 1.8 and 4 mA during 60 and 30 minutes, respectively. In the second one the anode was inserted at the center of the tumor and three cathodes at its periphery, and 4 mA were supplied during 21 minutes. In the third case the same distribution than in the first case was used and two 4 mA stimuli were applied during 30 minutes. It was concluded that DEC induces both electrochemical reactions and immune system enhancement, which produce tumor destruction.

INTRODUCTION

Since long ago, it has been known that direct electric current (DEC) can destroy tumors. This modality of treatment is characterized by its minimal invasiveness as well as extensive and immediate antitumoral effectiveness, as well as by its positive influence in the control of the metastatic dissemination [1-6].

In spite of being employed successfully in the Clinical Oncology [2,3], neither the way of DEC in the destruction of tumors nor the role of the immune system have been clarified yet. Several action mechanisms have been proposed, among which there are: electrochemical reactions [4-5], local pH changes [1-6] and so on.

The aims of this work are to demonstrate the antitumoral effect DEC for different therapeutic schemes (dose, number, polarity and position of the electrodes, type of therapy and repetitiveness of stimuli) and initial tumoral volumes as well as to propose a possible antitumoral mechanism of DEC.

MATERIALS AND METHODS

Balb/C male mice, between 7 and 8 weeks old and 18 to 22 g weightS, supplied by Laboratorio de Animales y Biomodelos Experimentales from Santiago de Cuba, Cuba, were used. Animals were maintained in plastic cages at a constant temperature of 23 ± 2 °C and a relative humidity of 65%.

The Ehrlich ascitic tumor cells suspension, transplanted to the Balb/C mouse, was prepared from the ascitic form of the tumor. Solid and subcutaneous tumors, located dorsilaterally in animals, were initiated by the inoculation of 5x10⁶ viable cells. The viability of the cells, was 95%.

Cell count was made with an hematocitometer. Tumor volume was calculated with the use of ellipsoid volume formula (V= πabc/6). Daily measurements of the three diameters of the tumor a, b, c, were made (mutually orthogonal), with a vernier calliper.

For supplying electrochemical treatment, a high stability and low noise DEC source was built at Centro Nacional de Electromagnetismo Aplicado (CNEA). Platinum electrodes of 0.7mm-diameter and 20 mm length were used. Three therapeutic schemes were applied, in which anode was always inserted at the center of the tumor. In the first scheme, the cathode was inserted subcutaneously, at a distance of 8-10 mm from the tumor margin. On the first day, the dose of DEC used was 1.8 and 4 mA during 60 and 30 minutes, respectively. Three experimental groups were formed, 15 animals each of them: the control group, the group treated with 1.8 mA during 60 minutes, and the one treated with 4mA during 30 minutes. Their initial volumes were 142 ± 0.86; 141.5 ± 0.78 and 139 ± 1.80 mm³, respectively.

In the second group, three cathodes were inserted at the tumor periphery. On the first day, 4 mA during 21 minutes were supplied. Two experimental groups were formed, each of them with 27 animals: control group and group treated with 4 mA during 21 minutes, with initials volumes of 849.8 ± 5.5 mm³ and 850.4 ± 3.7 mm³, respectively.

In the third group the same electrode distribution of the first group was used, but the dose of 4mA during 30 minutes was supplied on the first and second days.

Two experimental groups were formed, each of them with 27 animals: control group and treated group with 4 mA during 30 minutes. Initial volumes were 2 508 ± 58.33 and 2 525 ± 55.41 mm³, respectively. Animals from the control group were maintained under the same conditions, but without DEC. In all therapies the peritumoral and histopathological findings of organs were studied.

For the histopathologic analysis of tumors, they were fixed in a 10 % formal solution and processed by the paraffin method. Hematoxylin and eosin staining was used.

The necrosis percentage was calculated by means of the relation between the necrosis area and the tumor’s total area, multiplied by 100%.

In order to compare volumes and necrosis percentage of tumors, the statistical and non-parametric criterium one-
RESULTS

In the three therapeutic schemes and after DEC was supplied, an increase in the necrosis percentage and a decrease in volume were observed in the treated tumors. These changes were highly significant comparing them with their respective controls. In these tumors, a lymphocyte infiltrate was observed, and there were no significant differences.

Vascular congestion and the neutrophil infiltration were highly significant. Besides, an acute inflammatory process from moderate to severe and a great necrosis area around the anode was observed in all treated tumors.

In the different histopathological studies on the organs from treated animals, damages were not observed. However, in the spleen from these animals lymphoid hyperplasia was found greater to the one found in the control group. Death occurring in the treated animals is due to the fact that them tumor grew near their heads, so treatment was lethal.

The increase in the necrosis percentage and the decrease in the volume of treated tumors show the noticeable antitumoral effect of DEC, independently from the therapeutic scheme being used and the initial tumoral volume.

This could be explained by the production of electrochemical reactions (mainly those involving the reactive oxygen species) and from the immune system enhancement.

CONCLUSIONS

Electrochemical reactions generated in the tumor by DEC action are responsible for the initial induced necrosis in it, which brings about the stimulation of the acute inflammatory process, observed only in treated tumors. This necrosis stimulates the polymorphonuclear neutrophil migration to the peritumoral zone.

The immune system enhancement is corroborated by the remarkable presence of the neutrophil. Extension of necrosis with the passing of time is explained because the reactive oxygen species react (ROS) with organic compounds such as: lipids, proteins, etc, through a chain self-catalytic reaction causing damages at the membranes level. Damage of ROS to tumoral cells depends on its concentrations, which are dependent on the type of tumor, effectiveness of immune system and on the therapeutic schemes being used. ROS coming from the oxidative burst from polynuclear and mononuclear phagocytic cells, and from the electrochemical reactions generated in the tumor, in both cases induced by the cytotoxic action of DEC, could be the primary mechanisms responsible for the detection of tumoral cells.

REFERENCES


