Heat Perfusion for Malignancy

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Abstract Hyperthermia, total anoxia and low pH have shown selective lethal effect on malignant cells. A perfusion system was devised to combine these modalities and was tried in 4 cases of advanced malignancy. A perfusion lasting for 45 minutes was found safe for normal tissue and yet selectively injurious to malignant cells. Technically this is a very simple procedure and its principles can be utilized in regional infusion also. Though the clinical material is scanty, the method deserves further trial.

Keywords Heat · Exsanguination · Anoxia · Tumor

Surgery and radiotherapy have not provided the final answer in the management of cancer. Due to the lack of specific antitumor drugs, chemotherapy also has severe limitations. Selective lethal action of heat on malignant cells has been proved in experimental as well as clinical tumors [1, 2]. However, uncontrolled hyperthermia has its own complications. If heat is combined with other factors possessing similar antitumor characteristics, it maybe possible to reduce disadvantages and potentiate the tumorocidal effect of the combination. Anoxia and low pH seem to have such an antitumor action [3, 5]. HEAT (Hyperthermic, Exsanguination, Acidotic, Tumor) perfusion has been devised to combine these three agents in the treatment of malignancy. The experimental data showed that in mongrel dogs, the normal tissue of the limb can tolerate

such perfusion for 30 min without suffering a permanent injury [4]. The clinical experience with this procedure is presented here.

Methods and Materials

After heparinisation (1 mg/kg), the main vessels of the affected limb were cannulated and a tourniquet was applied proximally. The circuit was primed with heparinized 5% dextrose solution, which was pre heated to 43°C. this solution was infused into the artery till the limb was totally exsanguinated. After this, the circuit was completed and the perfusion was commenced. The temperature of the perfusate was maintained at 43°C and a flow of 75–150 ml/min. was given. The temperature of limb was maintained at 41–42°C for varying periods. After the perfusion was over, the cannulae were removed and the vessels were repaired. Parenteral antibiotics were given to all the patients. Pre- and post-perfusion biopsies were obtained from the tumor. Since we have had no experience with this procedure, only the patients with advanced disease were selected for the treatment. So far we have treated 4 patients with HEAT perfusion at the K.E.M. Hospital, Mumbai 12.

Results

Case 1 A man (60 years) presented with a large melanoma on the left foot. He had hard and fixed regional nodes. “HEAT” perfusion was performed through his left popliteal vessels for 30 min. Post perfusion, apart from minimal edema, there was no change either in the limb or the tumor. The histology did not reveal any change either.

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Case 2 A man (55 years) presented with a large, ulcerating melanoma on the left heel. The whole limb was swollen and satellite nodules were visible around the ankle. The inguinal nodes were hard and fixed. He underwent “HEAT” perfusion for 45 min. Following the procedure, the edema and satellite nodules disappeared. The ulcer remained stationary and showed granulation tissue at the periphery. Histology revealed vacuolation of malignant cells and degeneration. The patient succumbed to generalized disease after 6 months. Till that time, there was no local progression of the tumor.

Case 3 A female (58 years) was admitted with a huge epithelioma around left ankle. The inguinal nodes were metastatic and fixed. Due to technical problems, the first perfusion lasted for only 30 min. The post perfusion biopsy showed viable tumor. After a fortnight, the perfusion was repeated and was continued for 45 min. Following the second procedure, the tumor sloughed off and a clean healing ulcer was left behind. The biopsy revealed only inflammatory cells and fibrosis. During follow up, no local recurrence was noted for 6 months.

Case 4 A man (65 years) presented with a large melanoma involving left front foot. There was gross edema of the entire limb. The inguinal nodes were hard and fixed. He was subjected to “HEAT” perfusion for 60 min. During perfusion, there was considerable resistance to inflow. Within the next 24 h, the leg became gangrenous and had to be amputated. The histology revealed arteriosclerotic block in the popliteal artery and complete degeneration of malignant cells.

Discussion

The concept behind this procedure is to increase the metabolic needs of malignant cells by hyperthermia and at the same time, subject them to total oxygen lack and low pH, both of which are incompatible with cell life. All the three agents (heat, anoxia and acidosis) have shown selective antitumor action. At the same time, normal tissue can tolerate them to a certain extent. Since these factors are kept constant during perfusion, the cell damage depends on the duration of perfusion. The following considerations were given for selecting the optimum value of each agent.

Hyperthermia Human body can tolerate a temperature around 40°C during pyrexia, without suffering permanent damage. But the malignant cells are selectively injured at

this temperature [1, 2, 5]. Though temperatures higher than 40°C. kill malignant cells more rapidly, the normal tissue also suffers increasing injury [1, 2]. Therefore, the tissue temperature of 40–41°C was chosen as optimum hyperthermia. The priming solution was warmed to 43°C so as to compensate for loss of heat during perfusion.

Exsanguination The differential action of anoxia on tissue is well known in clinical practice. During irradiation of malignant tumors, anoxia has been used to protect normal tissue. Also the anoxia imposed by ligation of hepatic artery selectively injures the malignant cells [3]. In this procedure, total anoxia was achieved by complete exsanguination of the limb. This also helped to avoid complications like hemolysis and renal shut down which can occur during isolated perfusion.

Acidosis The cells need a near constant pH for survival and diminution below 7 is incompatible with life. However, the normal cells can tolerate acidosis of diabetic coma or cardiac arrest without irreversible injury. On the other hand, malignant cells are found to be more susceptible to chemotherapy and hyperthermia at lower pH levels [5]. in the “HEAT” perfusion, the dextrose solution was used because its pH is low (i.e. 4–5). In addition, due to isotonicity it was harmless to erythrocytes and tissues, in the event the tourniquet was ineffective in isolating the limb.

The number of patients in this series is very small to draw any definite conclusions. But it is obvious that the “HEAT” perfusion for 45 min has selective antitumor effect. The same principles can be employed in “HEAT” infusions, when the tumor arising in head, face or abdomen has a regional arterial supply. Cannulation of the artery after ligating it near its origin and infusion of warm dextrose solution will achieve local hyperthermia, exsanguination and acidosis.

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