Malignancy's Hyperthermia Vulnerability: A Therapeutic Advantage

Arka Bhowmik *

School of Medical Science and Technology, Indian Institute of Technology Kharagpur, India.

Accepted on 24 August 2018

Editorial

This editorial aimed to provide an insight on the therapeutic benefits of hyperthermia or supranormal temperature, refers to as temperature range above the normal body temperature, in the treatment of malignant tumor synergistically along with most common cancer treatment methods. The report highlights key evidences and reasons of the increased vulnerability of malignant cells to supranormal temperature, which has been shown to augment the sensitivity of malignant cells to radiation therapy and chemotherapy.

Malignancies in the human body have remained a serious threat from dates back in the 16th and 18th centuries, and they are more so these days. A malignant cell is a transformed form of a normal cell, which has evolved from multi-step mutations in genetic composition. These malignant cells actuate further alterations to the usual cellular signals, and thereupon refrain any changes due to the active immune system. These cells are capable to replicate faster and can metastasize to secondary locations via lymph and blood. To tackle this dynamic nature of the disease, the treatment strategy differs significantly between the type of cancer, stages, degree of spread, location and from person to person. Often the first choice of therapeutic measures includes neoadjuvent chemotherapy or radical/conformal radiotherapy followed by other methods including surgery. Chemotherapy uses targeting drugs that essentially affect the entire body and are sensitive to fast growing cells, for example, malignant cells and hair; radiotherapy on the other hand only targets specific areas, wherein ionizing radiation damages the DNA of the malignant cell. However, each treatment has its limitations and side effects [1-3]. For example, certain tumors are resistant to drugs and/or radiation due to decreased blood permeability, hypoxia situation, and deactivation of drug targeting enzymes. Further, the repeated exposure of body to chemotherapy and/or radiotherapy, a common clinical strategy for treatment, has indicated many side effects. Commonly found side effects include nausea, vomiting, mouth sores, toxicity, and loss of hair and risk of developing secondary cancer. In this regard, hyperthermia has demonstrated to increase the efficacy of the treatment in many recent clinical trials [4-6]; when administered individually, or in combination with either radiation therapy or chemotherapy. The term 'efficacy' here signifies the treatment's ability to cut down the number of scheduled radio- or chemo-sessions, side effects and increase in post treatment life expectancy. Especially, in case of adjuvant hyperthermia adding supranormal temperature (~ 39-44°C) to the unresectable and recurrent malignant tumor, in the standard schedule of radiotherapy and chemotherapy has shown the ability to treat cancer with less side effects and toxicity [6], also proved to increase the life expectancy of patients with superficial melanoma [7]. This improvement can be attributed to the facts and/or reasons suggesting the sublethal effect of hyperthermia to selectively kill cancer cells [8,9]. In fact, selective killing of cancer cell can be possible by various mechanisms; for example there are strong evidences of the harmful effect of supranormal temperature of 43-44°C on dividing cells (specifically the late S-phase and G2 phase of cell cycle) than non dividing cells [9]. Further, there are strong evidences of increase in blood perfusion and oxygenation within the tumors during and after hyperthermia [8-11], enhancing the drug uptake by cells and sensitizes the hypoxia/radioresistant tumors to radiotherapy, respectively. Depending on the supranormal temperature reached in the tumor various intrinsic distress contributes to the selective killing of malignant cells during bimodal (such as thermo-radiotherapy and thermo-chemotherapy) or trimodal treatment methods (such as thermochemoradiotherapy) [9,11]; such as destabilization of cell membrane which is responsible for increased drug permeability and antigenicity of heated tumor [9], synthesis of thermo-sensitive enzymes and inhibition of nucleic acid repair mechanism makes tumor cells more vulnerable to heat [9] post radiotherapy, and heat induced increase in immune responses and immunogenicity on local and systemic level [11]. In fact, the above therapeutic benefits of hyperthermia are identified in many *in vitro* and *in vivo* studies that include both loco-regional and whole-body sensitization and more clinical trials are presently undergoing for its widespread applicability.

Overall, this report intended to motivate researchers/clinicians to dig deeper into the topic by eagerness to bring improvements in the efficacy of present therapeutic measures of radiation and chemotherapy.

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***Correspondence to:**

Arka Bhowmik

School of Medical Science and Technology

Indian Institute of Technology

Kharagpur, India.

E-mail: arkabhowmik@yahoo.co.uk