Hyperthermia versus Oncothermia: Cellular effects in cancer therapy

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ABSTRACT

Hyperthermia means overheating of the living object completely or partly. Hyperthermia, the procedure of raising the temperature of a part or the whole body above normal for a defined period of time, is applied alone or as an additive in various established cancer treatment modalities such as chemotherapy and radiotherapy. The fact that hyperthermia is not generally accepted as conventional therapy is the problem of its commanders performance. This controversy is illustrated from the complications of the deep heating and the necessity of the heat-effect. The idea of oncothermia solution is an extensive deep action on cells and molecular interactions.

We would like to demonstrate the local and specific effects of oncothermia, as a highly specialized hyperthermic clinical modality. Our aim is to prove the ability of oncothermia to be a realistic and a widely accepted modality of the standard cancer care. We would like to show the proof and the challenge of the hyperthermia and oncothermia approaches to provide the presently available data and summarize the knowledge in the topic. In many early-stage therapies, oncothermia lacks adequate treatment experience and long-term, comprehensive studies that can help us optimize its use for all indications.

The concept of hyperthermia

The effectiveness of hyperthermia treatment is linked to the temperature achieved during the therapy, as well as the length of treatment and cell and tissue characteristics. To ensure that the desired temperature is reached, but not exceeded, the temperature is often measured and regulated throughout the hyperthermia procedure. The goal is to keep local temperatures under 46°C to avoid damage to surrounding tissue, and the whole body temperature under 42°C, which is the upper limit compatible with life.

Mechanism induced by hyperthermia

- Hyperthermia-induced cell death
  - It has been long recognized that hyperthermia at the 40–45°C temperature range kills cells in a reversible form, and temperature-dependent manner. At the hyperthermia region, there are three cellular responses for thermal therapy: apoptosis, autophagy, and necrosis.
  - The intensity of cell death in hyperthermia is dependent on cell death mechanisms. Both AP-1 and p53 pathway can induce a low level of cell death in hyperthermia. Cells dying at 45°C may follow a "cell cycle-dependent effect of hyperthermia."
  - Inhibitors
  - Certain inhibitors can block the effect of hyperthermia. Examples include inhibitors of DNA replication, apoptosis, and autophagy.

Cellular and molecular mechanisms of thermal effects in hyperthermia

Autothermia, hyperthermia, and hypothermia are characterized by specific cellular and molecular mechanisms. These mechanisms include changes in gene expression, protein localization, and metabolic pathways.

- Changes in gene expression
  - Hyperthermia can induce changes in gene expression, leading to the activation of specific genes and the repression of others.
  - Changes in protein localization
  - Hyperthermia can induce changes in protein localization, leading to the redistribution of specific proteins within the cell.

- Changes in metabolic pathways
  - Hyperthermia can induce changes in metabolic pathways, leading to alterations in cellular energy production and utilization.

Problems with hyperthermia

- High energy application could cause overheating of the target tissues and frequent inflammatory reactions.
- Cells die at a higher temperature than the malignant cells, but they are not affected by low temperatures.

Examples of hyperthermia

- In some cases, hyperthermia is used to treat malignant tumors by heating the affected area to a high temperature, which can lead to cell death and the destruction of the tumor.
- Hyperthermia can also be used to enhance the effectiveness of other therapies, such as chemotherapy or radiation therapy.

Change of Paradigm - The concept of oncothermia

Oncothermia technology is based on equally analyzing the absorbed energy to the normal and malignant cells. This method creates a temperature-dependent, microbe-controlled temperature difference for from thermal equilibrium. The definite large temperature gradient between the microbe and normal cells changes the microbe processes into rapid progress for normal programmed cell death, avoiding the toxic effects of the antibiotics.

Mechanism induced by oncothermia

- Oncoclinia promotes the programmed cell death of tumor cells
  - Destroying the cell cycle of DNA, RNA, and proteins can be achieved by hyperthermia. However, hyperthermia is highly limited in oncothermia. Consequently, the effect of oncoclinia is the opposite to the conventional hyperthermia, which depends mainly on heat. Hyperthermia suppresses the response by various methods (morphology, tumor nutrition, and pH). Consequently, the effect of oncoclinia is the opposite to the conventional hyperthermia, which depends mainly on heat.
  - Oncoclinia limits the destruction of normal cells
  - Oncoclinia limits the destruction of normal cells, which is more effective due to the lower energy input on the tumors. Oncoclinia reduces the cellular effects on normal cells, which is more effective due to the lower energy input on the tumors.

Oncothermia mimics the conventional hyperthermia, and at the same time, it reduces the toxicity of the treatment. Oncoclinia aims at imitating the effects of hyperthermia, minimizing the toxic effects of the conventional hyperthermia. The efficacy of hyperthermia is enhanced in the case of tumor cells, while the toxicity to normal cells is reduced. This makes oncothermia a promising approach for cancer treatment, especially for patients with limited treatment options.

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