Investigating the Role of Magnetic and Traditional Hyperthermia in Cancer Treatment

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Abstract

The results of traditional hyperthermia in combination with radiotherapy or chemotherapy were compared to results from treatments that just used chemotherapy or radiotherapy alone in order to determine if there was a statistically significant purpose of using traditional hyperthermia. Traditional hyperthermia trials were statistically analyzed and influenced the conclusion that they were significantly better than treatments without the traditional hyperthermia. Magnetic hyperthermia trials were analyzed and compared to each other in order to reach the conclusion that magnetic hyperthermia is, in fact, effective in cancer treatment but many limitations and side effects need to be considered before implementation of this method in humans.

Introduction

Cancer is one of the largest and most widespread of these diseases and causes many deaths around the world. It has been occurring since the 1700s and continues to kill millions every year (Cancer Statistics, 2018). Recently, a treatment for cancer known as hyperthermia or traditional hyperthermia (TH) has begun to be researched and experimented with. Magnetic hyperthermia (MH) has also become a new field of research for scientists but is completely theoretical in cancer patients at the moment. There are currently three different types of TH used in clinical trials: local hyperthermia, regional hyperthermia, and whole body hyperthermia. Local hyperthermia uses large amounts of heat in order to heat up up a small part of the body such as a tumor. It uses different types of energy in order to accomplish this such as microwaves, radio waves, and ultrasound (Hyperthermia in Cancer Treatment, 2011). Regional hyperthermia is used to treat larger parts of the body that have been affected by cancer. It is typically delivered intravenously as opposed to whole body hyperthermia which is conducted using thermal chambers and hot water blankets. Magnetic hyperthermia, on the other hand, is completely theoretical in humans. It is based off the fact that MNPs and MTB can convert electromagnetic energy from a high-frequency alternative magnetic field to heat. This heat is then used in order to heat up and kill the cancer cells by denaturing the enzymes.

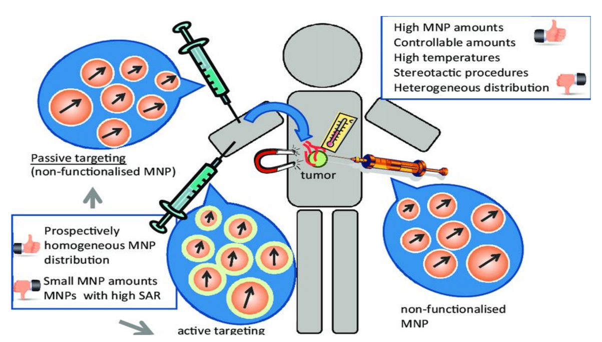

Fig. 3 Intravenous application of magnetic hyperthermia using MNPs and chemotherapeutic drugs in conjunction with each other (Yanase et. al).

Methods

Data Sources

The design of this study was a systematic literature review. Google Scholar, Ebscohost, PUBMED-NCBI, ResearchGate, Science Direct, PLOS, PLOS ONE, etc. were searched to gather studies investigating the role of magnetic hyperthermia in cancer treatment and its effectiveness

Filtering of Data Sources

This study focused primarily on the trials of magnetic hyperthermia which were done with MNPs as opposed to MTB.

Data Extraction

The data extracted focused on the temperature the MH was carried out at in degrees Celsius, the percentage of cancer cells that survived after the treatment, the number of patients that are reported to have a decrease in tumor size or number of cancer cells (percent response), or the state of the cancer cells after the treatment.

Statistical Analysis

In this study a one tailed t-test was used in which unequal variances were assumed. A p-value $\leq .05$ was considered to be significant, meaning that if the p-value was greater than .05 then the null hypothesis was accepted and the alternative hypothesis was accepted, and if the p-value was less than .05 then the null hypothesis was rejected and the alternative hypothesis was accepted.

Research Questions

A. Is magnetic hyperthermia with MNPs in combination with radiotherapy or chemotherapy effective in mice, F344 rats, and hamsters in cancer treatments?

B. Is traditional hyperthermia in combination with radiotherapy or chemotherapy effective as compared to radiotherapy or chemotherapy used alone in cancer treatments?

Hypotheses

Hypothesis (A)

Magnetic hyperthermia with MNPs in combination with radiotherapy or chemotherapy is effective in treating cancer in mice, hamsters, and F344 rats.

Alternative Hypothesis (B)

Traditional hyperthermia is more effective than current cancer treatments.

Null Hypothesis (B)

Traditional hyperthermia is not more effective than current cancer treatments.

Results and Discussion

Table 1. Data comparison showing the results from different studies in which MHT was applied to F344 mice that were injected with glioblastoma cells.

Study Extracted From	Temperature Reached (degrees Celsius)	Duration of AMF exposure (min)	Results
Yanase et. al (A)	43	60	Complete glioma cell death
Yanase et. al (B)	43-44	30	Necrotic tumor cells, some animals displayed complete tumor regression
Yanase et. al (C)	43-44	30	Some animals displayed complete tumor regression
Shinkai et. al	43-44	30	Some animals displayed complete tumor regression
Ito et. al	42	30	Reduced tumor growth
Ohno et. al	44.4	30	Significant tumor cell death
Jordan et. al	45	40	Necrotic tumor tissue

With the relevant success of each studies research and each different temperature tested, the ideal temperature range of these studies tended to be 43°-44°. This range also provided the most optimal results of tumor reduction and cancer cell death. This indicates that MH was a success in treating mice that were injected with glioblastoma cancer cells. The outliers within the data showed that as time of treatment increased, the results became more ideal and in some instances, led to complete treatment of the glioma.

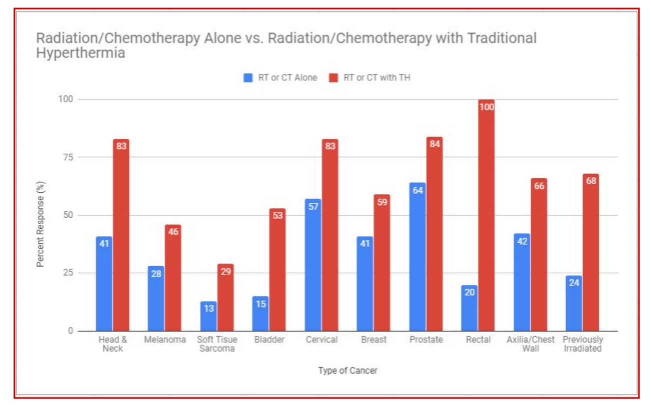

Fig. 5 This bar graph shows the treatment results in humans for traditional hyperthermia in different types of cancer. Percent response is the number of patients that were recorded to have a decreased tumor size. RT- radiotherapy, CT- chemotherapy, TH- traditional hyperthermia (Valdagni et. al, 1994; Overgaard et. al, 1995; Issels et. al 2010; Colombo et. al, 2012; Van der Zee et. al, 2000; Vernon et. al).

When comparing the control group to the combination group it is evident that a higher percentage of patients were reported to have some extent of success when they were treated, as shown in Figure 6. The combination treatment group had much better results overall, with a 36.6% better response rate on average. These trials were all conducted in real human cancer patients or voluntary cancer-injected patients, suggesting that TH also has the potential to be further implemented into humans.

Conclusion

This systematic literature review provides evidence supporting the hypotheses in this study. Statistical analysis resulted in a p-value of less than .05, indicating the rejection of the null hypothesis. MH trials were analyzed and compiled in order to show the effectiveness of their application mice, rats, and hamsters. Ultimately, MH was proven to be effective in treatments and TH was shown to be a significantly positive addition to the current cancer treatments.

Further Work

To further contribute to this study, MH can be further applied into more in vivo and in vitro experiments. Further research is required for MH to be fully viable in humans due to the toxicity of the nanoparticles and the MTB. Guidelines for further research include the increase of focus on the temperature range of 42°-44° as papers analyzed in this study were recognized to cover this temperature range. There is a large amount of cytotoxicity contained within the MNPs and MTB which can potentially result in large side effects. These side effects of this toxicity and what can be done to limit or eliminate it is also a field that requires further research.

As for the traditional hyperthermia, further research should focus on control of the temperatures achieved for tumors that are deep within the body. Currently, hyperthermia is not a standard treatment for cancer due to the fact that it is difficult to reach temperatures above 43°. The ideal temperature range that is theorized to achieve the best possible results is 44°-46° but this range cannot be implemented currently. Further research and developments are necessary in order for this temperature to be achieved, and future work can look into this.

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