Original Article

Review the effect of hyperthermia using iron and magnetic nanoparticles in cancer treatment in chemical injuries

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ABSTRACT

hyperthermia using different methods such as microwave and magnetic waves is one of the methods to treat cancer. In this method, iron and magnetic nanoparticles are used to increase the temperature and increase the effect of hyperthermia as auxiliary treatment with chemotherapy and radiotherapy. In this study, we review the results of studies that evaluated the role of iron and magnetic nanoparticles effects in increasing the tumor temperature and maintaining healthy tissue and thus increasing the efficiency of hyperthermia with radiotherapy in chemical injuries. The presence of both groups of iron and magnetic nanoparticles during microwave and magnetism waves irradiation increased tumor death. The results of our study showed that iron nanoparticles are less concentrated in comparison to magnetic ones, causing a rapid rise in temperature, which increases the efficiency of hyperthermia and reduces damage to healthy tissues around the tumor.

Keywords: Hyperthermia; nanoparticle; cancer treatment; chemical injuries

Introduction

Cancer is the second leading cause of death in the world[1]. In 2013, 8.2 million deaths due to cancer were reported[2]. The proportion of new cases of cancer diagnosed in less developed countries will increase from 56% in 2008 to more than 60% in 2030, which is due to an increase in the incidence of cancer, as well as an expected increase in the hope of Life and population growth[3]. Today, combining treatment regimens has become a major concern in eliminating cancerous tumors and improving treatment outcomes[4, 5]. Undoubtedly, the reason for using other therapy regimens concomitant radiation therapy is to prevent recurrence of the tumor. One of the most important reasons for the recurrence of the tumor is the presence of hypoxic cells (the low oxygen) in the central area of the tumors. These cells have fewer PHs than the peripheral tumor cells. These conditions make the cells of the central tumor more resistant to X and gamma rays. Because the oxygen enhancement ratio (OER) for these beams is about 2-3, in order to create a certain number of injuries in hypoxic conditions, the dose of radiation should be increased by 2-3 times, which also results in the absorption of healthy tissues will increase [5].

To overcome this problem, many attempts have been made, that The most important ones are: a) the use of oxygen in two to three atmospheres during radiation therapy; b) the use of drugs that specifically affect hypoxic cells; c) the use of beams With high LET: linear energy transfer; D) Use of hyperthermic technique [6, 7].

In cancer treatment, hyperthermia is a therapeutic method that uses an external heat source to increase tissue heat to kill or to prevent the growth of cancer cells, in which the heat is applied by electromagnetic or ultrasound waves with use of magnetic and iron nanoparticles and applied to the target tumor locally[8, 9]. Our aim is to review the results of studies using these nanoparticles. For this review article, we searched PubMed, Science Direct and Google scholar with cancer, hyperthermia, iron nanoparticles, magnetic nanoparticles as keywords. The term hyperthermia refers to the various heating techniques that used along with other common cancer treatments[10].

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According to studies, high temperatures highlight direct damage to cancer cells and sensitize them to treatments and increase the effectiveness of chemotherapy and radiotherapy, with minor damage and sometimes without damage to healthy tissues[11]. Therefore, hyperthermia is now considered as an auxiliary treatment for cancer[12].

The effect of hyperthermia depends on the temperature used in addition to the type of tissue and the length of treatment time. A good hyperthermic system should maximize the temperature of the tumor and minimize the temperature of the healthy tissue around to minimize tissue damage[13].

Today, more ultrasound or electromagnetic waves are used for heating. Usually hyperthermia aims to weaken tumor tissues so that they can be eliminated with other therapies[8].

The temperatures used in hyperthermia vary from 40 to 48 degrees Celsius, and may also be applied for one hour or more to the treated area[14]. Hyperthermy also has a number of limitations. These limitations include a failure to accurately heat tissues without damage to surrounding healthy tissues, problems of the uniform distribution of heat within the tumor, and inherent problems associated with targeting small hidden metastases present in tissues[15].

The complications of hyperthermia depend on the area under treatment, the type of treatment and the temperature. Very high temperatures can cause scorching, burn, pain or tissue necrosis. When hyperthermia is used alone, followed by blood clots or bleeding, inflammation of heated tissues or ischemia may occur, but in general hyperthermia complications are temporary[14].

In recent years, advances in the use of nanoparticles with hyperthermia have led to overcoming many of the limitations of this therapeutic approach, although the use of nanoparticles in this treatment is also a concern [15].

In the inner hyperthermia, the fluid containing nanoparticles is injected into the tissue to raise the temperature of the cancerous tissue by heat. Hyperthermia may be applied to a small tissue called local hyperthermia, and if it is applied to a larger tissue, it is called regional hyperthermia, and if it is all over the body, it is called the wholebody hyperthermia. nanoparticles used in hyperthermia is include ironlic and magnetic particles, each of which has different types, and the amount of heat produced in hyperthermia depends on the type of injected nanoparticles [16].

since the heat generated depends on the type of injectable material, so the type of injectable particle is of great importance. Therefore, we have studied the clinical and laboratory results of different nanoparticles used in hyperthermia.

As stated, the high and increasing incidence of cancer, the severity of its side effects and the lack of a definitive treatment strategy reveal the need for more effective therapeutic approaches for the treatment of disease; as many studies have examined the effects of various effective factors on the improvement of therapeutic outcomes from the therapies available in human, animal and laboratory samples and various studies have been conducted with different iron and magnetic nanoparticles, and different results have been obtained. But according to our studies, no study has been done to compare the results of these two types of nanoparticles. The purpose of this study is to investigate the results of these two types of nanoparticles in order to finally make suggestions on the subject.

Iron nanoparticles

As a less invasive experimental technique, Noble iron NPs have thoroughly been used as photothermal agents for in vivo therapy, that holds great promise for the treatment of cancer. hyperthermia with iron nanoparticles combines two key components that one of them is the light source, such as lasers with a spectral range of 650–900nm for deep tissue penetration and the other is optical absorbing iron NPs which efficiently transforms the optical irradiation into heat on a picosecond time scale, thus inducing photothermal ablation[17].

in few studies, Huang and coworkers demonstrated that Au-nanorods are effective photothermal agents due to their longitudinal absorption band in the NIR on account of their SPR oscillations[17-19].

For in vivo applications due to Au-nanorods high absorption cross-sections beyond the tissue absorption spectra, small diameter Au-nanorods are being used as photothermal converters of near infrared radiation (NIR). these nanorods can be used as ablation components for cancer because this NIR light transmits readily through human skin and tissue[20, 21]. Other gold nanostructures such as spherical AuNPs[22], Au-nanocages[23], and Au-nanoshells[24, 25] have also demonstrated the effective photothermal destruction of cancer cells and tissue. PEG-modified Au-nanoshells (Silica/Au core/shell NPs) injected intravenously in tumor-bearing mice showed to passively accumulate in the tumor tissue due to the leakiness of the tumor vasculature[26].

Magnetic nanoparticles

Studies show that dispersions of magnetic nanoparticle can be injected into tumors and subsequently heated in an externally applied alternating magnetic field. The overall surface and large number overall surface of the magnetic elements within such fluids result in excellent power absorption capabilities and make them particularly suitable for selective interstitial heating of tumors.

For hyperthermia using magnetic nanoparticles, the pathways developedso far have in common that they deliver the magnetic material directly into or adjacent to the tumor tissue. In very small portions, the magnetic fluid can be applied and therefore almost continuously within the targeted area, leading to high concentrations and homogeneous heat distribution. This addresses the major requirement for hyperthermia, namely that the heat is selectively targeted to the tumor region while sparing neighboring healthy tissue. Very precise heating of almost any part of the body is the result of the local application and the inductive excitation of the nanoparticles. Variation of the magnetic field strength enables an almost free choice of the treatment temperature, rendering both hyperthermia and thermoablation possible. Nevertheless, most of the techniques

in this field applied so far have only been evaluated in preclinical studies. Magnetic fluid hyperthermia (MFH) has been undergoing clinical testing. The safety and the feasibility of the technique has been proven in three clinical studies. Injection of the nanoparticles using different techniques (intraoperatively under visual control, stereotactically, CT or ultrasound guided) was excellently tolerated. The option to plan the magnetic fluid distribution prospectively and to calculate the heat distribution to a highly reliable degree thereafter, due to the density distribution of the nanoparticles in post-instillation CT and the known SAR of the particles is one particular advantage of this method.

This was confirmed by experimental data showing that about 90% of the injected amount of iron was detectable by CT in tissue samples. We speculate that the remaining 10% represent areas of low iron concentration, presumably in the periphery of larger deposits or needle tracks. A contribution of very low concentrations of iron to the heating process is physically negligible and the lack of detection does not significantly affect the thermal analysis based on CT data. The stability of the nanoparticle deposits is regarded as another advantage of the method. In an animal model of prostate cancer it was demonstrated that 10 days after injection of the magnetic fluid almost 90% of the dose of ferrites was still detectable in the tumor[27].

Magnetic fluid hyperthermia is feasible and can be safely applied in humans. Mean CEM 43°C T90 values achieved in our clinical studies compare favorably to the results of other groups using the same thermal dose definition[28-30].

Because survival benefit or time to progression were not defined endpoints of the finished feasibility studies. it is still too early to claim therapeutic advantages for the applied method.

Several strategies are available to further improve the effectiveness of treatment. Since field strengths of up to 18 kA/m can be applied with the applicator used and given the quadratic increase of SAR with increasing magnetic field strength, significantly higher temperatures should be achievable by elevating the H-field (after possible modifications of the applicator). Improvement of the instillation techniques resulting in higher concentrations and a more homogeneous distribution of the nanoparticles within the target area are further ways to optimize this promising approach. Furthermore, non-invasive temperature calculations based on the analysis of post-instillation CT data represent another area of ongoing research.

This new treatment approach is currently being investigated in two efficacy trials, namely recurrences of glioblastoma multiforme (in combination with radiotherapy) and prostate cancer (intermediate risk patients, in combination with LDR brachytherapy). The results of these trials will be of great help in the assessment of thermotherapy as an alternative or extension to the current standard procedures in cancer treatment. Current new developments include the implementation of target functions on the surface of iron oxide nanoparticles, which will be able to bind specifically to certain tumor cell epitopes or vascular target molecules or accumulate in lymph nodes after systemic administration. New classes of similar targeted particles have been developed for MR imaging. Therefore specific iron oxide nanoparticles could lead to advancements in thermotherapy, thermo chemotherapy and diagnostic imaging or combined as so called theranostic approaches. The controlled release of drugs from heat-sensitive particle-drug-conjugates has the potential to reduce side effects of conventional chemotherapeutic regimen[31].

Conclusion

The presence of both groups of iron and magnetic nanoparticles during microwave and magnetism waves irradiation increased tumor death. The results of our study showed that iron nanoparticles are less concentrated in comparison to magnetic ones, causing a rapid rise in temperature, which increases the efficiency of hyperthermia and reduces damage to healthy tissues around the tumor.

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