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Editorial

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Tumor control by targeted therapy using nanoparticles

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Editorial

Cancer is the second largest cause of death in human beings. Over one million new cases of cancer are reported every year world-wide. In spite of the spectacular developments in biology and medicine the incidence of cancer is alarmingly on the rise. Radiotherapy and chemotherapy are the most common modalities of treatments for human cancers. The success of radiotherapy of cancer depends on the radiosensitivity of the tumour cells. In solid tumours cells in the hypoxic region exhibit resistance to ionizing radiation. In case of chemotherapy the systemic toxicities of the therapeutics is a major problem.

One of the major problems encountered in radiotherapy of cancers is the radiation damage to normal cells surrounding the tumour. One of the approaches to circumvent this problem is the use of hypoxic cell radiosensitizers to enhance radiation damage to tumour cells and use of radioprotectors to preferentially reduce the deleterious effects of radiation and thereby imparting protection to the normal cells.[1] The goal of targeted therapy is to kill tumor cells selectively by delivering cytotoxic drugs or high radiation doses to a specific target while minimizing damage to normal cells.

Radionuclide therapy (RNT) involves delivering cytotoxic levels of radiation to tumour sites through administration of radionuclides bound to molecular carriers which get specifically accummulated at the tumour site and cause radiation-induced cellular lethality with short-range particulate radiations or gamma rays.[2] Unlike external beam radiation therapy, RNT targets disease sites at the cellular level rather than on a gross anatomical level.

In cancer chemo-therapy, biodistribution of a systemically administered drug depends on the physico-chemical properties like molecular weight, lipophilicity, etc and often results in sub therapeutic drug levels at the tumor site. The sub therapeutic exposure may not only fail to irradicate the lesion, but can even stimulate overgrowth of resistant malignant cells. Most chemotherapeutic agents possess poor selectivity toward the target tissue and can harm normal cells as well as cancer cells..

Targeted drug delivery is achieved by hybrid organic/ inorganic nanoparticles complexed with chemotherapeutics.[3] Nanoparticles due to their large surface to volume ratio, offer properties like tissue accessibility due to suitable interfacing. These hybrid nanoparticles have potential use as noval intravascular probes for diagnostic (imaging) purpose.[4] Magnetic nanoparticles can be administered intravenously or orally and transported through blood stream to the desired area of treatment. Super paramagnetic particles do not retain any magnetism after removal of magnetic field and they are physiologically well tolerated *in vivo*. Magnetic nanoparticles can be deposited on tumour tissues and heated in an alternating magnetic field to destroy the tumour.[5] It has been shown that magnetic nanoparticles are retained at tumour sites, after per-oral administration combined with a locally applied external magnetic field, due to the magnetic responsiveness of the iron oxide core, thereby enabling magnetic targeting.[6] The deleterious effects of conventional chemotherapeutic agent doxorubicin (having systemic toxicities such as cardiotoxicity and hepatotoxicity) were overcome by conjugating with magnetic ironoxide nanoparticles and application of magnetic field externally in an anmal model. Clinical application of magnetic targeting of epidoxorubicin with external magnetic field was demonstrated in patients with solid tumors.[7] Oxidative therapy using magnetic nanoparticles and D-amino acid oxidase has been demonstrated in an animal model, proving even enzymes can be specifically targeted to tumor using magnetc nanoparticles with the help of external magnetic field.[8] The physical targeting of the tumor by external magnetic field is effective in case of peripheral accessible tumors and may not be suitable for deep seated internal tumors and for these chemotargeting could be effective. Chemotargeting of cytotoxic drugs to tumor was achieved by utilizing the peculiar properties of tumour microenvironment. Hypoxia is a hallmark of malignant tumors and is associated with tumor aggressiveness and resistance to radiation and therapeutics.[3] The imbalance between the rapid rate of tumor growth and blood supply leads to an insufficient oxygen concentration in aggressively proliferating tumors, resulting hypoxic intratumor microenvironment. Aromatic nitro compounds such as nitroimidazoles and nitrotrazoles upon administration to tumour bearing animals get accumulated in the hypoxic tumor regions. This property of the nitrocompounds to get accumulated in tumor microenvironment is best utilized for targeting chemotherapeutics to the tumor tissiue. In tumour bearing mice, oral administration of a complex containing chemotherapeutic doxorubicin (DOX), iron oxide nanoparticles (NP) and the nitrotriazole compound, sanazole (SAN) result in accumulation of the nanocomplex (NP-DOX-SAN) specificallyin the tumor site, thereby enhancing the concentration of doxorubicin in tumor cells. Also, it was found that the cytotoxic phytoceutical, berberine (BBN) when complexed with SAN and iron oxide nanoparticles (NP-BBN-SAN) was effective in reducing tumor volumes upon oral administration to tumor bearing animals.[10] Thus nanoparticles can be effectively used for targeting cytotoxic drugs to cancer cells and achieve better therapeutic outcome. However, more studies are needed to initiate clinical trials.

Acknowledgments

None.

Conflicts of interest

Author declare that there is no conflicts of interest.

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