Annals of Materials Science & Engineering

Austin Publishing Group

Open Access Full Text Article

Editorial

Nanomedicine to Mitigate Toxic Side-Effects of Chemotherapy in Children

Rajasekaran AK* and Krishnan V

Department of Materials Science and Engineering, University of Delaware, USA

***Corresponding author:** Rajasekaran AK, Department of Materials Science and Engineering, University of Delaware, USA

Received: June 03, 2014; **Accepted:** July 25, 2014; **Published:** July 26, 2014

The field of nanoscience and nanotechnology is a multidisciplinary scientific undertaking of research, creation and application of nano-sized materials or devices for the treatment of human diseases. It is widely expected that nanoscience will bring about an inspiring and vital revolution in biomedical research. It encompasses a wide array of applications that range from bioimaging to treatment of incurable diseases to accelerated recovery from physical trauma. This could potentially be achieved by utilizing nanomaterials, nano-biosensors, nanorobots and many related devices. The practical application of any such technology in diagnoses, prevention and treatment of diseases is referred to as nanomedicine.

Unprecedented growth and research in cancer nanomedicine, is widely expected to achieve critical breakthroughs in early diagnosis and treatment of cancer. Applying nanotechnology for specific and controlled delivery of chemotherapeutics, small molecules, genes, proteins and peptides for cancer therapy has been viewed with unabated optimism [1]. Preliminary results based on pre-clinical and clinical trials of nanoparticle based "smart drugs" including liposomal formulations of anthracyclines, cytarabine, polymeric and nab based formulations of paclitaxel (Genexol-PM) have been encouraging [2]. The use of such systems has improved the pharmacological activity and therapeutic properties of clinically used anticancer drugs. The characteristic nano-dimensional structure of these "smart drugs" impedes its' rapid clearance from the body as compared to conventional chemotherapeutics. This is primarily due to tumor cells being able to retain nanoparticles on account of size and other physicochemical properties.

This prevents treatment related side-effects and reduces the need for repetitive high doses of the drug. A good example to be cited is the approval of Nab-paclitaxel (Abraxane) - a nanoparticle formulation of paclitaxel – by the United States Food and Drug Administration (FDA) for the treatment of metastatic breast cancer. The approval was primarily based on results of large randomized clinical trial investigations led by Dr. Gradishar at the Department of Medicine and Robert H. Lurie Comprehensive Cancer Center in Northwestern University, Chicago. The clinical trials revealed high response rates and significantly longer time to disease progression, with absence of hypersensitivity and reduced incidence of grade 4 neutropenia in patients who received Nab-paclitaxel in contrast to the group that received conventional paclitaxel [3]. Clinical trials based on other nanoformulations have also reduced treatment-related toxicity and enhanced life expectancy in cancer patients [2]. Overall, results are encouraging and have motivated the scientific community to take advantage of unique traits nanotherapeutics has to offer for applications in clinical oncology.

Despite the advancement of many nanotechnology applications to clinical trials for treatment of adult cancers, such approaches are not well developed for use in pediatric oncology. Childhood cancers are commonly treated by applying combinations of highly toxic chemotherapeutic agents. These agents were originally designed to treat adult cancers and adult treatment regimens were modified to accommodate for children with cancer. Since combination chemotherapy has proven to be effective in controlling cancer progression, its use in pediatric cancer therapy has not changed for the past couple of decades. The most common cancer in children is acute lymphoblastic leukemia (ALL). Significant improvements in treatment led to extraordinary success in achieving an overall five-year relative survival rate of over 90% for ALL [4]. The unfortunate aspect of this success is chemotherapeutics does not target and destroy cancer cells specifically. Combination chemotherapy therefore results in life threatening side-effects in more than 60% of childhood leukemia survivors. The side-effects can range from developmental problems to major organ damage (cardiotoxicity, deafness, nephrotoxicity) to higher risk for secondary cancers (acute myeloid leukemia) to infertility.

Intravenous administration of nanodrugs ensure continuous and long term delivery of chemotherapeutics specifically to leukemia cells in the peripheral blood. This enhances not only the drug efficacy but also improves survival and reduce treatment related toxicity during chemotherapy. For instance, incorporating dexamethasone into biodegradable polymeric non- targeted nanoparticles improved survival and reduced disease symptoms in preclinical models of ALL [5]. Results from Phase IIb clinical trials of CPX-351 - a liposomal system comprising of drugs used in childhood cancer treatments (Cytarabine and Daunorubicin) - revealed high response rates and reduction in 60-day mortality in adults receiving standard therapy for secondary acute myeloid leukemia [6]. Encouragingly, liposomal vincristine sulfate (Marqibo®) has entered into Phase 1 clinical trials for pediatric ALL therapy [7]. Marqibo® was recently approved by the FDA for treating a rare form of adult cancer (Ph- ALL).

Targeting chemotherapeutics using nanoparticles coated with a ligand, antibody or an aptamer that binds to leukemia cell-surface receptor achieves specific internalization and subsequent accumulation of drugs within the target cell. By manipulating the material composition, it is possible to alter the size, shape and surface chemistry of nanoparticles. By selecting targeting molecules exclusively or abundantly expressed on the surface of the leukemic

Karan et al. © All rights reserved

Citation: Rajasekaran AK and Krishnan V. Nanomedicine to Mitigate Toxic Side-Effects of Chemotherapy in Children. Ann J Materials Sci Eng. 2014;1(2): 2.

cells non-specific uptake of the nanoparticles by normal cells could be minimized to reduce treatment related toxic side-effects. Screening of individual patients' leukemic cells for selecting potential targeting moieties should further enhance the success of targeted delivery of drugs to leukemic cells. Such approach will pave the way for "personalized nanotherapeutics" and should significantly reduce side-effects and improve the quality of life of children treated for cancer.

Pediatric nanomedicine is still in its infancy and well-designed pre-clinical and clinical trials are essential to advance the development of novel systems to treat any form of childhood malignancy. Achieving this goal requires systematic approaches combined with long-term efforts and commitments by interdisciplinary biomedical researchers and clinicians. Minimal research funding for pediatric cancer research has impeded the progress of pediatric nanomedicine. In conjunction with advances in drug discovery, biotechnology and molecular biology, delivery and targeting obstacles can be surmounted to achieve 100% incident free survival in children treated for cancer. The future lies in developing nanosystems that can deliver chemotherapeutics in combination and cure childhood leukemia with reduced treatment-related side-effects.

References

1. Nanotechnology in clinical trials -http://nano.cancer.gov/learn/now/clinical-trials.asp.
2. Krishnan V, Rajasekaran AK. Clinical nanomedicine: a solution to the chemotherapy conundrum in pediatric leukemia therapy. Clin Pharmacol Ther. 2014; 95: 168-178.
3. Gradishar WJ, Tjulandin S, Davidson N, Shaw H, Desai N, Bhar P, et al. Phase III Trial of Nanoparticle Albumin-Bound Paclitaxel Compared With Polyethylated Castor Oil–Based Paclitaxel in Women With Breast Cancer. J Clin Oncol. 2005; 23: 7794-7803.
4. Facts 2014. The Leukemia & Lymphoma Society
5. Krishnan V, Xu X, Barwe SP, Yang X, Czymmek K, Waldman SA, et al. Dexamethasone- loaded block copolymer nanoparticles induce leukemia cell death and enhance therapeutic efficacy: a novel application in pediatric nanomedicine. Mol Pharm. 2013; 10: 2199-2210.
6. J Lancet, J Cortes, T Kovacsovics, D Hogge, JE Kolitz, MS Tallman, et al. CPX-351 is effective in newly diagnosed older patients with AML and with multiple risk factors [abstract]. In 54th ASH Annual Meeting and Exposition. 2012; 120. (Blood- ASH Annual Meeting Abstracts, Atlanta, GA, 2012).
7. National Library of Medicine -http://www.ClinicalTrials.gov.

Ann J Materials Sci Eng - Volume 1 Issue 2 - 2014
ISSN : 2471-0245 | www.austinpublishinggroup.com
Karan et al. © All rights reserved

Citation: Rajasekaran AK and Krishnan V. Nanomedicine to Mitigate Toxic Side-Effects of Chemotherapy in Children. Ann J Materials Sci Eng. 2014;1(2): 2.