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Nanoparticles in Peritoneal Carcinomatosis

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Abstract

The management of peritoneal metastasis remains controversial. The local regional treatments are Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and recently the Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC).

Both methods were improved the survival and quality of life in precisely selected patients. On the other hand major progress has been made through nanoparticles.

In this short review presented the use of nanoparticles a novel tool increase drug delivery and penetration and may be more effective in patients with peritoneal metastasis.

Keywords

Nanoparticle; Peritoneal Carcinomatosis; Peritoneal Cavity; HIPEC; PIPAC

Introduction

The main problem in the management of peritoneal metastasis is the limitation using systemic chemotherapy. Nanoparticles (carriers) are the most important new tool as rational drug design

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optimized the mode of delivery offers an exciting prospect for improving the therapeutic index of chemo-drugs.

To optimize the mode and efficacy of delivery nanoparticles it's important to well now the permeability of blood-peritoneal barrier, and exceeded the expectations of this new tool.

Nanoparticles as Carriers in the Peritoneal Cavity

The conventional therapeutic approaches for cancer are surgery, chemotherapy, radiation therapy, targeted drugs and immunotherapy and sometimes hormonal therapy. The demand for the advancement of novel strategies for precise therapy have been proposed to address for using nanoparticles as drug delivery system [1].

Nanoparticles offer a good pharmacokinetics and peruse targeting and at the same time reduce the phenomenon of tumor multidrug resistance.

The capacity to enter intracellularly and the advantall when delivered intraperitoneally to act selectively to the tumor deposits by active and passive mechanisms. The basic composition of nanoparticles is quiet complex with surface Payer, the shell layer and the core. Specific moieties on the surface layer can interact to enhance tumor localization with an ACTIVE mechanism.

Passive accumulation of nanoparticles is mediated by Enhanced Permeability and Retention effect (EPR), which relies on imperfections in tumor architecture for intratumoral accumulation, and retention due to diminished lymphatic recovery by the tumor [2].

The nanoparticles are different structures with synthesis methods categorized as bottom-up approach or top-down approach with different subclasses both of them. For the drugs within nanoparticles delivery into the peritoneum there are limited studies with Paxcliraxel or Abraxane. The cellular active targeting includes cellular recognition of cell surface receptors and medical endocytosis. Then release of nanoparticle drug in the cytoplasm.

Acts of Nano-drugs in Peritoneal Cavity

Normally for I.P chemotherapy the “ideal” Nano-drug must be with high molecular weight, transporting by the Basel membrane of peritoneal blood barrier which works with trans mesothelial cells and lymphatics.

Previously considerable effort has been devoted to develop a Nano carrier that optimized for peritoneal delivery, including manipulation of size, surface charge and PEG coating.

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The most important is to develop Nano-drugs that optimized the peritoneal delivery according diameter molecular weight, surface charge. Then release of nanoparticle drug in the cytoplasm.

Drug Candidates for Nanoparticles

The search for molecular targets to enhance target the tumor by the nanoparticle has yielded several candidates with potential for clinical utilization. These candidates include folic acid and transferrin which are showing the most effective enhancers [3-7]. An alternative targeting strategy involves is encapsulation of targeted therapeutic agent in non-targeted Nano carrier [8]. Currently, the bevacizumab and pemetrexed only target therapeutics have been used in the peritoneal cavity. Bevacizumab was successfully used as a palliative treatment of malignant ascites in peritoneal carcinomatosis of ovarian origin [9]. Pemetrexed (folic acid targeting drug) used in Phase I trial for treatment of optimally debulked ovarian, peritoneal, and tubal cancers showed lower toxicity and efficacy compare to other chemotherapeutic agents [10,11].

Nanoparticles in HIPEC/PIPAC

The role of intraperitoneal chemotherapy is to maximize tumor penetration and optimize cell death while minimizing systemic toxicity.

HIPEC and PIPAC are two treatments methods that serve this role and have been shown to improve survival [12].

The molecular targets to enhance the tumor by nanoparticles are several but recently we used folic acid and transferrin with encouraging results [5-7]. Two drugs as pemetrexed (Alimta) and bevacizumab (Avastin). Successfully used intra abdominally for ovarian, colorectal, gastric and ascites with excellent response rates.

Various advances in drug delivery System for intraperitoneal therapy such as implants and injectable depots to extend the residence time of chemotherapeutic agents in the peritoneal cavity have been discussed [14]. Based on nanofibers, carbonaceous nanomaterials and polycaprolactone materials were evaluated and termed nano-desings or hybrid beads with anticancer properties [13,15,16].

The administrations immediately offer cytoreduction allows the entire abdominal cavity to be bathed with perfusate and Nano carrier.

This timing prevents the compartmentalization and inadequacy exposure of the entire peritoneal cavity due to post-operative adhesion.

Conclusions

The role of NPs will be very important to the future.

The latest advances in the field of nanoparticles and their application to precision diagnostics and improved treatment strategies for Peritoneal Carcinomatosis (PC) will be discussed. These advances will likely develop both the HIPEC and PIPAC methods that were tested in *in-vitro* and *in-vivo* studies. 1) Nanoparticles as drug delivery systems; 2) Nanoparticles and Near Infrared (NIR) Irradiation; 3) use of nanoparticles in perioperative diagnostic and individualized treatment planning; 4) use of nanoparticles as anticancer dressing's, hydrogels and as active beads for optimal recurrence prevention; 5) finally the current *in-vitro* and *in-vivo* studies and clinical trials of nanoparticles.

Conflict of Interest

The author declares no conflicts of interest.

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