Analysis of the effect of liquid viscosity on the aerosol distribution during Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) using computational modeling

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BACKGROUND

Peritoneal metastases (PM) are a common manifestation of gastro-intestinal and gynecological cancers. Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) has been proposed as a new drug delivery technique to treat patients with PM. During this procedure, a CO_2 pneumoperitoneum (12 mmHg) is established. Subsequently, a nebulizer (Capnopen®, Zimmern, Germany) aerosolizes the chemotherapy into the inflated peritoneal cavity using a high-pressure injector (Injektron™ 82 M, Medtron, Saarbrücken, Germany) with the aim to obtain a homogeneous aerosol droplet distribution. The goal of the present work was to investigate the effect of liquid viscosity on the homogeneity of aerosol distribution during PIPAC using Computational Fluid Dynamics (CFD) modeling.

MATERIALS AND METHODS

Saline (NaCl 0.9%) and Icodextrin solution (Baxter Healthcare Ltd, Illinois, US), a glucose polymer preparation, with concentrations of 4% and 7.5% were used. The liquid viscosity was measured using a capillary viscometer (Paragon Scientific, Birkenhead, UK) according to the protocol of the European Pharmacopoeia 10.0. Experiments were repeated three times; the flow time of the liquid was assumed to be the mean of the three measurements. For the CFD simulation of PIPAC, a box model was generated using COMSOL Multiphysics (COMSOL, Inc., Burlington, VT), representing the peritoneal cavity. It was subdivided in 4 regions, corresponding to dorsal (bottom) to ventral (top) regions of the abdomen, with the nebulizer positioned on top. After mesh generation, the box was first filled with CO_2 gas to reach a pressure of 12 mmHg. Then, liquid (20 mL) was nebulized at a flow rate of 0.5 mL/s and droplet diameter of 30 µm, assuming freeze conditions at the walls. Aerosol droplet behavior during PIPAC for saline and two different concentration of Icodextrin (4% and 7.5%) was compared.

RESULTS

The dynamic viscosity of Icodextrin was 1.88 and 2.24 mPa·s at room temperature for concentrations of 4% and 7.5%, respectively. CFD results revealed that the aerosol droplet distribution for liquids with lower viscosities is more homogenous than liquids with a higher viscosity. As expected, aerosol droplets tended to move more to the dorsal region (bottom) of the box model when viscosity increased, while the ventral region (top) remained unexposed. In addition, the nebulization cone angle decreased by increasing the liquid viscosity, narrowing the aerosol droplets deposition pattern.

CONCLUSIONS

Aerosol droplet transport during PIPAC is affected by the liquid viscosity. A more homogenous distribution of aerosol droplets was found for liquids with lower viscosities.