Nanotherapy Methods for Treating Malignant Pleural Effusion: A Meta-Analysis & Systematic Review of 110+ Tumor Biopsies, Cell Lines, and Murine Models

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ABSTRACT

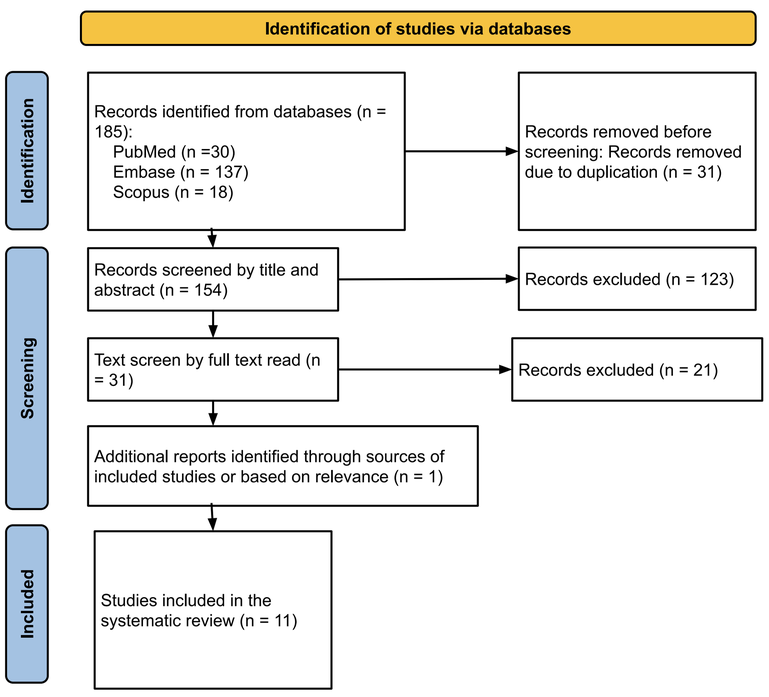
BACKGROUND: A pulmonary embolism is an obstruction of the pulmonary artery by a thrombus structure that forms an embolus and blocks respiratory functionality. In the extreme case of the complications that would normally arise, pulmonary embolisms can turn malignant. These can cause increased pressure in the pulmonary vasculature, which causes fluid leakage in pleural space, or malignant pleural effusion (MPE). A variety of complications include chest pain, productive bloody cough, tachycardia, lung damage, and infection. A modern treatment procedure involves nanotherapy: a treatment with involvement at the nanoscale. **METHODS:** A systematic review investigated the latest nanotherapy methods for malignant pleural effusion. This systematic review utilizes the following databases: Embase, PubMed, and Scopus. Articles were selected based on numerous well-processed searches to reduce redundancy and increase relevance. **RESULTS:** Many viable nanotherapy methods were found to be very effective in drug delivery and the detection of MPE. **CONCLUSION:** Nanoparticles presented for drug delivery and treatment have proved a strong therapeutic efficacy in combating pleural effusion. Further research into nanotechnology in the world of healthcare can develop a new understanding of treatment and diagnostic methods.

INTRODUCTION

A pulmonary embolism is an obstruction of the pulmonary artery by a dislodged blood clot. In the extreme case of the complications that would normally arise, pulmonary embolisms can turn malignant. These can cause increased pressure in the pulmonary vasculature, which causes the leakage of fluid in pleural space, or pleural effusion. Malignant pleural effusion (MPE) impacts nearly 1 million people globally each year. Additionally, it had a high mortality in one study: with 22% mortality at 30 days and 74% mortality at 1 year. This demands more treatment options. There is promising research in the field of nanotechnology for cancer and infections in general. Therefore, some researchers have decided to test it in malignant and non-malignant pleural effusion. This novel method utilized nanoparticles to deliver drugs to infection sites for various diseases, including cancer, diabetes, and neurodegenerative disease. This approach has various benefits, including targeted drug delivery, reduced side effects, and individualized treatments. This paper examines the effectiveness of nanoparticles in treating a malignant pleural effusion.

METHODS

In order to conduct the systematic review, a comprehensive search method was developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines following a PICO (Population, Intervention, Comparison, Outcomes) analysis. Four databases were used in the systematic search: PubMed, Embase, and Scopus. The search string used in all databases was: "(nano OR nanoparticles OR nanotechnology) AND (therapy OR prevention) AND (pleural effusion)." The systematic review software, Covidence, was used for de-duplication and title/abstract and full-text screening. Following this, data extraction was done with Microsoft Excel. Studies implementing nano therapy in pleural effusion, studies measuring the outcome of the therapy, and studies published in English were included in the review. An ethical approval was not deemed to be necessary for this study as it is a systematic review and did not involve living participants. We assessed the quality of non-randomized studies using the ROBINS-I tool. Two independent authors performed the assessments, and any disagreements were resolved through discussion and consensus.



RESULTS

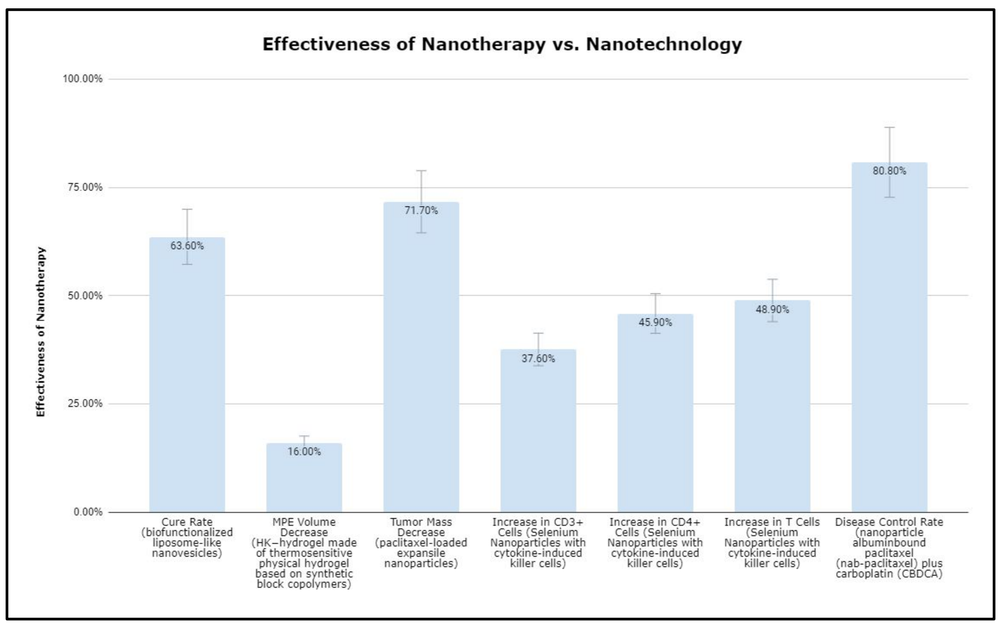


Figure 1: This graph explains the effectiveness of specific nanotechnologies with different statistics reported from each study.

Nanotherapy Methods
radiotherapy-derived microparticles (RT-MPs) in combination with α-PD-1, an immune checkpoint inhibitor
liposomal nanoparticle loaded with cyclic dinucleotide (LNP-CDN)
Nanoparticle albumin-bound paclitaxel
Honokiol Nanoparticles: HK–hydrogel made of thermosensitive physical hydrogel based on synthetic block copolymers
Empty and paclitaxel-loaded expansile nanoparticles (eNP and pax-eNP)
Pemetrexed-loaded gold nanoparticles (GNP-HCPe) targeting CD146 surface markers on MPM cells to enhance drug delivery and efficacy.
Selenium Nanoparticles, which provide Selenium as a drug delivery vector, when γδ T cells pretreated with SeNPs, and combined SeNPs with cytokine-induced killer cells have enhanced efficacy for cancer-killing and tumor growth inhibition
nanoparticle albumin bound paclitaxel (nab-paclitaxel) plus carboplatin (CBDCA)
PEG-coated small unilamellar vesicle (SUV) liposomes labeled with a dye (DiR) to track retention in the pleural cavity and target MPE
a nano system by amalgamating high-molecular-weight Lentinan (LET) (derived from shiitake mushroom polysaccharide) with SeNPs, denoted as LET-SeNPs
drug/gold nanoparticles (AuNPs) conjugates

Table 1: Outlines the nanotherapy methods discovered through the systematic review

DISCUSSION

After an analysis of each of the *Nanotherapy Methods for Treating Malignant Pleural Effusion*, we found that these nanotechnologies were significantly effective in reducing tumor size and spread, leading to better survival rates in the sample and population. **RT-MPs**, in utilization **with α-PD-1**, intrapleurally injected, led to tumor regression and delay in the progression of MPE with a 63.6% MPE cure rate. There were no striking limitations, as it even resulted in significant T-cell infiltration, with immune memory, protecting against future malignant growth. Another nanoparticle with beneficial outcomes in helping treat MPE is **LNP-CDN**, which was shown to improve therapeutic efficacy, especially in individuals not fit for chemotherapy. Intrapleurally injected LNP-CDN targets phagocytes in MPE, enhances anti-PD-L1 immunotherapy, reprograms myeloid immune cells, and promotes cytotoxic effector CD8+ T cells and NK cells. Although specific statistics weren't explicitly stated, a significant increase in immune response to Pleural Effusion was recorded. Another study was done on murine models, focusing on **HK-NP Hydrogel** (Honokiol-Hydrogel) Intrapleural Injections. The mice were first inoculated with Malignant Pleural Effusion, and afterward, on days 4 and 11, were injected with HK-NP Hydrogel, resulting in an overall lifespan increase from 18 to 24.9 days with a definite decrease in pleural effusion size. This demonstrates another nanoparticle drug-delivery system as an effective model to help diminish Pleural Effusion, especially since no striking negative effects were found. **PEG-coated small unilamellar vesicle (SUV) liposomes** were also used in a mouse model. It was found that SUVs were effective in staying in the pleural cavity longer, as well as specifically targeting tumor cells, making them an effective form of treatment. Another nanoparticle delivery system is **SeNPs (Selenium Nanoparticles)**. After Lentinan (LNT), known for antitumor, immune regulation, and anti-infection regulation, was pretreated with SeNP, it was tested on 20 subjects and illustrated positive results in the decrease of Malignant Pleural Effusion. It was noted that this study required more subjects to be fully conclusive, but it illustrates potential. In a study with empty and **paclitaxel-loaded expansile nanoparticles** detonated eNP and pax-eNP. pax-eNP showed superior efficacy demonstrating the potential of nanoparticle drug delivery in pleural effusion while also noting a significant drop in tumor mass. Finally, in the study that utilized **GNP-HCPe** (pemetrexed-loaded gold nanoparticles), the GNPs reduced cell viability for MPE cells; however, something important to note in this study was that some cell lines had different effects which may be the same for patients. *In conclusion, many of these nano-therapy methods should be further assessed via clinical trials to confirm their potential clinical implementation, but they all show potential in helping treat Malignant Pleural Effusion in larger cohort studies.*

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