The current data on nanoparticles and pleura

Öner DİKENSOY, Hasan BAYRAM

Gaziantep Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, Gaziantep.

ÖZET

Nanopartiküller ve plevra hakkında güncel veriler

Nanopartikül çapı 0.1 nm ve 100 nm arasında olan partiküllere verilen genel isimdir. Son zamanlarda çoğu çalışmanın odağı olan karbon nanotüpler, yeni bir tür teknolojik kristal karbon olup sahip oldukları özel fiziksel ve kimyasal nitelikler nedeniyle elektronikten tıbba kadar çoğu alanda kullanılmaktadır. Günümüzde karbon nanotüpler akciğerler dahil çoğu organ üzerindeki etkileri çok sayıda çalışmada araştırılmış olmakla birlikte plevra üzerindeki etkileri kısıtlı sayıdaki hayvan çalışması ve in vitro çalışmalarda araştırılmıştır. Bu derlemede nanopartiküllerin ve özellikle de karbon nanotüplerin plevra üzerindeki etkileri gözden geçirildi.

Anahtar Kelimeler: *Nanopartiküller, plevra, karbon nanotüpler.*

SUMMARY

The current data on nanoparticles and pleura

Öner DİKENSOY, Hasan BAYRAM

Department of Chest Diseases, Faculty of Medicine, Gaziantep University, Gaziantep, Turkey.

Nanoparticle is the general name given to particles with a size between 0.1 nm and 100 nm. Carbon nanotubes, which have been the focus of many studies recently, are a new type of technological crystal carbon, having specific physical and chemical properties and being used in a wide array of fields from electronics to medicine. To date, the effects of carbon nan-

Yazışma Adresi (Address for Correspondence):
Dr. Öner DİKENSOY, Gaziantep Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı,
GAZİANTEP - TURKEY
e-mail: dikensoy@yahoo.com

otubes over various organs including the lungs have been investigated by many studies, while their influence on pleura has been analyzed only by a limited number of animal and in vitro studies. The current data on the effects of nanoparticles and particularly carbon nanotubes to pleura is reviewed in this article.

Key Words: *Nanoparticles, pleura, carbon nanotubes.*

Nanotechnology is one of the most important industrial advances in which engineering is integrated with biology, chemistry, and physics (1). The investments in this field are estimated to reach billions of dollars by 2015. Nanotechnology focuses on changing the physical properties of a material by miniaturization. As the size of a given material is reduced, its physical and chemical properties vary from the original bulk material (2).

Nanoparticle is the general name given to particles with a size between 0.1 nm and 100 nm (1). In order to be called as a nanoparticle, at least one dimension of a particle should be smaller than 100 nm. Currently, nanoparticles and nanofibers are among the most commonly investigated materials for their harm potential over humans, because, in the future, those will be the most frequently used nano-scale materials. Targeted treatment methods and body implants can be mentioned among the technologies that will probably demonstrate breakthrough developments by the use of nanoparticles and nanofibers in the near future (1).

Carbon nanotubes (CNTs), which have been the focus of many studies recently, are a new type of technological crystal carbon, having specific physical and chemical properties and being used in a wide array of fields from electronics to medicine. To date, the effects of CNTs over various organs including the lungs have been investigated by many studies, while their influence on pleura has been analyzed only by a limited number of animal and in vitro studies (1).

Hazard Potential of CNTs to Pleura

One of the most suspected aspects of CNTs is their potential which can cause a tragedy similar to that of asbestos. The reason behind this potential is the structural similarities of CNTs and asbestos (having a form of fiber or rod along with similar length/diameter ratios). On the other hand, in a recent study conducted in People's Republic of China, pleural fluids and materials of seven women that have been subjected to nanomaterial for 5-17 months in a factory were examined by electron microscopy, and presence of nanoparticles with 30 nm size, supportive of the above mentioned suspicion, was determined (3).

Malignant mesothelioma (MM) is a very aggressive tumor originating from mesothelial surfaces such as pleura and it occurs as a result of exposure to asbestos mineral fibers (1). However, epidemiological studies show that MM may arise due to exposure to other fibers, called as asbestiform, which include non-asbestos or asbestos-like fibers (4,5). Moreover, some animal studies have shown that MM might be seen because of vitrous fibers produced by humans, as well (6). Particularly, the high ratio of length/diameter in asbestos types, increases the carcinogenic properties (5,7,8). Currently, the mechanisms leading to MM due to asbestos exposure, are not clearly understood.

In Vivo and In Vitro Studies

To date, the effects of CNTs over mesothelial cells have been investigated by seven studies. Three of those were animal studies, whereas four were performed in vitro on cells. In one of the animal studies, inflammatory response and pathological changes occurring after the peritoneal injection of CNTs, were studied (9). Investigators subjected C57B1/6 mice to four types of multi-walled carbon nanotubes (MWCNTs) with varying size and aggregation phases. They also tested two amosite fiber samples. The primary target of the study was the quantification of inflammation by analyzing peritoneal lavage and diaphragm. Consequently, only MWCNT samples and amosite fibers were found to cause inf-

lammation and granuloma. Histologic analysis demonstrated presence of frustrated phagocytosis in the macrophages. Only long fibers were responsible from the frustrated phagocytosis and granuloma development. Ichihara et al. published a study focusing on long-term effects of MWCNTs on animals (10). In that study, MWCNTs were injected into the periosteal space of C57Bl/6 p53+/- mice, while the other group (control) received crocidolite asbestos. Since those mice carry *Trp53* gene mutation in one of their alleles, they are susceptible to cancer development. The autopsies performed after 25 weeks revealed equal amount of peritoneal MM development in both of the groups (10). In another very recent study, MWCNTs were injected intrascrotally to 7 Fischer 344 rats and the animals were observed for 52 weeks (11). Eighty two percent of the MWCNTs had a diameter of 70-100 nm, whereas 72.5% had a length of 1-4 μm. While 5 rats were included as the control group, crocidolite was injected to 7 rats as a positive control group. Mesothelioma incidence in the MWCNT group was 86%, whereas none of the control groups (including the crocidolite group) demonstrated mesothelioma. However, in those studies, the mechanisms and the role of mesothelial cells in MM development are not known.

In the literature, there are only four in vitro studies focusing on the effects of nanoparticles on mesothelial cells. In one of those studies exposure of normal mesothelial cell rows and MM cell rows to single-wall CNTs was investigated (12). In that study, investigators reported DNA damage both in the normal mesothelial cells and MM cells along with cell activation through (AP)-1, NF-κB, and Akt . In another study, similarly, normal human mesothelial cell rows were subjected to single-wall CNTs which led to alterations in the cellular viability and reduction of cell proliferation (13). Three of the previous studies reported CNTs as cytotoxic for normal human mesothelial cell rows, MM cell rows, and TSV-40-transformed mesothelial cells (12-14). It was remarkable that the same CNT material exhibited various levels of cytotoxicity over human mesothelial cell rows as a result of being dispersed in various degrees (14). In that study, the cytotoxicity of CNT bundles (having a diameter of aproximately 20 nm at best dispersion) were reported to be lower than those of CNT aggregates (having a diameter at μm levels). While in vitro studies demonstrate uptake of CNTs by various cell types, they also show some contradictory results (15,16). On the other hand, several studies report that cells do not uptake those particles (17). Cellular uptake is probably associated with cellular receptors and cell surface functions along with the reactivity between surfaces of CNTs (4). Depending on the cell type, many cell surface functions can be identified (4).

Moreover, CNTs may be carrying various reactive groups. Different types of chemicals and biological molecules used for dispersing CNTs, may be modifying the surface of CNTs (4). Therefore, cellular CNT interactions appear to be dependent on many intrinsic and extrinsic parameters. Also, surface modification of asbestos fibers alters the cellular responses, as well (18-22). The receptor (MARCO), cleaning the collagenous structure in macrophages, is believed to play a role in lung damage associated with inorganic particles, and this mechanism may have an effect on the interaction between the plasma membranes of macrophages and MWCNTs (23,24). Integrin receptors in mesothelial cells have been reported to interact with asbestos fibers (20,25). Most recently, large TSV40-transformed mesothelial cells exposed to MWCNTs, have not demonstrated particular internalization despite the cytotoxicity (13).

CONCLUSION

In conclusion, although it is one of the most popular fields of science, there is not much study focusing on the effects of CNTs over mesothelial cells and further investigations are definitely needed. However, detection of nanoparticles in the human pleura and development of mesothelioma in animal studies due to nanoparticles delivered through inhalation or direct injection, raise suspicions about nanotechnology which enters our lives more and more each day.

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