Effect of Nanodisperse Ferrite Cobalt ($CoFe_2O_4$) Particles on Contractile Reactions in Guinea Pigs Airways

L. V. Kapilevich, E. Yu. D'yakova, A. V. Nosarev, T. N. Zaitseva*, Z. R. Petlina*, L. M. Ogorodova, B. G. Ageev*, A. A. Magaeva, V. I. Itin**, and O. G. Terekhova****

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 149, No. 1, pp. 77-79, January, 2010
Original article submitted March 19, 2009

The effect of nanopowder $CoFe_2O_4$ on contractile responses of smooth-muscle segments of guinea pigs airways was studied by mechanography. Both *in vivo* inhalation of nanopowder aerosol or *in vitro* application of nanopowder to isolated airway segments increased the amplitude of contractile responses to histamine and potentiated the dilatory reaction to adrenergic salbutamol.

Key Words: *nanodisperse structures; contractile response; airways*

Modern industrial development is closely related to advances in nanotechnology, which can shape the overall technical progress in the nearest future. However, alongside with evident benefits, wide use of nanotechnology can be accompanied by negative side effects for the environment and human health. The nanoparticles penetrate into human organism via the digestive tract, mucosae, and mainly via the lungs [3]. The most important property underlying the negative effects of nanoparticles on human health is their ability to pass into the alveolar regions of the lungs and induce mechanical, toxic, and immunological damages. Aerosol nanoparticles are characterized by large specific surface area and in some cases by high degree of imbalance determining high concentration of radical centers on the surface and high toxicity [5].

Disorders in the respiratory system can manifest in inadequate responsiveness of the airway wall to various physiological and biological stimuli leading finally to bronchospasm.

Our aim was to examine the effect of nanoparticle suspension on contractile activity of smooth muscle segments isolated from guinea pig airways (AW) during inhalatory or direct application of nanoparticles.

MATERIALS AND METHODS

The experiment was carried out on mature male guinea pigs (n=26).

Nanopowder $CoFe_2O_4$ was obtained by mechanochemical synthesis in salt systems performed in Department of Structural Macrokinetics, TRC SD RAS. The size of the nanoparticles was 5-20 nm. Cobalt ferrite was chosen for preparation of nanoparticles, because it is an inert substance [4] and does not react with the biological tissues and fluids.

Group 1 animals (n=6) inhaled the suspension of $CoFe_2O_4$ nanoparticles, which was prepared in distilled water. Inhalation was performed with a Musson-1M ultrasonic nebulizer (OJS Altay Instrumental Factory Rotor) 30-min per day for 4 days.

After inhalation course, the animals were sacrificed by cervical dislocation, 3-4-mm AW rings were

Siberian State Medical University, Russian Ministry of Health; *Institute of Atmospheric Optics, Siberian Division of the Russian Academy of Sciences, **Department of Structural Macrokinetics, Tomsk Research Center, Siberian Division of the Russian Academy of Sciences, Tomsk, Russia. ***Address for correspondence:*** adyakova@yandex.ru. E. Yu. D'yakova

0007-4888/10/1491-0070

prepared from the trachea and major bronchi. The epithelium was removed mechanically by rotation of a wood spatula in the segment lumen for 1 min.

Group 2 animals (n=8) were killed by cervical dislocation. AW rings prepared as in group 1 were incubated in the suspension of $CoFe_2O_4$ nanoparticles (0.5 mg/ml) for 30 min.

The control group animals (n=12) inhaled distilled water aerosol by the same scheme as in the experimental group 1 animals.

In all groups, mechanical tension of smooth muscle in AW segments was measured by mechanography using an FT10G isometric force transducer.

Before the experiments, the segments were tested with high-potassium Krebs solution (40 mM KCl). The amplitude of the response to this stimulus was taken as 100%. The amplitude of contractile responses to histamine and salbutamol was measured in percents of control contraction and dose-response curves were constructed.

The data were processed with Statistica 6.0 software and presented as mean and SEM ($X \pm m$).

RESULTS

In experimental series I, we examined the effect of nanopowder suspension on histaminergic contractile responses of AW smooth muscle ring segments.

All examined segments responded by dose-dependent contractions to histamine applied within the concentration range of 1-100 μM. In these tests, the amplitude of contractile responses of the segments incubated with nanopowder suspension (n=9) and the segments isolated from guinea pigs inhaling nanopowder (n=8) was significantly higher than in the control group (p<0.05 for both groups, Fig. 1). It is noteworthy that the responses of group 2 segments (incubated in nanopowder suspension) were 2-fold more potent than the responses of group 1 segments isolated from animal subjected to inhalation of nanoparticles (p<0.05).

In experimental series II, we examined the effect of nanopowder on the adrenergic contractile responses of AW smooth muscle ring segments. The test solution contained β_2 adrenoceptor agonist salbutamol. It was applied after conditioning solution with histamine (100 μM), which induced preliminary contraction.

Deepithelized segments responded to salbutamol (0.1 nM-10 μM) by dose-dependent relaxation. In both experimental groups (incubated segments, n=14; segments from pigs subjected to inhalation of nanoparticles, n=8), relaxation was more pronounced than in the control group (Fig. 2, p<0.05).

Thus, both *in vivo* and *in vitro* application of $CoFe_2O_4$ nanoparticles potentiated the contractile responses to histamine and dilatatory reactions to salbutamol of isolated AW segments.

A number of reasons can cause the described effects. First, inhalation of nanoparticles could provoke unspecific inflammation in the AW wall. Similar potentiation of contractile responses was observed during the formation of AW hyperreactivity in experimental animals [2,6]. Some investigators reported respiratory problems in experimental animals inhaling carbon nanotubes [7], which can be associated with up-regu-

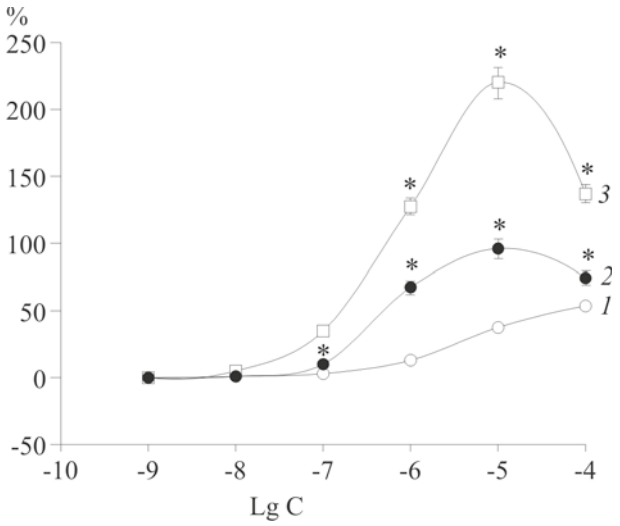

Fig. 1. Dose-dependent effect of histamine on contraction amplitude of guinea pig airway smooth muscle segments. Abscissa: decimal logarithm of histamine concentration. Ordinate: mechanical tension in percentage of preliminary response to high-potassium Krebs solution. Here and in Fig. 2: *1*) control AW segments; *2*) AW segments isolated from the animals subjected to nanopowder inhalation; *3*) AW segments incubated in nanopowder suspension. *p<0.05 compared to the control AW segments.

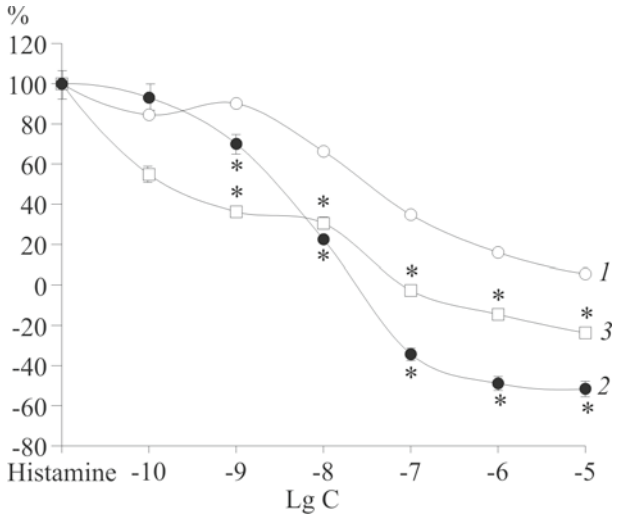

Fig. 2. Dose-dependent effect of salbutamol on the amplitude of dilatatory responses of guinea pig airway smooth muscle segments. Abscissa: decimal logarithm of salbutamol concentration.

lation of the expression of receptors to histamine and salbutamol or with increased sensitivity of these receptors. Second, application of nanopowder to isolated AW segments can directly damage cell structures, *e.g.* cytoskeleton. We made such an inference from comparison of the contractile responses to high-potassium Krebs solution in AW segments preconditioned with non-selective cytoskeleton disintegrator colchicine or with a nanomaterial [1]. The present data attest to similar mode of action of the nanomaterials. The data on erythrocyte distortion under the action of ultradispersive structures also favors the hypothesis of cytoskeleton lability under the action of nanostructures.

This work was supported by the Russian Foundation for Basic Research, grant No. 09-04-99124-r-ofi.

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