Abstract

Optimizing of anesthetic dosing to reduce side effects is the major challenge of modern anesthesiology [237,238]. Understanding the mechanism of action of anesthetic molecules on the molecular level is essential to understand this process [239-241]. It is postulated that anesthetics can interact with the ion channels on the conductivity-reduced way. Still is the question: are the molecules of anesthetics bind directly to the transmembrane proteins or indirectly influence their activity by perturbation the structure of lipid membranes? The research [96,97,106,115,130-139] confirmed that the ability to dissolve in fats is related to the degree of anesthetic effect. It suggests that anesthetics may interact with lipids of biological membranes and, by modifying their structure, indirectly influence on the conduction of nerve impulses through ion channels. Therefore, the aim of the study was to investigate the effect of four selected inhalation anesthetics (halothane, enflurane, isoflurane and sevoflurane) on the structure of lipid membranes consisting of dipalmitoylphosphatidylcholine (DPPC) or dipalmitoylphosphatidylglycerol (DPPG) with or without cholesterol (Chol) molecules inside, which are the model of natural biomembranes. The comparison of phospholipids characterized by different physic-chemical properties was aimed to obtain various and objective perspectives of the phenomena observed in model lipid membranes and relating them to those occurring in different areas of natural bilayers.

The implementation of the task set in this experiment was possible by the use of the mid-infrared (MIR) and near-infrared (NIR) vibrational spectroscopy techniques as a function of increasing temperature. These techniques were supported by the chemometric analysis (PCA). NIR range infrared spectroscopy was used for the first time to monitor modifications in the hydrophobic region of model lipid bilayers. It has been shown that NIR range infrared spectroscopy can be an alternative technique to the commonly used MIR range infrared spectroscopy in the study of this type of systems. In addition, in the systems of anesthetic-doped DPPC model membranes, the EPR spectroscopy allowed us to track the dynamics of the examined systems.

NIR range infrared spectroscopy, thorough analysis of changes in the hydrophobic region of lipid membranes, monitoring the evolution of the phase transitions of lipid bilayers was performed. This process was based on conformational changes within the hydrocarbon lipid chains. It has been proved that all analyzed general anesthetics exert a significant influence on the analyzed model lipid membranes. Moreover, a gradation of the influence caused by halogenated hydrocarbon components on the conformational state of the hydrophobic region of the liposome systems was achieved. The

halothane was the strongest modifier of the conformational state and temperature of main phase transition of the lipid bilayers, the weakest was sevoflurane, while enflurane and isoflurane caused a middling modulating effect. It has also been shown that the type of lipid components which constituting the bilayer, which changes the membrane charge, are of significant importance for the strength of the interaction between the molecules of anesthetics and the lipids forming the model membranes.

The use of the EPR technique allowed us to extent the information obtained by the method of NIR spectroscopy about the processes taking place in various regions of the model DPPC membranes in the presence of inhalation anesthetics. It has been shown, that the molecules of anesthetics modify the hydrophilic region of the lipid bilayer more strongly, middling affecting the nonpolar region of the model DPPC membrane. On the other hand, the data obtained from EPR spectra on the influence of individual anesthetics on DPPC liposome systems confirm conclusions from the NIR tests that halothane is the strongest, sevoflurane the weakest, and enflurane and isoflurane with is modifier of the structure of model DPPC membranes with an intermediate strength.