

EPIGENETIC APPROACHES BY ANALYSIS OF CIRCULATING MIRNAS AND GLOBAL DNA METHYLATION IN VETERINARIANS OCCUPATIONALLY EXPOSED TO VOLATILE ANESTHETICS

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ABSTRACT

INTRODUCTION: Several professionals around the world face occupational exposure to inhalation anesthetics, and chronic occupational exposure to waste anesthetic gases (WAGs) is associated with DNA damage. Circulating microRNAs (miRNAs) are potent post-transcriptional regulators involved in molecular changes associated with exposure to occupational toxicants; however, miRNAs and global DNA methylation have not yet been investigated in relation to occupational exposure to WAGs, showing the novelty of the present study. **OBJECTIVE:** To measure urinary levels of isoflurane and sevoflurane (exposure levels) and investigate epigenetic profiles via circulating miRNAs and DNA methylation in professionals who worked in veterinary operating theaters and were occupationally exposed to WAGs. **MATERIALS AND METHODS:** 29 individuals exposed to at least one year to WAGs and 28 matched-controls were investigated. Urine was collected to identify both halogenated anesthetics by gas chromatography combined with a mass spectrometry. DNA methylation levels were quantified by high-performance liquid chromatography. Total RNA was extracted from plasma samples, and miRNA expression was analyzed using the *NanoString nCounter® Human v3 miRNA Expression Panel*. Data were normalized and submitted to differential expression and functional analyses using standard bioinformatics tools. **RESULTS AND CONCLUSION:** High levels of urinary anesthetics were identified. No difference was observed between groups in relation to global DNA methylation status ($p > 0.05$). However, comparison between the exposed and control groups revealed eleven differentially expressed miRNAs, with seven upregulated in the exposed group (fold change ≥ 1.5). Functional analyses indicated the involvement of these miRNAs in pathways related to inflammation, oxidative stress, apoptosis, cell proliferation, and cell cycle regulation, including PI3K-Akt, MAPK, TGF- β , and FoxO signaling. The identification of these molecular events contributes to a better understanding of the biological effects of chronic exposure to WAGs and highlights the importance of miRNAs as potential biomarkers. In conclusion, our study suggests that occupational exposure to WAGs is associated with modulation of expression of

circulating miRNAs, but not with global DNA methylation, and suggests that urinary isoflurane and sevoflurane can be considered suitable biomarkers for monitoring occupational exposure to WAGs in veterinarians.

Keywords: circulating microRNAs; occupational exposure; anesthetic gases; differential expression; epigenetics

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