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Identification of putative biomarker for early detection of meloxicam-induced kidney injury in cats: a metabolomic and lipidomic approach

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Abstract

Statement of the Problem: The repeated administration of the nonsteroidal anti-inflammatory meloxicam damages kidneys in cats. Serum creatinine and symmetric dimethylarginine are used to detect and monitor changes in kidney function. However, these biomarkers do not detect alterations in kidney function earlier than 10 days after the onset of kidney damage. Early detection of meloxicam-induced kidney damage would provide the best chances of maximizing the clinical use of this drug in cats. Unfortunately, biomarkers for detecting early NSAID-induced kidney damage in cats are yet to be discovered. The purpose of this study is to identify biomarker candidates for detecting early renal changes within 4 days after starting the repeated administration of meloxicam. Methodology & Theoretical Orientation: Cats (n=12) were treated subcutaneously with either saline solution or a labeled dose of meloxicam every 24 h for up to 4 days to induce acute kidney injury. The plasma and urine metabolome and lipidome were determined before and after the administration of the treatments by LC- and GC-MS/MS. Findings: The repeated administration of meloxicam altered the feline plasma and urine metabolome and lipidome as demonstrated by multivariate analysis. By using random forest and receiving operating characteristic analyses, we identified 24 compounds in plasma and urine that could serve as biomarker candidates for discriminating meloxicam-treated from saline-treated cats. In addition, we identified 23 biomarker candidates using the group of meloxicam-treated cats as its own control. Notably, phenylethylamine, nicotinic acid, and oxalic acid were common biomarker candidates observed between and within groups. Conclusion & Significance: This is the first report on the identification of lipidomic and metabolomic changes in urine and plasma induced by the repeated administration of meloxicam to healthy young-adult cats. Early diagnosis of kidney diseases will facilitate effective inter-ventions that may slow down the progression of kidney disease.

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