

METHODS OF IDENTIFYING PATHOMORPHOLOGICAL LESIONS IN THE KIDNEYS OF OFFSPRING BORN UNDER CONDITIONS OF CHRONIC POISONING IN THE MOTHER

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The purpose of the study: Acute kidney injury is the leading cause of nephrology consultation and is associated with high mortality rates. The primary causes of AKI include ischemia, hypoxia or nephrotoxicity. An underlying feature is a rapid decline in GFR usually associated with decreases in renal blood flow. Inflammation represents an important additional component of Acute kidney injury leading to the extension phase of injury, which may be associated with insensitivity to vasodilator therapy. It is suggested that targeting the extension phase represents an area potential of treatment with the greatest possible impact. This article provides information on the methods of identifying pathomorphological lesions in the kidneys of offspring born under conditions of chronic poisoning in the mother.

Contents of the study :The kidneys are one of the most frequently injured retroperitoneal organs during abdominal trauma with blunt objects. The main task

of forensic medical research in mechanical injuries is to establish the mechanism, lifetime and duration of injury . One of the most important functions of the kidney is the filtration and excretion of nitrogenous waste products from the blood. The measurements of elevated blood urea nitrogen (BUN) and creatinine serve as indicators of decreased renal function indicative of the decreased clearance of these waste products. AKI is currently defined as a rapid decline in the glomerular filtration rate (GFR) resulting in retention of nitrogenous wastes, primarily creatinine and blood urea nitrogen. Consequently, the diagnosis currently is dependent on the serial measurement over time of these substances in the blood of patients. The rapidity of this decline may occur over a time course of hours to months, but typically occurs over the course of hours to days. The ability of these measurements to serve as a surrogate marker of GFR is relatively imprecise and improved methods for evaluating GFR and a direct assessment of renal injury are sorely needed in the practice of medicine .

Research methods and materials: In recent decades, work has appeared devoted to kidney injury, but remains unexplored morphology of damage to this organ to resolve the issue of the peculiarities of the mechanisms of injury formation points. In addition, in the literature there are no reliable criteria by which one can establish the lifetime and duration of formation of kidney damage, including taking into account the influence on the development of reactive changes in some additional factors, such as shock. A second emerging marker used increasingly to assess acute renal injury is the presence of neutrophil gelatinase-associated lipocalin (NGAL, also known as lipocalin-2). Levels of NGAL expression in the kidney are normally low, but increase markedly as a result of renal cell damage. Elevated early in the etiology of acute kidney injury, resulting from ischemia or cisplatin exposure, NGAL was found to rise earlier than other, more commonly used urinary kidney injury markers such as creatinine, albumin, or cystatin C. Exposure to stressors during development has been shown to result in physiologic changes to the developing offspring, changes that promote in utero survival. While such changes enhance survival in utero, they may result in greater disease risk later in life. However, few studies have examined such outcomes following exposure to NP. An investigation that examined the effects of titanium dioxide exposure during pregnancy in rats revealed microvascular impairments in the maternal uterine arterioles that resulted in cardiac mitochondrial insufficiency in the offspring that persisted through adulthood. In our previous studies, pregnant mice were exposed by inhalation to CdO NP, and while Cd was not measurable in the fetus, there were

effects on neonatal growth and sex-dependent dyslipidemia in adult offspring fed a high-fat diet (report in preparation). Changes arising from stressors from development have also been associated with adult hypertension and kidney disease in humans. The primary goal of this offshoot study was to test the hypothesis that short-term, repeated inhalation exposure of pregnant mice to CdO NP results in kidney injury in the mother and neonate, as evidenced by changes in urinary levels and/or mRNA expression of Kim-1 and NGAL in neonatal kidneys.

Results and reasoning :Maternal kidneys recovered from dams at GD 10.5 ($n = 3-4$ /treatment group) were fixed in formalin and shipped to Colorado Histo-Prep for embedding, sectioning (5 μm), and staining with hematoxylin and eosin. Tissue sections were viewed by light microscopy using a Nikon E400 epifluorescent microscope. Images were captured with a 40 \times objective using an Evolution MP digital air-cooled color camera equipped with Image Pro Plus (v. 7.0) image acquisition software. The scale bar indicates a length of 100 μm . To evaluate consistency of these morphologic changes from one tissue sample to another, three images were captured from random fields of the renal cortex from each sample. Statistical analyses were performed using SAS. All data were analyzed by one-way analysis of variance with treatment and time as main effects. Real-time PCR values were compared for each treatment group by calculating the ΔCt values for each individual sample and subtracting the Ct value for 18S rRNA from the Ct values for both Kim-1 and NGAL. Real-time PCR expression data, presented as ΔCt values, were used for comparison between treatment groups using one-way ANOVA. A lower ΔCt value represents a higher level of expression. Fold changes presented in the text were computed using the formula $2^{-\Delta\Delta\text{Ct}}$. When appropriate, post hoc testing was performed using Fisher's least significant difference (LSD) test. Data presented are means \pm SE.

Summary :Under normal conditions, animals have sufficient renal function to survive with only one functioning kidney. Unfortunately, this is not always the case for animals with kidney damage. In some cases, the ability to measure the individual renal function is important because such cases may include the prospect of nephrotomy or nephrectomy. An assessment of the individual renal function can have a significant impact on the plan to surgically remove kidney stones or the entire kidney damaged by an infection or tumor. Non-invasive means of determining renal function in individual kidneys may be advantageous during planning for medical management or surgical intervention of renal diseases.

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