[Mechanisms of hepatocyte multinucleation in rats exposed to N-nitrosodimethylamine].

Автор:Shalakhmetova, T M; Umbaev, B A; Kolumbaeva, S Zh; Kudriavtsev, B N

Tsitologiia

Том:51

Выпуск:1

Стр.:34-42

Опубликовано:2009

Аннотация
Mechanisms of hepatocyte multinucleation were investigated in rats exposed to N-nitrosodimethylamine (NDMA).Using immunohistochemical reaction to y-tubulin it was established that the number of cells containing three and more centrosomes increased in 48 h after NDMA injection. It was shown that formation of extra-centrosomes in hepatocytes was enhanced by oxidative stress induced by cytochromes P450 superfamily in the course of NDMA metabolism. NDMA administration led to a sharp increase in cytochrome P450 content in the liver, especially in 24 and 48 h (3.3 and 2.8 times respectively) after NDMA injection. Extensive staining of cytoplasm in the centrolobular hepatocytes was revealed by immunohistochemical reaction to cytochrome P450 2E1 in 24 and 48 h after the NDMA injection. Malone dialdehyde (the derivative of lipid peroxidation) was shown to increase 1.1-2.0 times, whereas catalase activity as of the antioxidative agent reduced to 1.1-1.3 times in that time. In 72-120 h after NDMA treatment, the number of cells with three or more centrosomes, the intensity of cytoplasmic staining, cytochrome P450 and malone dialdehyde contents in the liver were shown to decrease, whereas catalase activity increased. In 48 h after treatment, binucleated hepatocytes with various 3H-thymidine distribution in nuclei appeared in NDMA-treated cell populations evidencing of asynchronous DNA synthesis. Immunohistochemical reaction against Ki-67 proliferation marker revealed asynchronous nuclear proliferation activity in binucleated cells spreading not only to S-phase, but also to other phases of cell cycle, and namely G1, G2 and M. Thus, main mechanisms of hepatocyte multinucleation under NDMA exposure are accounted for hyperamplification of centrosomes as a consequence of oxidative stress and for asynchronous DNA synthesis in the nuclei of binucleate hepatocyte followed by asynchronous acytokinetic mitosis.
Категории/классификация

Направления исследования:Cell Biology; Biochemistry & Molecular Biology; Toxicology; Pharmacology & Pharmacy; Microscopy; Gastroenterology & Hepatology (предоставленные Thomson Reuters)

Термины MeSH:

Заголовок	Классификатор
Animals	
Cell Nucleus	*metabolism
	ultrastructure
Centrosome	ultrastructure
Cytochrome P-450 CYP2E1	metabolism
Dimethylnitrosamine	pharmacokinetics

	*toxicity
Hepatocytes	*drug effects
	enzymology
	ultrastructure
Immunohistochemistry	
Lipid Peroxides	metabolism
Liver	*drug effects
	enzymology
	ultrastructure
Male	
Oxidative Stress	*drug effects
Rats	
Tubulin	analysis

Химические:

Реестровый номер	**Содержимое**
0	Lipid Peroxides
0	Tubulin
EC 1.14.13.-	Cytochrome P-450 CYP2E1
M43H21IO8R	Dimethylnitrosamine

Информация о документе

Тип документа:English Abstract; Journal Article; Research Support, Non-U.S. Gov't

Язык:Russian

PubMed ID:19281047

Уникальный идентификатор NLM:0417363

Дата создания: 13 Mar 2009 Дата завершения: 13 Apr 2009 Дата проверки: 20 Nov 2014

Страна: Russia (Federation)

ISSN:0041-3771

Другая информация

Подвыборка цитирования:Index Medicus

Состояние:MEDLINE