

Evaluation of effects of methamphetamine repeated dosing on proliferation and apoptosis of rat germ cells

Alavi, S.H.^a, Taghavi, M.M.^b, Moallem, S.A.^c

^a Department of Anatomy, School of Medicine, **Mashhad University of Medical Sciences, Mashhad, Iran**

^b Department of Anatomy, School of Medicine, Rafsanjan **University of Medical Sciences, Rafsanjan, Iran**

^c Department of Pharmacodynamics and Toxicology, School of Pharmacy, **Mashhad University of Medical Sciences, P.O. Box 91770-1360, Mashhad, Iran**

[View references \(7\)](#)

Abstract

Methamphetamine (MAMP) is a central nervous system stimulant that is increasingly abused especially by teenagers and young adults, a group in its reproductive age. MAMP effects on the male reproductive system are not clear. In this experimental study, we evaluated the effects of MAMP administration on proliferation and apoptosis in seminiferous tubules of rat testis. Methamphetamine hydrochloride was synthesized by iodination of norephedrine hydrochloride and reduction to methamphetamine. Mature male rats were randomly divided into four groups (n=7) and were injected intraperitoneally with MAMP (1, 2 or 10 mg/kg) or saline at the same time, once daily for 14 consecutive days. Twenty four hrs after the last injection, perfused testis were fixed, sectioned and stained by TUNEL labeling or proliferating cell nuclear antigen (PCNA) immunostaining. Apoptosis and proliferation indices were calculated and ratios of proliferation/apoptosis in the seminiferous tubules were obtained. Cell proliferation and the ratio of proliferation to apoptosis decreased significantly in all experimental groups compared to the control group. Conversely, apoptosis was increased in these groups. Such differences were observed in both spermatogonia and primary spermatocytes. In the control group, more than 90% of spermatogonia were PCNA-positive. However, 10 mg/kg of MAMP caused a reduction to approximately 50% PCNA staining in spermatogonia. In some tubules of the experimental groups, more than 10 TUNEL-positive germ cells were seen, although in the control group, the tubules with 2 TUNEL-positive germ cells were rarely observed and the majority of tubules were without such cells. There were significant differences in the indices between the 1 mg/kg group and the higher dose groups, but there was no such difference between the 2 mg/kg and 10 mg/kg groups. In some tubules of the experimental groups, significant gaps in the epithelium between the spermatogonia layer and other cell layers were observed. These results show that repeated administration of MAMP, especially at higher doses, may cause a decrease in cellular proliferation, induce apoptosis and change the proliferation/apoptosis ratio in testis. This might explain the MAMP effect on the spermatogenesis process. It is suggested that studies on the consequence of MAMP consumption on male fertility is warranted. Copyright © Informa Healthcare USA, Inc.

Author keywords

apoptosis; male reproductive system; methamphetamine; proliferating cell nuclear antigen; proliferation; rat; spermatogenesis

Indexed Keywords

EMTREE drug terms: central stimulant agent; cycline; methamphetamine

EMTREE medical terms: animal; apoptosis; article; cell proliferation; dose response; drug effect; immunohistochemistry; immunology; intraperitoneal drug administration; male; nick end labeling; pathology; rat; seminiferous tubule; spermatozoon; Sprague Dawley rat

MeSH: Animals; Apoptosis; Cell Proliferation; Central Nervous System Stimulants; Dose-Response Relationship; Drug; Immunohistochemistry; In Situ Nick-End Labeling; Injections, Intraperitoneal; Male; Methamphetamine; Proliferating Cell Nuclear Antigen; Rats; Rats, Sprague-Dawley; Seminiferous Tubules; Spermatozoa

Medline is the source for the MeSH terms of this document.