INVolvement of nitric oxide in the hypnotic effects of benzodiazepines in mice.

Sylwia Talarek, Sylwia Fidecka

Department of Pharmacodynamics, Medical University School, Saszica 4, PL 20-081 Lublin, Poland


The influence of nitric oxide (NO) on hypnotic activity of diazepam, chlordiazepoxide and clonazepam was studied in mice. Administration of both non-selective NO synthase inhibitors: Nω-nitro-L-arginine methyl ester (L-NAME), Nω-nitro-L-arginine (L-NOARG) and selective NO synthase inhibitor 7-nitroindazole (7-NI) resulted in significant increase in the duration of diazepam-, chlordiazepoxide- and clonazepam-induced sleep. The effects of co-administration of the examined inhibitors with benzodiazepines were not changed by L-arginine, a substrate for NO formation. Administration of L-arginine alone had no effect on the duration of sleep induced by benzodiazepines. Methylene blue, the guanyl cyclase inhibitor, was able to increase the duration of benzodiazepine-induced sleep. These findings suggest that the cGMP/NO system may participate in hypnotic effects of benzodiazepines.

Key words: nitric oxide, benzodiazepines, sleep, mice