Ethanol-Ecstasy (MDMA) Interactions in Rats: Effect on MDMA Pharmacokinetics and Body Temperature

Takeshi Saito*, Shigeaki Inoue, and Sadaki Inokuchi
Tokai University School of Medicine, Department of Emergency and Critical Care Medicine, Kanagawa, Japan

AIMS: Recreational use of Ecstasy, (±)-3,4-methylenedioxymethamphetamine (MDMA), is often associated with other drugs, among which ethanol is one of the most commonly used in dance clubs and rave cultures. We investigated the effects of ethanol co-administration on MDMA pharmacokinetics and body temperature in male Sprague-Dawley (SD) rats.

METHODS: Male SD rats (220 - 260 g) were obtained from CLEA Japan Inc. (Tokyo, Japan) and randomly divided into 6 groups (3 - 5 animals per group). The plasma concentration-time profiles were characterized after intraperitoneal (i.p.) administration of 10 mg/Kg and 30 mg/Kg MDMA alone and MDMA with 1.5 g/Kg ethanol to rats (4 animals per group). The rats were sacrificed 4 h after i.p. MDMA administration, and the plasma and brain samples were collected and analyzed using gas chromatography-mass spectrometry (GC-MS).

RESULTS: With 1.5 g/Kg ethanol, the maximum ethanol concentration in plasma was approximately 1.6 mg/mL after 0.3 h, and the average half-life was 2 h. Ethanol was not detected in the rat plasma after 4 h. However, ethanol concentration in the rat plasma did not statistically differ after the administration of MDMA in the presence or absence of ethanol. Following i.p. administration, the peak MDMA plasma concentrations (Cmax) were obtained 0.189 - 0.275 h after the administration of both concentrations. The MDMA concentration in plasma significantly increased when co-administered with ethanol than when administered alone (p < 0.05). The pharmacokinetic parameters of MDMA in rats were adequately described by a 2-compartment open body model. Although Nα,α-dimethyl-(3-methoxy-4-hydroxybenzene) ethanamine (HMMA) and MDA are most abundant metabolites, we did not analyze HMMA. However, the (±)-3,4-methylenedioxymethamphetamine (MDA) and MDMA concentrations in the brain did not differ among the 4 groups after 4 h. MDMA and MDA are well distributed in the brain when administered with ethanol. Although the temperature decreased after i.p. ethanol injection, it increased after the i.p. injection of MDMA.

CONCLUSIONS: After MDMA i.p. administration, plasma MDMA and MDA concentration will be increased and reach a higher value than p.o. administration. The enhancement of the effects of MDMA in the ethanol combination may be due to the initial increase in the MDMA plasma concentrations followed by the effect of MDMA and MDA in the brain.

Keywords: MDMA, Ethanol, Pharmacokinetics