LACK OF INTERACTION BETWEEN THE BEHAVIORAL EFFECTS OF KETAMINE AND BENZODIAZEPINES IN MICE

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The effect of co-administration of ketamine at the sub-effective dose with diazepam, chlordiazepoxide and clonazepam on their antinociceptive and protective efficacy against pentetrazole-induced seizures were studied in mice. Ketamine alone produces dose-dependent antinociception manifested as reduction in the number of writhing episodes evoked by acetic acid. In the writhing test, the antinociceptive effects of the threshold doses of diazepam, chlordiazepoxide or clonazepam were not changed by ketamine, whereas that of morphine was intensified by ketamine. In the hot plate test, slight antinociceptive effects of the threshold dose of diazepam, but not that of chlordiazepoxide (except the results at 120 min of observation), were significantly intensified by ketamine vs ketamine alone. Ketamine alone was able to protect mice, in the dose-related manner, against pentetrazole-induced seizures. The anticonvulsant effects of the threshold doses of diazepam, chlordiazepoxide and clonazepam were not changed by ketamine. These findings indicate that co-administration of ketamine (at the sub-effective dose) with diazepam, chlordiazepoxide and clonazepam (at non-effective doses) resulted in an intensification of neither antinociceptive nor protective effect against pentetrazole-induced seizures in mice. These data seem to indicate the lack of interaction between ketamine and benzodiazepines with respect to their antinociceptive and anticonvulsant efficacy.

Key words: benzodiazepines, ketamine, nociception, seizures, mice