HUMAN PSYCHOPHARMACOLOGY
Hum. Psychopharmacol. Clin. Exp. **14**, 355–356 (1999)

CASE REPORT

Acute Olanzapine Overdose

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Olanzapine, a thiobenzodiazepine derivate, is a recently released novel antipsychotic medication. The authors report the first case of overdose of olanzapine in an apparent suicide attempt. A 38-year-old schizophrenic patient was brought to a hospital emergency room following the ingestion of 12 10-mg tablets of olanzapine. There were no serious clinical adverse effects. Copyright © 1999 John Wiley & Sons, Ltd.

KEY WORDS — olanzapine; overdose

INTRODUCTION

The novel or atypical antipsychotic drugs have a favourable side effect profile, with low incidence of extrapyramidal signs, non-extrapyramidal complications and tardive dyskinesia (Umbricht and Kane, 1996; Casey, 1997). The first of them, clozapine, has been known for over 30 years, but relatively few cases of intoxication due to clozapine overdose have been reported (Keller *et al*., 1997; Ishii *et al*., 1997).

The present case describes the ingestion of 10-fold the daily therapeutic dose of olanzapine, a clozapine-like thiobenzodiazepine derivate. Searches of Medline and Current Contents show only one case report of a fatal overdose due to an unknown amount of olanzapine (Elian, 1998).

Case report

A 38-year-old, unemployed, divorced woman with a history of severe, therapy-resistant chronic, paranoid–hallucinatory schizophrenia for 12 years, was treated with olanzapine up to 10 mg/day. Her mental state improved considerably. Her speech and movement problems disappeared; paranoid ideation lessened in intensity and affective instability also improved. She was admitted to a rehabilitation facility for 5 months. The patient was discharged to her home and agreed to outpatient maintenance on olanzapine 10 mg/day. Three months later she attempted suicide by taking 12 tablets of olanzapine (120 mg). Reported symptoms were fatigue, dizziness and headache. Overdose management included gastrointestinal lavage with 0·9 per cent saline, activated charcoal, diuretics and cardiovascular monitoring. The patient's condition and vital signs were stable and unchanged. She was discharged after one day and remained well on maintenance therapy with olanzapine 10 mg/day. The laboratory results and electrocardiogram on admission, on the day following the overdose and one-week later, were normal.

DISCUSSION

Traditional antipsychotics have a high ratio between therapeutic and fatal doses, lowest for phenothiazines (20–200) and in excess of 1000 for the more potent antipsychotics (Goodman and Gilman, 1992). A small number of fatal and non-fatal cases of intoxication due to clozapine overdose have been reported with a lethal dose between 2·5 and 4 g, which is 5–10 times the mean daily dose (Keller *et al*., 1997; Ishii *et al*., 1997; Ganssmann *et al*., 1998).

Olanzapine has a wide pharmacological profile that is marked by high affinity for the dopamine

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CCC 0885–6222/99/050355–02$17·50

receptor (D2 subtype) and the serotonin receptor (5-HT-2A subtype). Olanzapine also has a high affinity for a variety of other receptors, including the dopamine D1 and D4 receptors, the serotonin 5-HT2C and 5-HT3 receptor subtype, the alpha 1-adrenergic and H1 histaminic receptors, the cholinergic (muscarinic m4) receptors (Bymaster *et al*., 1997). It is surprising that this profile of multiple effects did not lead to more serious problems on overdose

Olanzapine is extensively metabolized via *N*-glucuronidation, allylic hydroxilation, *N*-oxidation, *N*-dealkylation and their combination. Metabolites are excreted within 3–7 days in faeces and urine (Ereshefsky, 1996; Kassahun *et al*., 1997).

Our case report corroborates preliminary data about the relatively high therapeutic index (Beasley *et al*., 1997) of the novel antipsychotic drug olanzapine.

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