

Title: THE USE OF RO 15-1788: A BENZODIAZEPINE ANTAGONIST IN THE DIAGNOSIS AND TREATMENT OF BENZODIAZEPINE OVERDOSE

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**INTRODUCTION:** Several drugs including naloxone; physostigmine and aminophylline have been tried with only partial success in an attempt to reverse the CNS effects of benzodiazepines (BDZ). Recently newly synthesized imidazodiazepines were described which act at the BDZ receptor level to specifically inhibit the central effects of BDZ(1). Of these compounds RO 15-1788 was shown to possess very low toxicity in animals as well as in studies in man.(1,2) We present our experience using this compound in treating five patients comatose due to BDZ overdose.

**METHODS:** All five patients were treated in our ICU under ECG and intra-arterial pressure monitoring. Three patients (no. 1,3,4 in the table) also had central venous pressure measured. Patients No 1, 2, 4 were mechanically ventilated. The use of RO 15-1788 in all patients was approved by the committee for human research of our medical center and consent of the patients' families was obtained.

**RESULTS:** All patients, except patient no. 4 who had high barbiturate blood levels, regained full consciousness within minutes after RO 15-1788 injection. Patients were fully awake, recognized their families and responded to commands. No significant changes in hemodynamic parameters or any other adverse effects were observed. Generally

within 1-2 hours the effect of the antagonist began to wear off necessitating additional doses (see table).

**DISCUSSION:** The prompt and complete reversal of all BDZ central effects by RO 15-1788 in patients with BDZ overdose is of extreme importance. In two of our patients the immediate availability of the BDZ antagonist prevented endotracheal intubation and mechanical ventilation. In the first two patients where the vital question of ischemic brain damage versus drug induced coma had to be clarified, the antagonist proved to be extremely useful. The lack of side effects following the administration of the BDZ antagonist to our patients is in agreement with previous reports in the literature(2,3). We believe that RO 15-1788 will be an important tool in the diagnosis and treatment of BDZ overdose.

**REFERENCES:**

1. Hunkeler W, Mohler H, et al: Selective antagonists of benzodiazepines. *Nature* 290:514-516, 1981.
2. Darragh A, Lambre R, et al: Investigation in man of the efficacy of a benzodiazepine antagonist RO 15-1788. *Lancet* 2:8-10, 1981.
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PATIENT NO.	SEX	AGE
1	F	66
2	F	65
3	M	54
4	M	62
5	F	31

CAUSES OF COMA	TOTAL IV ANTAGONIST
S/P intraoperative cardiac arrests Iatrogenic diazepam overdose	300 mg over 4 days
Prolonged BDZ sedation preoperatively. Low cardiac output state.	2 mg over 3 hours
Suicide attempt with flunitrazepam.	5.7 mg over 24 hours
Suicide attempt with BDZ and barbiturates	21. mg over 12 hours
Suicide attempt with diazepam and nitrazepam	1.4 mg over 2 minutes