

RARE PARADOXICAL REACTION WITH LORAZEPAM IN A PSYCHIATRIC PATIENT**Dr. Pratik Awake*, Dr. Fiona Mahapatro and Dr. Sanjiv Kale**¹Junior Resident, Department of Psychiatry, Dr.D.Y.Patil Hospital and School of Medicine, Sector-5, Nerul, Navi Mumbai, Maharashtra.²Professor, Department of Psychiatry, Dr.D.Y.Patil Hospital and School of Medicine, Sector-5, Nerul, Navi Mumbai, Maharashtra.³HOD and Professor, Department of Psychiatry, Dr.D.Y.Patil Hospital and School of Medicine, Sector-5, Nerul, Navi Mumbai, Maharashtra.***Corresponding Author: Dr. Pratik Awake**

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ABSTRACT

Benzodiazepines are commonly used as adjunctive treatment alongwith antipsychotic medications in psychiatric patients. They are also used in hostile, aggressive and agitated patients to calm them. However in some less than 1 % of patients, benzodiazepines can cause paradoxical reaction ,(also called disinhibitory reactions) characterised by acute excitement and an altered mental state: increased anxiety, vivid dreams, hyperactivity, sexual disinhibition, hostility and rage.^[1,11] Here we present a known psychiatric case who showed sudden paradoxical reaction to lorazepam during the course of hospitalisation, given as adjunctive with his antipsychotic medication; and which occurred despite patient been exposed to lorazepam in the past without any such paradoxical effects.

KEYWORDS: Paradoxical reaction, Benzodiazepines, Lorazepam.**INTRODUCTION**

Benzodiazepines bind to the GABA_A receptor, reducing the quantity of GABA required to open the chloride channel, hyperpolarise the neuron and inhibit neurotransmission.^[1]

In the majority of recipients, benzodiazepines have a calming effect but in a minority they can cause paradoxical reactions (also called disinhibitory reactions) characterised by acute excitement and an altered mental state: increased anxiety, vivid dreams, hyperactivity, sexual disinhibition, hostility and rage.

The mechanism by which paradoxical reactions occur is not completely understood, but several theories exist.

The most likely explanation is that the anxiolytic and amnesic effects of benzodiazepines lead to a loss of the restraint that governs normal social behaviour and a reduced ability to concentrate on the external social cues that guide appropriate behaviour.^[1,10,12]

Known risk factors include high-potency drugs, high doses being administered by parenteral routes to the very young, elderly, those with pre-existing CNS damage and those with a history of aggression or impulsivity.^[6]

CASE REPORT

A 43 year male, known case of Schizoaffective disorder, was admitted in psychiatry ward with irritability, violent, aggressive behaviour, suspiciousness and sleep disturbances for three months with past history of admission and treated with psychotropics and ECTs with good improvement in symptoms and functionality, however he stopped medications since eight months.

During the course of hospitalisation, patient was given benzodiazepines in form of lorazepam as adjunctive alongwith his antipsychotic medications (haloperidol, risperidone and promethazine) for aggression and sleep disturbance on two separate occasion ,one week apart , first time as 2mg intramuscular injectable and second time as 4mg orally.

On both occasions, patient exhibited symptoms of delirious behaviour with sleep disturbances, irritability, confusion, disorientation, excitability and pacing around. Patient didnot have any fever. No alcohol consumption. Patient was investigated for other causes, however his blood counts, electrolytes, liver function and ammonia was within normal limits. MRI brain too revealed only age related changes.

Patient was managed conservatively both times, kept in quiet place, loosely and briefly restrained with relatives consent and all medications were withheld. Patient returned back to his previous mental state both times with no residual symptoms within 24 hours.

Interestingly patient was given injection lorazepam 4mg intramuscularly 2 weeks prior during admission process and also lorazepam was given multiple times during his previous hospitalisation with no apparent paradoxical reaction effects seen at these times.

DISCUSSION

Thus it was seen in this patient case that even low doses of lorazepam could cause paradoxical reactions and the route did not matter much.

Also as benzodiazepines are used commonly as behavioral control or to augment the antipsychotic drugs, it is imperative to keep the potential risk of paradoxical reactions in mind.

In this case the patient was male, with known psychiatric disorder and aggressive hostile behaviour.

However surprising thing was patient had tolerated lorazepam effectively in the past.

Thus it is important to be aware of the ability of benzodiazepines to cause behavioural disinhibition and to maintain a high degree of vigilance when these drugs are administered to patients known to be at risk.^[1,12]

Failure to recognise such a reaction could lead to the administration of higher doses of benzodiazepines in an attempt to control the behavioural disturbance.

In patients who have experienced a paradoxical reaction to benzodiazepines, behavioural emergencies should be managed with antipsychotic drugs in the future.

Short *et al* (1987) reported similar disinhibitory reactions to benzodiazepines in monozygotic twins and Dietch & Jennings (1988) reported that a mother and daughter both experienced behavioural disinhibition with temazepam.^[2]

Acute alcohol consumption is known to increase feelings of hostility and competitive and retaliatory behaviour, and epidemiological data show that alcohol is involved in over 50% of acts of violence (Miczek *et al*, 1997).^[3]

In a placebo-controlled study of alprazolam in the treatment of panic disorder, 13.7% of patients randomised to alprazolam experienced paradoxical reactions compared with none given placebo (O'Sullivan *et al*, 1994).^[4]

In a further study of the efficacy of alprazolam in borderline personality disorder, 58% of patients randomised to alprazolam experienced paradoxical

reactions compared with 8% with placebo (Gardner & Cowdrey, 1985).^[5]

Benzodiazepines can reduce 5HT neurotransmission, which may in turn precipitate aggressive behaviour. It therefore follows that people with antisocial personality disorder may be at increased risk of paradoxical reactions to benzodiazepines (Bond, 1998).^[6]

In a review of this subject, Dietch & Jennings (1988) conclude that, in the general population, the incidence of aggressive dyscontrol after administration of a benzodiazepine is less than 1%.^[11]

Blair & Curran (1999) found that when diazepam was administered to healthy volunteers, it selectively impaired the ability of subjects to recognise angry facial expressions.^[7]

Weisman *et al* (1998) reported that healthy volunteers who had taken diazepam 10 mg were more likely to behave aggressively under low levels of provocation than those who had taken clorazepate, oxazepam or placebo.^[8]

Dåderman & Lidberg (1999) reported that, in a population of young violent offenders, flunitrazepam abuse led to self-reported feelings of power, overwhelming self-esteem and increased suggestibility.^[9]

Bond *et al* (1995) highlighted four factors associated with benzodiazepine-induced aggression: it occurs in response to provocation; it is recognised by others but not by the patient; it usually occurs with high doses; and high-potency drugs cause particular problems.^[6]

Blair & Curran (1999) postulated that disinhibition may be mediated via GABA_A pathways in the right orbitofrontal cortex.^[7]

Thus according to different studies and reports, many of the Benzodiazepines could cause paradoxical reactions and caution should be taken while using the drug in the susceptible population.

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