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Benefit of Loxapine in substance abuse patients

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Case report

The phenomenon of psychomotor agitation concerns a clinical condition characterized by excessive activity that manifests itself with a multifaceted series of emotional, ideational, motor and behavioral alterations, sometimes afinalistic in relation to the state of consciousness.

Psychomotor agitation states can also occur independently of psychiatric pathology. Psychomotor agitation, in fact, can recognize medical causes, it can be triggered by intoxication or abstinence from psychoactive substances, but it can also occur in the daily life of an otherwise healthy person without requiring medical intervention 1.

Today the abuse of drugs or psychotropic drugs (drug addiction) is a widespread phenomenon worldwide.

Some episodes of psychomotor agitation of subjects who come to the Emergency Department often present triggers, such as alcohol and drug abuse. These factors are just some of the causes that are being grafted into the onset of psychiatric diseases that appear increasingly widespread specially among young people.

Even if the data available at national level are few and fragmented, we are faced with an alarming scenario that sees a huge and constantly increasing number, with a very high percentage of minors that exhibits mental disorders. Episodes of agitation are frequent in patients with dual diagnosis, and such patients generally experience greater consequences of and additional substance use disorder than those with a psychiatric disorder alone, including a greater exacerbation of psychiatric symptoms, medication nonadherence, increase in aggressive and violent behaviors, emergency room (ER) visits, and inpatient psychiatric placements.

Agitation may range from mild to severe, with rapid fluctuations, reaching extreme agitation in some cases that can derive into aggressive behavior in a relatively short period. Rapid intervention is needed to treat the psychotic agitation at a mild stage to prevent the escalation to an aggressive behavior but also to proceed with further investigations for each particular case and to properly treat such disorders 2.

The treatment of drug addictions and drug abuse is multidisciplinary, namely: medical-health, socio-rehabilitation and psychotherapy.

Today the prevention of drug-related problems, particularly among young people, represents an essential political objective.

In this case report, we describe our experience with inhaled loxapine to calm psychomotor agitation in 6 patients with double diagnosis during hospitalization at the Papa Giovanni XXIII Hospital in Bergamo (Italy) in the year 2019.

All patients presented a diagnosis of "Psychotic disorders" in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition. All of these patients are substance abusers. A single dose of inhaled loxapine was required for all patients, which was effective a few minutes after administration. No other concomitant medications were used during the acute agitation episode. In one



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case only mild dizziness was reported. No respiratory adverse events or bronchospasm have been reported for any patient.

Discussion

To our knowledge, this case series constitutes one of the first reports of inhaled loxapine use in patients with double diagnosis outside the context of the clinical trial. Inhaled Loxapine was rapid, effective and well accepted in patients with double diagnoses who presented acute agitation and did not want the drug sedation effect but only tranquillization. Data have confirmed the efficacy, rapid onset of action, and safety and tolerability of this agent in the psychiatric emergency and hospital settings. Emerging data have indicated the potential for inhaled loxapine as a self-administered agent for use in the community setting without the direct supervision of a healthcare professional ³.

However, it is important to understand the right timing to be able to use Loxapina. That is, the psychiatrist must understand the exact moment when, during an episode of psychomotor agitation, he can propose such administration to the patient. In fact, if the moment is poorly assessed, there is a risk of receiving a patient's refusal which will appear uncooperative due to the same symptoms of agitation.

Thanks to the non-invasive route of administration and the rapid calming effect, inhalation loxapine confers significant advantages in the control of agitation, representing a valid alternative to other intramuscolar formulations not always well experienced by the patient. In addition, an inhaler involves the patient in the collaboration and improves the doctor-patient therapeutic alliance. The risk of drug-related bronchospasm should always be kept in mind when planning to use loxapine by inhalation, leading to a careful evaluation of the patient before and after administration ⁴.

In our case series, psychiatric conditions were represented by schizophrenia, bipolar disorder type I, other psychotic disorders, comorbid substance-induced psychotic disorder with personality disorders. The mean age of the sample was 39,6 years old and gender was adequately represented. All patients had substance use disorders, alcohol abuse, cannabinoids and cocaine abuse as the most prevalent. Everyone was a cigarette smoker. After initial verbal de-escalation a first dose of inhaled loxapine was offered and administered in all patients. The choice of treatment with Loxapine was carefully considered for

each patient based on the psychiatric diagnosis, good health conditions and the absence of respiratory or lung problems in the past history. During the attempts of verbal de-escalation, the psychiatrist assessed the severity of the psychomotor agitation, the absence of respiratory or pulmonary symptoms at that specific moment and the absence of actual drug intoxication.

Agitation intensity was assessed on-site based on clinical evaluation and using the *Clinical Global Impression - Severity scale* (CGI-S) ⁵. Regarding the severity of the agitation, two patients were classified as "mild", three as "moderate", one as "moderately severe". Therefore, no patient was identified as "severe" or with "extreme agitation".

Almost all patients (N=5) received just one dose of inhaled loxapine, which was effective within minutes after administration (mean: 6 minutes, range: 2-10 minutes). Just one patient required the second dose to control agitation.

Monitoring the risk of drug-related bronchospasm was even more careful since loxapine was administered to smoking patients with dual diagnoses. No clinically significant adverse events were observed.

Although our data refer to a limited number of cases, this case series represents general clinical practice and demonstrates the efficacy of inhaled loxapine for agitation in double patients who have been seen in hospital. Subsequently, adequate management of comorbidity disorders with the integrated resources available would be needed to improve adherence and outcome of treatment in patients with double diagnosis.

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