

Multiple Drug Ingestion For Suicidal Purpose: Alprazolam, Citalopram, Risperidone, Oxcarbazepine And Alcohol

İntihar Amacı İle Çoklu İlaç İçilmesi:
Alprazolam, Citalopram, Risperidone, Oxcarbazepine Ve Alkol

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Özet

Hipnotik ajanlar, antidepresan ve antipsikotik ilaçlar uykusuzluk, depresyon ve psikotik hastalıkların tedavisinde yaygın olarak kullanılmaktadır. Bu ajanların aşırı dozda alınımının rapor edilmesi giderek artmasına rağmen alprazolam, citalopram, risperidone, oxcarbazepine ve alkolün hep birlikte alınımı kapsayan bir vaka şu ana kadar gösterilmemiştir. Gelişmekte olan ülkelerde bu ilaçların reçete edilmesi artmaya devam ettiği için bu ilaçların klinik toksisitelerini ve klinik yaklaşımlarını değerlendirmek gereklidir. Biz, intihar amacı ile aşırı dozda alprazolam, citalopram, risperidone, oxcarbazepine ve alkol alan ve destek tedavisi ile iyileşen 20 yaşında bir kadın olguyu bildirdik. Kadın hastanın yüksek dozda alprazolam (18 mg), citalopram hidrobromur (80 mg), risperidone (16 mg), oxcarbazepine (600 mg) ve aynı zamanda alkol aldığı ev arkadaşı ve uyanık iken kendisi tarafından bildirilmiştir. Hastaya standart detoksifikasyon prosedürü ve destek tedavisi uygulandı. **Anahtar Kelimeler:** Alprazolam, citalopram, risperidone, oxcarbazepine, alkol, çoklu ilaç zehirlenmesi

Abstract

Hypnotic agents, antidepressant and antipsychotic drugs are commonly used for the treatment of sleeplessness, depression, and psychotic disorders. Although overdose intake with these agents is increasingly being reported, no case of co-ingestion including alprazolam, citalopram, risperidone, oxcarbazepine and alcohol has been demonstrated so far. As prescription of these drugs continues to increase in developing countries, it is necessary to evaluate their clinical toxicity and clinical approach. We reported a case of overdose with alprazolam, citalopram, risperidone, oxcarbazepine and alcohol in a 20-year-old female for suicidal purpose who recovered with supportive management. It was reported by her room-mate and patient when conscious that she had taken high doses of alprazolam (18 mg), citalopram hydrobromur (80 mg), risperidone (16 mg), oxcarbazepine (600 mg) and alcohol also. She was managed with standard detoxification procedures and supportive treatment. **Key Words:** Alprazolam, citalopram, risperidone, oxcarbazepine, alcohol, multiple drug intoxication.

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INTRODUCTION

Among young people, poisoning is a leading cause of injury mortality in the United States. One of the major causes of death is a suicidal attempt. It is commonly seen in patients who take antidepressant medications (1). Prevention and management of such overdose are of increasing clinical relevance as prescription of these kinds of drugs continues to increase (2). Though, little is known about these drugs (3), several cases reported about overdose of these agents (4-7).

Many variable medication combinations may be used in a suicidal attempt. Most commonly we see one or two kinds of drugs taken. We mentioned here is a patient under antidepressant treatment who taken multiple drug combinations which are not seriously toxic if taken alone but may have severe toxic effects when taken together. Each drug has a central nervous system (CNS) depressant effect. First of them is alprazolam (an antidepressant), the second one is risperidone (a type of phenothiazines), third one is citalopram hydrobromur (a selective serotonin reuptake inhibitor-SSRI), fourth one is oxcarbazepine (an anticonvulsant and hypnotic agent) and the last one is alcohol.

There is a lack of knowledge in the literature about the management of multiple drug ingestion in emergency and intensive care unit. The treatment was effective because of the rapidly introducing of patient to the hospital, emergent evaluation and routine medications done immediately. It is aimed to discuss a case of intoxication with the multiple drugs; all of them were almost depressants of CNS.

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CASE REPORT

A 20-year-old girl was taken to the emergency unit with an semi-unconscious situation. It was learned from her roommate and patient when conscious that she took high doses of alprazolam (18 mg), citalopram hydrobromur (80 mg), risperidone (16 mg), oxcarbazepine (600 mg) and alcohol approximately 90 minutes before being admitted to the emergency department.

On the initial examination she had a heart rate of 150 beats/min, respiratory rate of 22 breaths/ min. Body temperature was 36.8 C. Systemic blood pressure was 90/50 mm Hg. Pupils were mydriatic and positive to light reflexes. She was semi-conscious and Glasgow Coma Scale Score was 9. Her arterial blood gas analysis showed metabolic acidosis with a-13.5 base excess, and PaO₂ 87 mm Hg, PaCO₂ 52 mm Hg and SpO₂ 80%. She was administered 100% oxygen via the face mask. In the pulmonary examination, wheezing was auscultated in the basal zones. For the radiological assessment, chest X-ray examination was applied and it showed a pneumonic infiltration which was thought to be a pulmonary aspiration in the lung.

Pulmonary aspiration may have happened while vomiting before transferred to hospital. Blood glucose level was 75 mg/dl. Serum CPK enzyme level was normal. Electrocardiogram showed negative T waves in the V2 and V3 derivations. It was thought to be the result of co-ingestion of these drugs. In order to exclude an intracranial pathology, cranial CT scan was performed and was reported as normal.

As she was not unconscious completely and was able to obey our commands, gastric lavage was performed via a nasogastric catheter of 14 G. As the aspiration material was not enough, we decided to give 50 grams of active charcoal and laxafenol (300 mg, 2x1) via the nasogastric catheter in the supine-sitting position. It was repeated for every six hours. Flumazenil, the antagonist of alprazolam, was given in titrated doses of 0.5 mg intravenously. For supportive treatment fluid replacement therapy, antibiotics (seftriaxone; 1 grX1, clindamycine; 600 mg, 1X1), gastric acid inhibitor agent (ranitidine, 150 mg X2), bronchodilator agents and n-acetyl cystein (Asist; 4X1) applied in routine doses.

After six hours from the beginning of the treatment she became conscious completely and orally cooperated. Blood pressure was improved and arterial oxygen saturation increased to 81% at the sixth and 96% at the twelfth hours. T waves in the V2 and V3 derivations and other abnormal parameters returned to normal in 48 hours. Oral feeding was begun on the second day and she referred to psychiatry clinic on the sixth day.

DISCUSSION

Alprazolam is a triazolobenzodiazepine that appears both to exhibit a high affinity for BZ receptors and activate brain a₂-adrenoceptors. Because it acts as benzodiazepine and a₂-adrenoceptor agonist also it may be particularly efficacious in the treatment of the alcohol withdrawal syndrome (1).

Alprazolam has been shown to produce improvement in patients with panic disorder (4). It has also been reported useful in alcohol withdrawal (5) and in some types of pain syndromes (6).

Although alcohol increases simple reaction it has much more effect on central activity at this dose. Combination of benzodiazepines and alcohol has more effect on tests of motor function and coordination than would be predicted from the sum of the single effects and that alcohol is the dominant partner in this combination (7).

Patients receiving psychotropic medications are often cautioned against the use of ethanol. 2 mg alprazolam in combinations with ethanol produced additive decrements in performance on all cognitive and psychomotor tasks (8). Benzodiazepines and ethanol may act partially on the same receptor; the lack of the interaction may be due in part to acute cross tolerance (9).

In our case chemical causes of CNS depression were alprazolam (Xanax), risperidone (Risperdal), citalopram hydrobromur (Cipram), oxcarbazepine (Trileptal) and alcohol. She wasn't tolerant to the effect of that dose alcohol. Although doses of all drugs ingested were not toxic level, their doses higher than their therapeutic doses. Their combination resulted in clinical toxicity. This may be due additive or potential effects of drugs ingested together. These drugs have a potential of CNS depression (10).

Risperidone (Risperdal) (a phenothiazine) is used for its antiemetic, antipsychotic and sometimes analgesic and hypnotic effects. Serious symptoms may be occur after 1mg/kg dose. Higher doses can cause liver injury, cirrhosis, and agranulocytosis. Risperidone toxicity manifests primarily with mild central nervous system effects and reversible neuromuscular and cardiovascular effects (11).

Citalopram hydrobromur (Cipram) is a selective serotonin reuptake inhibitor drug and may be efficacious in the treatment of depression, senile dementia, alcohol withdrawal syndrome and bipolar disorder. Minimum lethal level of its blood concentration was reported 5200 mg. After using with other CNS depressant agent risk of arrhythmia and convulsion increases. Acute toxicity with this drug results in rhabdomyolysis, renal failure, hypoxia and seizures (12).

Oxcarbazepine (Trileptal) has an anticonvulsant and hypnotic effect via CNS depressant effect. Overuse causes respiratory insufficiency and coma. There is no antidote agent to use in oxcarbazepine toxicity (13).

Flumazenil is a benzodiazepine antagonist and can be used in addition to supportive care at iv doses of 0.01 mg/kg. It binds to the benzodiazepine receptor, where it competitively displaces benzodiazepines and reverses sedative and anxiolytic effects (14). It reverses sedation, respiratory depression, amnesia and psychomotor effects of benzodiazepines (e.g., midazolam, alprazolam, diazepam, flurazepam, lorazepam) (15). Flumazenil only has a 1 hour half-life and may need to be repeated (16).

In this case use of alprazolam, ethanol, Risperidone, citalopram and Oxcarbazepine together and in overdoses produced syncope, hypotension, tachycardia, metabolic acidosis, tachypnea and pulmonary aspiration.

Our goal in treating those drugs' overdoses was to prevent hypotension and severe CNS depression. Gastric lavage was performed and activated charcoal was given for the ingestion of large doses. If the patient had been unconscious we wouldn't perform gastric lavage because of the aspiration possibility. Rajkumar et al. Reported an other multi-drug overdose and they intubated the unconscious patient without performing gastric lavage and then they started the supportive treatment (17). Heart rate, blood pressure, body temperature, and respiration rates were monitorized. Intravenous fluid was needed for prevention of hypotension. The unique antidote, flumazenil, was used treating alprazolam overdose. However, toxicity may be worsened by extremes of age (18), substance abuse, medical co-morbidity, co-ingestion of other agents (2) and obesity, our patient had none of these worsening factors and co-ingestion of alprazolam (18 mg), citalopram hydrobromur (80 mg), risperidone (16 mg), oxcarbazepine (600 mg) and alcohol didn't prove fatal. As multiple overdoses may be common, our report provides an information regarding the toxicity of these drugs.

It is rare to see a patient who had taken overdoses of these kinds of drugs together. Probably the doses taken for each drugs alone may not have toxic effects but when they are taken together they have synergistic effects and cause severe toxicity.

IN CONCLUSION

The multiple drug overdose reported here showed that prompt supportive treatment, early detection of overdose, the rapid, correct and optimal management can provide a successful outcome.

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