

Delayed Respiratory Depression After Risperidone Overdose

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Risperidone is an atypical antipsychotic drug used for the treatment of schizophrenia. Both positive and negative symptoms are prominent with its use. Metabolism occurs mainly in the liver, where risperidone is changed by CYP2D6 to an active metabolite, 9-hydroxyrisperidone. The half-lives of risperidone and its metabolite are 3 and 7 h, respectively. Genetic

polymorphism is seen in the 6%–8% of white patients who are considered poor metabolizers. In poor metabolizers, the half-life extends to 20–30 h. We present an unusual case of unanticipated delayed respiratory depression after risperidone overdose.

(Anesth Analg 2005;101:1490–1)

Antipsychotic drugs, also called major tranquilizers and neuroleptics, are used to treat schizophrenia and other types of psychoses. Toxicity of these drugs may result from suicidal overdose or from adverse reactions after therapeutic administration. Risperidone overdose is rare but life-threatening. All antipsychotics produce extrapyramidal side effects (EPS), such as acute dystonic reactions, which can cause respiratory difficulty by pharyngeal and laryngeal muscle spasm. The introduction of drugs that produce minimal EPS and of atypical antipsychotics (e.g., risperidone) has allowed separation of antipsychotic from neuroleptic effects and prevents the interchange of terms. The serotonin-dopamine antagonist concept contends that antipsychotics that are more potent at 5-hydroxytryptamine 2A receptors than at D2 receptors (e.g., risperidone) have a low EPS liability (1).

Case Report

A 26-yr-old woman who had been treated with risperidone for 3 mo was found unconscious on the street. The patient was admitted to a state hospital where it was determined that she had ingested 30 mg of risperidone (a suicide attempt after an argument with her husband) rather than her usual amount of 6 mg/d. Her medical history included long-term schizophrenia.

On Day 3 (after 52 h), respiratory distress developed, and the patient was transferred to our university hospital. On admission, she was hypotensive, with an arterial blood pressure (BP) of 80/50 mm Hg, and she had a Glasgow Coma Scale (GCS) score of 8 of 15. A chest radiograph showed no abnormality. Serum electrolytes and her electrocardiogram were normal (heart rate, 50 bpm). The slow heart rate and BP responded initially to treatment that included IV fluids and a single dose of 0.5 mg of atropine.

Two hours after arrival in the intensive care unit (ICU), the patient's respiratory drive began failing, and she started gasping. The blood gas analysis at this time, under O₂ 6 L/min with face mask, showed a pH value of 7.39, Po₂ of 51 mm Hg, Pco₂ of 54 mm Hg, and HCO₃ of 24.3 mmol/L, with a respiratory rate of 5 breaths/min. After 10 min, the patient had a respiratory arrest and was endotracheally intubated and ventilated. Sedation was maintained by propofol infusion. A computed tomography scan of the head was performed and showed no abnormalities. There were no other causes of respiratory depression, and she was not receiving any other respiratory depressant drugs. The patient remained hemodynamically stable, and laboratory tests were normal.

The patient started to make respiratory efforts on Day 5. Her reported GCS was 13. After 6 h, she managed to breathe spontaneously with a continuous positive airway pressure mode. She was tracheally extubated on Day 6 and discharged from the ICU on Day 8.

Discussion

Toxicity of antipsychotic drugs results from unintentional or intentional overdose or from adverse reactions after therapeutic administration. EPS are a result of basal ganglia dopamine D2 receptor blockade and consist of four main drug-induced syndromes. These can be divided into reversible syndromes, which occur within days to weeks of the onset of antipsychotic

Accepted for publication April 22, 2005.

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DOI: 10.1213/01.ANE.0000180195.57760.E9

therapy (acute dystonia, parkinsonism, and akathisia) and a potentially irreversible syndrome that occurs after months to years of therapy (tardive dyskinesia).

Acute dystonic reactions (dyskinesias) consist of intermittent spasmodic or sustained involuntary contractions of muscles in the face, neck, trunk, and occasionally the extremities. Resulting clinical manifestations include trismus, tongue protrusion, torticollis, opisthotonos, and respiratory difficulty. Pharyngeal and laryngeal muscle spasm may produce respiratory distress and asphyxia (2,3).

Reported side effects of risperidone are lethargy, dystonia, hypotension, tachycardia, dysrhythmia, impaired concentration, and abnormal temperature regulation (4-7). The recommended dose is 2 mg on Day 1, 4 mg on Day 2, and 6 mg on Day 3; however, in the elderly (or in patients with hepatic or renal failure), the dose is 0.5 mg up to 2 mg on Day 3. This patient was under treatment with risperidone for three months, and her usual medication was 6 mg/d.

Delayed respiratory failure has not been a prominent feature in overdose cases. Rassam and Srinivasa (8) reported a 72-year-old patient with respiratory depression after accidental risperidone overdose, and Acri and Henretig (9) reported cases of impaired respiration when risperidone was given concomitantly with other respiratory depressant drugs resulting in no additive side effects.

In this case, we evaluated whether acute dystonic reaction contributed to the clinical course of our patient, who demonstrated lethargy, tongue protrusion,

and pharyngeal-laryngeal muscle spasm, all of which were related to respiratory dysfunction.

Experience with risperidone overdose is limited and the clinical presentation difficult to predict after an overdose. Therefore, patients who are being treated for risperidone overdose should be monitored for hypotension, sedation, and respiratory depression. It should be noted that respiratory depression may be seen as late as the third day after risperidone overdose.

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