

SURVIVAL AFTER OLANZAPINE OVERDOSE COMPLICATED WITH SEVERE BRONCHOPNEUMONIA AND LEUKOPENIA

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BACKGROUND

Olanzapine is a thienobenzodiazepine-derived neuroleptic, chemically and pharmacologically closely related to clozapine, an atypical antipsychotic because of its serotonin-dopamine antagonist actions while typical antipsychotics are only D2 antagonists. Atypical antipsychotics not only block the dopamine receptors but also block the 5-HT_{2A} receptor this being responsible for the reduction or absence of extrapyramidal symptoms such as Parkinsonism, akathisia and dystonia. They also show multiple other pharmacologic actions at other receptors sites such as alpha 1 and alpha 2 noradrenergic, muscarinic cholinergic, histamine 1 and norepinephrine reuptake pumps explaining the additional favourable or unfavourable clinical properties. Understanding the clinical toxicity of olanzapine is important since it is typically used in a population at risk for intentional overdose and the safety of this drug in overdose has not been yet completely evaluated. Very common symptoms of overdose with olanzapine alone include agitation, dysarthria, tachycardia, extrapyramidal symptoms and reduced level of consciousness ranging from sedation to coma. Less common are some potentially medically serious events such as aspiration, cardiopulmonary arrest, cardiac arrhythmias, delirium, neuroleptic malignant syndrome, respiratory depression, convulsions and even death.

CASE REPORT

A 29-year-old woman, with a diagnosis of schizophrenia for several years, with a history of other four suicidal attempts, currently on a regimen with sertraline, olanzapine and alprazolam, ingested 24 hours before admission the whole content of her olanzapine prescription. She was admitted in a near-by hospital, was lavaged, but no tablet fragments were recovered, and activated charcoal was administered. In the next hours the patient lost consciousness, respond only to deep painful stimuli and so the decision for transfer in our hospital was taken. The transfer crew intubated the patient for airway protection before transport. On arrival in our hospital she was in deep coma (GCS=5), HR 140 bpm, BP 100/60 mmHg, RR 22/min., oxygen saturation 98%. There were no significant acid-base changes (pH=7.41, pO₂=140 mmHg, pCO₂=37 mmHg, HCO₃=23 mmol/l at a 98% O₂ saturation). On auscultation crackles were heard in her right inferior lung field and the X ray revealed infiltration in this area. Laboratory data on admission included Na 142 mmol/l, K 2.72 mmol/l, BUN 14 mg/dl, creatinine 0.59 mg/dl, glucose 136 mg/dl, ALT 42 u/l, AST 27u/l. With a diagnosis of pneumonia antibiotic therapy was initiated, but

the patient respiratory state deteriorated rapidly and mechanical ventilation was needed. In the next days she developed septic syndrome with fever 39-40 °C, circulation instability and moderate leucocytosis. The X ray showed infiltration in the entire right lung and portions of the left lung. The next days her state remain very unstable, with high fever and high levels of PEEP and FiO₂ needed to reach an acceptable level of pO₂. In spite of the clinical poor condition the leucocyte level become normal and continued to decrease to 3500-4000/mm³. After microbiological tests an antibiotic regimen with meropenem and linezolid was established. With this treatment the circulatory and respiratory state improved gradually, the catecholamine supply was stopped, the share of spontaneous breathing increased and the X ray of thorax showed a considerable improvement. The patient was extubated, she was awake and several days later she was discharged.

CONCLUSION

Olanzapine profile as a atypical neuroleptic is well established. It has a high affinity for dopamine, adrenergic, serotonergic, histamine and muscarinic cholinergic receptors this being responsible for both its clinical efficacy and adverse effects. Although, because of her high affinity for the serotonin receptors the extrapyramidal effects are very low, she is not devoid of adverse pharmacologic effects, including tachycardia, hypotension, somnolence, and anticholinergic side effects due to binding to muscarinic, adrenergic and histamine receptors. Also there is still discussed controversially whether olanzapine can induce hematotoxic side-effects. Case reports of olanzapine therapy associated with WBC decrements, ranging from leucopenia to agranulocytosis have been described in the published literature.

This case of intentional overdose resulted in significant sequelae necessitating management in an ICU setting. Until more accurate experience can be established with this new antipsychotic medication suspected significant ingestions warrant observation in an intensive care setting.

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