We describe a patient who ingested 5 g of atenolol with ethanol. After awakening, with repeat toxicology screen only showing atenolol, and in spite of normal voluntary breathing mechanics, he had marked suppression of his spontaneous respirations as measured by minute ventilation and by occlusion pressure with no incremental response to hypercapnic challenge. Subsequently, he recovered. Although we are unable to prove a causal relationship, future patients with atenolol overdose should be observed carefully for ventilatory failure, even if fully conscious.

Self-poisoning with large doses of propranolol, a beta adrenergic antagonist, have been reported frequently. Physiologic effects include bradycardia, heart failure, hypertension, bronchospasm, hypoglycemia, and seizures. Only one case has been reported of self-poisoning with atenolol, a new adrenergic receptor blocking agent with greater beta selectivity. We report a patient who ingested 5 g of atenolol, four times the previously reported amount and who temporarily had marked suppression of spontaneous ventilation while awake. This drug-induced ventilatory suppression was similar to the central nervous system-mediated alveolar hypoventilation which has been given the eponym, Ondine's curse.

**CASE REPORT**

A 42-year-old man had been taking atenolol for two years for treatment of mild hypertension. In a suicide attempt, he ingested

Marked Suppression of Ventilation While Awake following Massive Ingestion of Atenolol

A. Bruce Montgomery, M.D.;* Marie A. Stager, B.S.N.; and Robert B. Schoene, M.D.†

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Paramedics found him to be minimally responsive, lacking a gag reflex. Vital signs were: blood pressure 112/50 mm Hg; pulse rate, 80; respirations, 14. An endotracheal tube was inserted, and he was transported to Harborview Medical Center. On arrival, he was lethargic but responsive to voice command. Gastric lavage did not return pill fragments. Results of admission blood toxicology screen revealed only alcohol (blood level of 220 mg/dl) and atenolol level (9.4 \( \mu g/ml \), therapeutic range 0.2 to 1.0). After transfer to the medical intensive care unit, he was mechanically ventilated overnight and was hemodynamically stable with only a sinus bradycardia to 59. He did not receive any medication during this period. By morning, he was alert and oriented, and on the following morning, voluntary breathing mechanics were obtained: tidal volume, 600 ml; vital capacity, 3.6 L; respiratory effort, \(- 60 \) cm \( H_2O \); \( V_t \) 6.0 L/min. Static and dynamic compliances were 77 and 50 ml/cm \( H_2O \) respectively.

Arterial blood gas levels on mechanical ventilation with tidal volume of 1,000 ml, rate of 8, \( F_{CO_2} \) of 0.3, were: pH, 7.45; \( P_{CO_2} \), 27 mm Hg; and \( P_{O_2} \), 150. He subsequently failed a 20 minute \( T \)-piece trial, exhibiting a lack of spontaneous respirations while awake. Results of repeat toxicology screen revealed a blood alcohol level of zero and an atenolol level of 5.6 \( \mu g/ml \). After informed consent was obtained, his respiratory drive was studied on a protocol approved by the University of Washington human subjects' committee. Minute ventilation (\( V_t \)) and airway occlusion pressures at 0.1 sec after inspiration (\( P_{E}} \)) were studied by methods described previously.\(^5\) His spontaneous breathing pattern was random with tidal volumes ranging from 200 to 400 ml. Without continuous verbal prompting to breathe, spontaneous hyperventilation ensued over a three-minute period. \( V_t \) decreased from 13.4 to 0.29 L/min, \( P_{E}} \) from 4.4 to 1.2 cm \( H_2O \) and end-tidal \( CO_2 \) rising from 30 to 44 mm Hg. With repeat prompting, he was able to breathe spontaneously for a 20-minute period before mechanical ventilation was reinitiated. After five hours, repeat arterial blood gas levels on mechanical ventilation with \( F_{CO_2} \) of 0.30, tidal volume of 1,000 ml, rate of 6 were: pH, 7.41; \( P_{CO_2} \), 36; \( P_{O_2} \), 142 mm Hg. The study was repeated using \( F_{CO_2} \) of 0.30. Again, without continuous verbal prompting to breathe, spontaneous hyperventilation ensued over a three-minute period with \( V_t \) decreasing from 6.7 to 0.22 L/min, \( P_{E}} \) from 4.8 to 1.0 cm \( H_2O \) and end-tidal \( CO_2 \) rising from 30 to 47 mm Hg. Respiratio was again supported by mechanical ventilation until the following morning.

Arterial blood gas levels on assisted mechanical ventilation were: pH, 7.45; \( P_{CO_2} \), 27; and \( P_{O_2} \), 141 mm Hg. A repeat study revealed a regular pattern of respiration, with \( V_t \) increasing from 11.7 to 16.1 L/min and \( P_{E}} \) increasing from 1.4 to 3.2 cm \( H_2O \) during exogenous hyperventilation that raised end-tidal \( CO_2 \) from 32 to 41 mm Hg. Atenolol level was 4.3 \( \mu g/ml \). He was subsequently extubated, did well, and was discharged to a psychiatric facility.

**Discussion**

In the intensive care unit setting, alveolar hypoventilation resulting in hypercapnic respiratory failure can occur commonly by three mechanisms: obstruction of air flow; failure of respiratory muscles, and inadequate ventilatory drive. In this case there was no evidence of obstruction from his static and dynamic compliance measurements. Respiratory muscle weakness was an unlikely cause since spontaneous breathing mechanics were excellent and the patient was able to maintain normal minute ventilation when asked. Decreased \( V_t \) and \( P_{E}} \) values in the presence of hyperventilation suggest a central drive dysfunction. The latter variable, \( P_{E}} \), has been found to correlate well with central respiratory drive and is independent of muscle weakness.\(^6\) Although a single case report cannot prove causality, other CNS events such as a transient ischemic event are unlikely in a patient who was not hypotensive and had otherwise normal results of neurologic examination. Another possibility is ventilator-induced hypocapnia. We find this unlikely, as the patient was eucapnic for five hours prior to the second study that documented continued decreased respiratory drives and the patient had a normal respiratory drive the following day even though he was hypocapnic prior to that study.

Previous reports have implicated beta blockers as respiratory depressants. Both timolol and propanolol have been implicated in neonatal respiratory depression, the former by ophthalmologic administration, the latter by a transplacental route.\(^7\) Furthermore, when adrenergic agents have been investigated as ventilatory stimulants, the antagonist propanolol has been shown to cause respiratory depression, although the decrement was not always statistically significant.\(^8\)

In the previously reported case of self-poisoning with atenolol, no major problem occurred. Interestingly, in our patient, serial serum levels of atenolol, although decreasing, remained elevated after return of a normal ventilatory response to \( CO_2 \) suggesting a threshold effect. This may explain why this effect was not seen in the previous 1 g ingestion.\(^9\)

In conclusion, a 5 g ingestion of atenolol was associated with marked suppression of spontaneous ventilation which required continuous conscious effort on the part of the patient to breathe until he was placed back on mechanical ventilation. Physicians managing a similar patient should maintain mechanical ventilation until certain of spontaneous respirations, even in the presence of excellent spontaneous weaning mechanics and full consciousness. Furthermore, with the widespread use of beta-adrenergic antagonists in chest medicine, physicians should be aware of the possible ventilatory depressant effects of these agents.

**References**


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