Case 1

Acute Aspirin Overdose: Relationship to the Blood Buffering System

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Focus concept

The response of the carbonic acid/bicarbonate buffering system to an overdose of aspirin is examined.

Prerequisites

- Principles of acids and bases, including pK_a and the Henderson-Hasselbalch equation.
- The carbonic acid/bicarbonate blood buffering system.

Background

You are an emergency room physician and you have just admitted a patient, a 23-year-old female, who had been hospitalized for psychiatric treatment for the past six months. She was out on a day pass when she was brought to the emergency room around 9 pm. The patient was disoriented, had trouble speaking, and was suffering from nausea and vomiting. She was also hyperventilating. The patient admitted to taking an entire bottle of aspirin, which contained 250 tablets. The patient said that she took the tablets around 7 pm that evening. You draw blood from the patient and the laboratory performs the analyses shown in Table 1.1. The patient is experiencing mild respiratory alkalosis.

Table 1.1: Arterial blood gas concentration in patient

	Patient, two hours after aspirin ingestion	**Patient, ten hours after aspirin ingestion**	**Normal values**
p_{CO_2}	26 mm Hg	19 mm Hg	35-45 mm Hg
HCO_3^-	18 mM	21 mM	22-26 mM
p_{O_2}	113 mm Hg	143 mm Hg	75-100 mm Hg
pH	7.44	7.55	7.35-7.45
Blood salicylate concentration, mg/dL	57	117	

In the emergency room, the patient is given a stomach lavage with saline and two doses of activated charcoal to adsorb the aspirin. Eight hours later, nausea and vomiting became severe, and her respiratory rate increased; she was in severe respiratory alkalosis, and further treatment was required. You carry out a gastric lavage at pH = 8.5 and administer further activated charcoal treatments, one every 30 minutes. A bicarbonate drip was required to prevent the blood bicarbonate concentration from dropping below 15 mM. After 12 hours, blood salicylate concentrations began to decrease. The patient's blood pH begins to drop around 24 hours after the aspirin ingestion and finally returned to normal at 60 hours after the ingestion, although salicylate concentrations did not fall to zero until about 80 hours after aspirin ingestion.

Questions

1. Aspirin, or acetylsalicylic acid (structure shown in Figure 1.1), is hydrolyzed in the presence of aqueous acid and stomach esterases (which act as catalysts) to salicylic acid (the pharmacologically active form of the drug) and acetic acid. Write the balanced chemical reaction for this transformation.

Figure 1.1: Structure of aspirin.

2. Since the patient was brought into the emergency room only two hours after the overdose, you suspect that her stomach might contain undissolved aspirin that is continuing to be absorbed. The fact that she is experiencing severe respiratory alkalosis 10 hours after the ingestion confirms your suspicion and you decide to use a gastric lavage at pH 8.5 to effectively remove any aspirin that still remains in the stomach.
   a. Calculate the percentage of protonated and unprotonated forms of salicylic acid at the pH of the stomach, which is usually around 2.0.
   b. Calculate the percentage of protonated and unprotonated forms of salicylic acid at the pH of the gastric lavage. How does the gastric lavage at pH 8.5 facilitate removal of aspirin from the stomach? Explain. (Note: Assume that the pK_a values for the carboxylate group in salicylic acid and acetylsalicylic acid are the same.)

3. It has been shown that salicylates act directly on the nervous system to stimulate respiration. Thus, our patient is hyperventilating due to her salicylate overdose.
   a. Explain how the salicylate-induced hyperventilation leads to the values of pO_2 and pCO_2 symptoms seen in the patient.
   b. Explain how the salicylate-induced hyperventilation causes the pH of the patient's blood to increase. Illustrate your answer with the appropriate equations.

c. Why was the bicarbonate drip necessary?

4. a. Determine the ratio of HCO_3^- to H_2CO_3 in the patient's blood 10 hours after aspirin ingestion. How does this compare to the ratio of HCO_3^- to H_2CO_3 in normal blood? Can the H_2CO_3/HCO_3^- system work effectively as a buffer in this patient under these conditions? Explain.

   b. Compare the concentration of HCO_3^- in a normal person and in our patient. Then calculate the concentration of H_2CO_3 in the patient's blood 10 hours after aspirin ingestion. Again, compare this value to the concentration of H_2CO_3 found normally, and again address the question of buffer effectiveness in the patient.

5. Sixty hours after aspirin ingestion, the patient's blood pH returned to normal (pH = 7.4). By what mechanism(s) was the patient's blood pH return to normal?

6. Are there other substances in the blood that can serve as buffers?

Reference

Krause, D. S., Wolf, B. A., and Shaw, L. M. (1992) *Therapeutic Drug Monitoring* **14**, pp. 441-451.