Accidental Salicylate Intoxication in a Hemodialysis Patient

Kenneth S. Kleinman, MD; Suzanne Schweitzer, MPH; Allen R. Nissenson, MD

• A 61-year-old woman receiving long-term hemodialysis presented with symptoms of tinnitus, insomnia, malaise, and disequilibrium. On close questioning, it was discovered that she had received a prescription for salsalate (Disalcid) from a consulting physician who had evaluated her for joint pain. This tablet was similar in appearance to a dried aluminum hydroxide gel preparation (Alu-tab) that the patient was taking as a phosphate binder. She had mistakenly been taking six Disalcid tablets with each meal. Her salicylate level was 5.86 mmol/L, but she had no change in her serum electrolyte levels or acid-base status. When the salsalate treatment was stopped and regular dialysis treatments were continued, the symptoms of salicylism resolved. This case illustrates one of the potential dangers of polypharmacy in patients with chronic disease. The mild course was probably due to ongoing hemodialysis, which prevented the appearance of the usual acid-base abnormalities of salicylate intoxication.

(*Arch Intern Med* 1988;148:2277-2278)

Salicylate intoxication is a common form of accidental poisoning and therapeutic impropriety in children and the elderly.[1] Among adults, excessive ingestion of salicylates often occurs inadvertently.[2] The large number of medications that patients with chronic diseases use therapeutically can frequently lead to confusion over the proper dosing schedule.

The usual signs and symptoms of salicylism include dizziness, tinnitus, nausea, vomiting, mental confusion, and lassitude when mild intoxication is encountered. When the poisoning is more severe, the signs and symptoms can be life-threatening and include hyperpnea and tachypnea with corresponding respiratory alkalosis, although a mixed acid-base disorder with a marked anion gap metabolic acidosis may be seen.[3] Nevertheless, the classic symptoms and signs may be more subtle, and diagnosis of the intoxication may be delayed and associated with an increased mortality in comparison with those patients for whom early diagnosis and therapy are instituted.[4] The peak plasma salicylate level is probably the best measure of clinical severity. When salicylate levels exceed 4.34 mmol/dL, a forced diuresis is indicated, but when levels are in excess of 6.52 mmol/L and the clinical condition is severe, hemodialysis should be considered.[5]

A patient in our dialysis center accidentally confused two similar-appearing medications prescribed for totally dissimilar reasons; one was prescribed by a consultant without our knowledge. This medication is a commonly prescribed nonsteroidal anti-inflammatory agent that is predominantly of the salicylate class. Since the therapy for both chronic renal failure and salicylate poisoning in a patient with renal failure is hemodialysis, the ongoing hemodialysis not only delayed early diagnosis but also prevented more severe morbidity.

REPORT OF A CASE

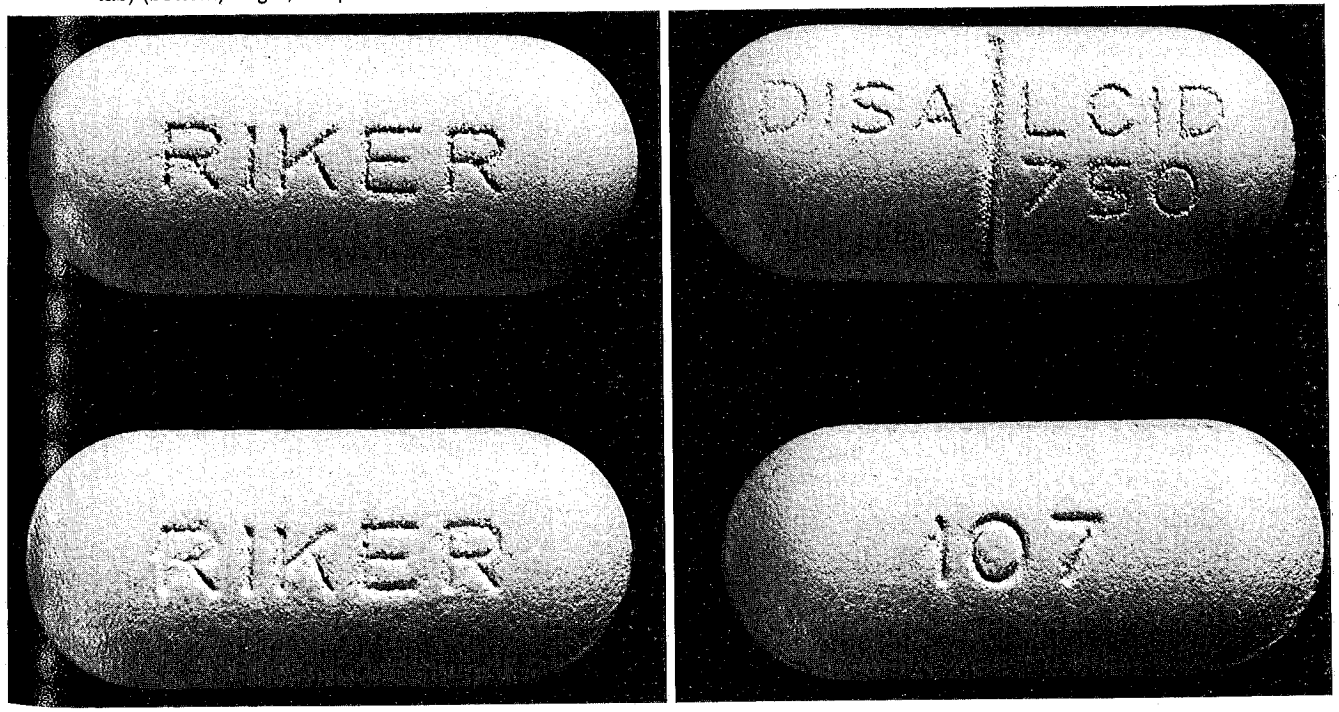
A 61-year-old woman had end-stage renal disease secondary to chronic glomerulonephritis. In 1968, a successful cadaveric renal transplant was performed, and the kidney functioned well until 1975, at which time thrice-weekly four-hour hemodialysis treatments were reinstituted with a cellulosic membrane. Complications of chronic renal failure included secondary hyperparathyroidism and renal osteodystrophy. Carpal tunnel surgery was performed in 1985. Chronic bronchitis was treated intermittently

Accepted for publication May 12, 1988.

From the Division of Nephrology, Department of Medicine (Drs Kleinman and Nissenson) and Pharmacy Services (Ms Schweitzer), UCLA Center for Health Sciences and UCLA School of Medicine, Los Angeles.

Reprint requests to UCLA, CHS 57-143, 10833 Le Conte Ave, Los Angeles, CA 90024 (Dr Nissenson).

Left, Manufacturers' embossed identifications on salsalate (Disalcid) (top) and aluminum hydroxide preparation (Alu-tab) (bottom). Right, Respective other sides of same medications.



with oral antibiotics. The patient complained frequently of diffuse aches and pains in multiple joint areas. Although she had received hemodialysis for a number of years, no evidence of hemodialysis-related amyloidosis had been discovered. Severe anemia necessitated frequent blood transfusions, which led to non-A, non-B hepatitis. Although the patient complained of intermittent fatigue, no evidence of jaundice or chronic hepatic dysfunction had been discovered. Usual medications included the following: a dried aluminum hydroxide gel preparation (Alu-tab [600 mg of aluminum hydroxide per tablet]), six tablets with each meal; calcium carbonate (500 mg/tablet), one with each meal; propranolol hydrochloride, 40 mg twice daily; calcitriol (Rocaltrol), 0.25 μg every day; theophylline, 100 mg twice daily; folic acid, 1 mg daily; a zinc sulfate vitamin prepation (Z-bec), one tablet daily; and naproxen (Naprosyn), 250 mg by mouth as needed for severe joint pains.

In December of 1986, the patient commenced therapy with recombinant human erythropoietin in a clinical trial for the treatment of the anemia of end-stage renal disease. At approximately the same time, she began to experience symptoms of tinnitus, difficult breathing, disequilibrium, insomnia, and generalized malaise. These symptoms occurred intermittently and in no consistent fashion. Because recombinant human erythropoietin was the only known new medication, the drug was withheld for several doses. This medication was re-introduced without side effects and was believed not to be responsible for her symptoms. It was discovered in February 1987 that the patient had been seen in the orthopedic clinic four months previously for joint pains and had been prescribed salsalate (Disalcid) in a dosage of two tablets twice daily (750 mg/tablet). After refilling a prescription, the patient realized that her salsalate medication was similar in appearance to that of her Alu-tab (Figure) and that she had been inadvertently taking salsalate in the dosage and frequency that was intended for the phosphate binder Alu-tab (six tablets with each meal). A predialysis salicylate level was 5.86 mmol/L (therapeutic level, 1.81 to 2.32 mmol/L). Unfortunately, a specimen for an arterial blood gas determination was not drawn at this time. The physical examination was remarkable only for scars from previous surgeries and an effusion of the left knee. Kussmaul's respirations and hyperpnea were not noted. Review of the hemodialysis flow sheets over the previous month showed a respiratory rate of 20 to 22 breaths per minute.

Six days prior, when the patient was already symptomatic and mistakenly ingesting large quantities of salsalate, serum electrolyte levels were as follows: sodium ion, 142 mmol/L; potassium ion, 4.1 mmol/L; chloride ion, 103 mmol/L; total carbon dioxide, 27 mmol/L. The salsalate treatment was discontinued, and the patient was admitted to the hospital, where hemodialysis was performed daily for four additional days. Following the first hemodialysis treatment, the salicylate level fell to 2.90 mmol/L. Subsequent levels fell by approximately half of the prior level. At the end of this four-day period, the tinnitus and disequilibrium had resolved, and she no longer complained of difficulty breathing. The patient continued to receive hemodialysis and her usual medications without further symptoms.

COMMENT

To our knowledge, this case is the first report of accidental salicylate poisoning in a patient receiving long-term hemodialysis therapy. The absence of severe metabolic alterations and the association of subtle symptoms emphasize how difficult the diagnosis of salicylate overdosage can be without the benefit of pertinent historical information.[2] The variations in the symptoms presented by this patient were probably due to an oscillation between mild and severe salicylism caused both by intermittent dialysis treatments and irregular misuse of the similar-appearing tablets.

The symptom of tinnitus was typical of salicylism. However, other physical signs, especially the respiratory pattern (eg, hyperpnea and tachypnea), were not dramatic enough to be noted by the staff. A predialysis arterial blood-gas determination when the salicylate level was 5.86 mmol/L would have been of interest, in particular, to see how much compensation for salicylate-induced respiratory alkalosis might occur in this setting. Unfortunately, this information was not available.

This case emphasizes the hazards of polypharmacy in patients with chronic medical illnesses. This danger is especially true when medications are similar in appearance. Improper and inadvertant use allows therapeutic regimens to become toxicologic emergencies.

References

1. Winchester JF, Gelfand MC, Knepshield JH, et al: Dialysis and hemoperfusion of poisons and drugs—update. *Trans Am Soc Artif Intern Organs* 1977;23:783-786.
2. Greer HD, Ward HP, Corbin KB: Chronic salicylate intoxication in adults. *JAMA* 1965;193:85-89.
3. Narins RG, Jones ER, Townsend R, et al: Metabolic acid-base disorders: Pathophysiology, classification, and treatment, in Arieff AI, DeFronzo RA (eds): *Fluid and Electrolyte and Acid-Base Disorders*. New York, Churchill Livingstone Inc, 1985, pp 269-384.
4. Anderson RJ, Potts DE, Gabow PA, et al: Unrecognized adult salicylate intoxication. *Ann Intern Med* 1976;85:745-747.
5. Lawson AA, Proudfoot AT, Brown SS: Forced diuresis in the treatment of acute salicylate poisoning in adults. *Q J Med* 1969;38:31-35.

Marked Hyperprolactinemia in Subclinical Hypothyroidism

Maj Kenneth E. Olive, MC, USAF,
Maj James V. Hennessey, MC, USAF

• Hyperprolactinemia is common in primary hypothyroidism but, to our knowledge, marked elevation of serum prolactin in subclinical hypothyroidism has not been previously reported. A 45-year-old woman presenting with carpal tunnel syndrome was found to have a minimally elevated level of thyrotropin with a normal level of thyroxine. Thyrotropin releasing hormone stimulation testing revealed hyperresponsiveness consistent with primary hypothyroidism. An unstimulated prolactin level was 187 μg/L and returned to normal with levothyroxine therapy. Results of visual field testing were normal, and a computed tomographic scan of the pituitary gland revealed no evidence of a macroadenoma. This case demonstrates the occurrence of significant hyperprolactinemia in the absence of overt primary hypothyroidism.
(*Arch Intern Med* 1988;148:2278-2279)

Elevated serum prolactin levels have been reported frequently in patients with primary hypothyroidism. Indeed, patients with primary hypothyroidism have pre-

Accepted for publication June 30, 1988.

From the Departments of Medicine, US Air Force Medical Center, Wright-Patterson Air Force Base, Ohio, and Wright State University School of Medicine, Dayton, Ohio.

Presented in part at the Air Force Regional Meeting of the American College of Physicians, San Antonio, Tex, Feb 29, 1988.

The information contained in this article is the opinion of the authors and should not be construed to represent Department of Defense policy.

Reprints not available.