Acute Renal Failure Due to Sulfadiazine in Patients with AIDS

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Dear Sir,

Sulfadiazine (Adiazine®) has been extensively used from the mid 1930s, mainly for treating pulmonary infections, till the introduction of penicillin and other modern antibiotics. By that time, numerous cases of acute renal failure due to crystallization of the drug in the urinary collecting system were reported [1–4]. In recent years sulfadiazine has come into utilization again as therapy for toxoplasmosis in patients with AIDS [5, 6]. We report here on 3 patients who developed acute renal failure while being treated with sulfadiazine in our institution during the last year.

Case Reports

Case No. 1.
He was a 44-year-old man with AIDS known since February 1986 and Kaposi sarcoma since December 1986. Toxoplasmosis with right arm monoparesis developed in March 1986 and was treated with sulfadiazine (6 g/day) and pyrimethamine 50 mg/day. At the start of this treatment his serum creatinine concentration was 100 µmol/l. One month later he suffered from intense back pain and became oliguric (500 ml/day). His serum creatinine concentration had increased up to 350 µmol/l. Urinalysis disclosed no infection. Renal ultrasound showed a multitude of small stones in both kidneys. Following intravenous rehydration and alkalinization (2 liters of isotonic sodium bicarbonate and 1 liter of isotonic glucose with 5 g of NaCl and 2 g of KC1 during the first 48 h), serum creatinine concentration came down to 115 µmol/l. Analysis of the stones that were eliminated spontaneously showed them composed of sulfadiazine cristals.

Case No. 2
He was a 46-year-old homosexual man with AIDS and Kaposi sarcoma. Therapy was started with sulfadiazine (4 g/day), inter-feron (18 million units/day) and pyrimethamine 50 mg/day for a choroiditis due to toxoplasmosis. Serum creatinine concentration was 79 µmol/l. 21 days after onset of this treatment, the patient complained of intense headache, abdominal pain and hand shaking. The patient was afebrile, normally hydrated, oliguric (500 ml/day) his blood pressure was 120/80 mm Hg. Serum creatinine concentration was 1,551 µmol/l, sodium, potassium and carbon dioxide concentration were 122, 7.1 and 10 mmol, respectively. A plain abdominal film revealed two symmetric kidneys whose size was slightly enlarged. No obstruction of the urinary tract was
found by renal ultrasound, which however disclosed numerous small hyper-echogenic images in
the medulla of both kidneys (fig. 1). Two hyperechogenic images were also visible in the
bladder. The patient underwent two hemodialysis sessions associated with hydration and
alkalinization (2 liters of isotonic glucose with 16 g NaCl and 6 g KC1, 1 liter of isotonic
bicarbonate, associated with 500 mg furose-mide during the first 48 h). His serum creatinine
concentration returned to normal in 3 days.

Case No. 3
She was a 23-year-old woman from Zaire with AIDS who was operated on for a cerebral abscess
due to toxoplasmosis. Postoperatively the treatment comprised sulfadiazine (6 g/day),
pyrimethamine (50 mg/day) and sodium valproate (1,500 mg/day), her serum creatinine
concentration at that time was 96 µmol/l. 6 days after start of treatment, the patient decided to
leave the hospital. She was readmitted as an emergency 15 days later, afebrile but feeling sick
and her hands shaking. Her daily urinary output was 1,500 ml and plasma creatinine
concentration was 1,550 µmol/l. Renal ultrasound showed two kidneys of enlarged size (14 cm
right, 13.5 cm left) without any dilatation of renal pelvises or calyxes. A stone was detected in
the upper left pyelon. The patient was treated by intravenous hydration and alkalinization. Her
renal function improved rapidly and on the 7th day after admission, serum creatinine
concentration had decreased down to 173 µmol/l.

Comments
The 3 patients reported herein who developed acute renal failure while being submitted to
sulfadiazine had a normal serum creatinine concentration prior to drug administration. Acute
renal failure developed after 15–45 days of high-dose sulfadiazine (80–100 mg/kg/day) therapy.
Sharp elevation of serum uric acid concentration in the genesis of renal dysfunction is unlikely,
the peak uric

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Fig. 1. Hyperechogenic images in the medulla of the left kidney due to sulfadiazine crystals.
acid levels recorded in the patients being 487, 691, 490 µmol, respectively. Sulfadiazine crystals
were evidenced in the urinalysis of patient 1. Renal ultrasound appears superior to plain
abdominal X ray examination for detecting radiolucent and small calculous elements located in
the renal parenchyma or renal urinary cavities.
Acute renal dysfunction due to sulfadiazine has in some cases been attributed to an acute
interstitial nephritis secondary to an allergic or hypersensitivity reaction. However the
mechanism most commonly involved is the formation of crystalline aggregate in the renal
parenchyma or along the urinary tract from calyxes down to the bladder, causing tubular damage
and/or urinary tract obstruction [7, 8]. The rapid reversal of this type of acute renal failure is
particularly noteworthy, being recorded within 3, 4 and 10 days in our 3 cases, respectively.
Improvement of renal function follows discontinuation of sulfadiazine, abundant hydration
and alkalinization of the urine via parenteral route. Severe oliguric renal insufficiency
may render dialysis treatment mandatory as was the case in our patient 2. The urinary pH
must be raised over 7, an alkaline milieu being requested for transforming sulfadiazine into a soluble
salt [9].
A careful monitoring of patients treated with sulfadiazine appears thus mandatory in order to
avoid the development of acute renal dysfunction due to intrarenal urinary tract crystallization
of the drug, especially in dehydrated patients. This cause of acute renal failure can thus be easily
prevented by maintaining in the patients an alkaline daily urinary output of at least 2,000 ml.
References