SELECTED REPORTS

Trimethoprim with Sulfamethoxazole for Treatment of Infection with Pneumocystis carinii in Renal Insufficiency*

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Pneumonia due to Pneumocystis carinii developed in an immunosuppressed patient with a renal transplant who had substantial renal failure. Successful treatment was achieved with administration of trimethoprim plus sulfamethoxazole at a dosage adjusted to the degree of renal failure. There were no significant adverse effects from this therapy.

Infection with Pneumocystis carinii has been successfully treated with pentamidine isethionate and, more recently, with large doses of trimethoprim plus sulfamethoxazole. Treatment with pentamidine, particularly in patients with renal failure, is troublesome. Recent studies suggest that therapy with trimethoprim plus sulfamethoxazole can be used safely for bacterial infections of the respiratory and urinary tracts in patients with impaired renal function. To our knowledge, there has been no report on treatment with trimethoprim plus sulfamethoxazole for pneumonia due to Pneumocystis in patients with substantial renal failure.

CASE REPORT

An 18-year-old man who was receiving hemodialysis for treatment of chronic renal failure underwent bilateral nephrectomy and splenectomy in September 1975 and received a renal transplant from his father in November 1975. Chronic rejection of the transplant followed. On Oct 8, 1976, a kidney from a cadaver was transplanted, and the original allograft was removed on Oct 18, 1976. To prevent rejection of the transplant the customary high doses of methylprednisolone and azathioprine were administered. On Nov 19, 1976, fever and a nonproductive cough developed, followed by severe dyspnea during the next 48 hours. On examination, the patient, who weighed 80 kg (132 lbs), had blood pressure of 140/90 mm Hg, pulse rate of 122 beats per minute, respiratory rate of 44/min, and temperature of 38.9°C (101.2°F). The lungs were clear to auscultation.

Studies in the laboratory gave the following results: hemoglobin level, 4.8 gm/100 ml; white blood cell count (WBC), 10,700/cu mm; serum level of creatinine, 4.5 mg/100 ml; arterial pH, 7.46; arterial oxygen pressure, 36 mm Hg; and arterial carbon dioxide tension, 30 mm Hg. The chest x-ray film revealed diffuse bilateral infiltrates.

Blood, sputum, and urine were cultured for bacteria and fungi. Infection with P carinii was suspected. The dosages of azathioprine and methylprednisolone were reduced. Because of the severe clinical deterioration, a decision was made on the evening of Nov 21, 1976 to administer trimethoprim plus sulfamethoxazole; an open biopsy of the lung was to be performed on the next morning. An initial dose of 2,800 mg of sulfamethoxazole and 560 mg of trimethoprim was given at approximately 1 AM on Nov 22. This dose was considered to be approximately half of the daily dosage indicated for this patient if renal insufficiency had not been present. Therefore, 1,200 mg of sulfamethoxazole (20 mg/kg of body weight) and 240 mg of trimethoprim (4 mg/kg of body weight) were given daily in three divided doses. These doses were approximately one-fifth of the usual daily dosage for treatment of pneumonia due to P carinii.

The open biopsy of the lung revealed subacute interstitial and alveolar pneumonitis. Cysts of P carinii were identified in sections stained by the Gomori methenamine silver technique. Cultures of pulmonary tissue were negative for bacteria, fungi, mycobacteria, and viruses, including cytomegalovirus and herpesvirus. The patient's condition responded well to therapy, with resolution of the fever, dyspnea, and pulmonary infiltrates.

No side effects from trimethoprim plus sulfamethoxazole were noted. Serum levels of sulfamethoxazole and creatinine, the hematocrit reading, and the WBC are shown in Figure 1. During the 14-day course of therapy with trimethoprim plus sulfamethoxazole, the hematocrit reading remained stable. The WBC decreased from 10,700/cu mm to 3,300/cu mm on the eighth day of treatment and increased to 5,900/cu mm thereafter. No thrombocytopenia was demonstrated.

The serum level of creatinine decreased from 4.5 to 3.5 mg/100 ml. There was no crystalluria on examination on seven occasions. The mean pH of the urine during treatment was 5.8. Samples of blood for determination of the levels of trimethoprim and sulfamethoxazole were obtained one hour after the oral administration. The level of trimethoprim was measured by the microbiologic assay of Bushby; and the level of sulfamethoxazole was determined by the method of Bratton and Marshall. The serum levels of sulfamethoxazole determined on six occasions ranged from 43.6 μg/ml to

![Figure 1. Serum levels of sulfamethoxazole (SMX) and creatinine and values for hematocrit reading and WBC related to treatment with trimethoprim-sulfamethoxazole mixture.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21010/ on 06/03/2017)
172 μg/ml. Unfortunately, the serum level of trimethoprim was measured only once, on the tenth day of therapy, when the level was 12.6 μg/ml.

**Discussion**

Studies by Hughes et al. and by Lau and Young have reported the effectiveness of trimethoprim plus sulfamethoxazole in pneumonia due to *P. carinii*. The daily doses given were 100 mg of sulfamethoxazole per kilogram of body weight and 20 mg of trimethoprim per kilogram of body weight. With this schedule of dosage, Hughes et al. reported serum levels ranging from 80 μg/ml to 120 μg/ml for sulfamethoxazole and from 4 μg/ml to 10 μg/ml for trimethoprim; in the study by Lau and Young, these levels ranged from 21 μg/ml to 144 μg/ml and from less than 1 μg/ml to 9.6 μg/ml, respectively. This latter report also suggested that a good response to treatment was associated with levels of trimethoprim exceeding 5.5 μg/ml. Neither group mentioned the presence of renal failure in their patients.

Tasker et al. demonstrated that patients with renal impairment could be safely treated for bacterial infections, provided that adjustment was made for renal insufficiency. Bennett and Craven treated six patients who had a mean clearance of creatinine of 14.8 mg/min/1.73 m², 1,000 mg of sulfamethoxazole and 320 mg of trimethoprim per day for two weeks, with no decrease in renal function. These investigators obtained mean antimicrobial levels of 65 μg/ml for sulfamethoxazole and 3.1 μg/ml for trimethoprim; however, some of their patients were receiving treatment with hemodialysis. Barclay et al. treated seven patients who had clearances of creatinine between 15 and 30 ml/min with 500 mg of sulfamethoxazole and 160 mg of trimethoprim twice daily for four days. These investigators noted levels in the blood of up to 140 μg/ml for sulfamethoxazole and up to about 2.2 μg/ml for trimethoprim; however, the timing of assay in relation to the previous dose was not given in either of these last two reports.

Our values for the serum levels of sulfamethoxazole have fluctuated widely, ranging from 43.6 μg/ml to 172 μg/ml. The low levels can possibly be explained by an improvement in renal function, with a decrease in the serum levels of creatinine from 4.5 to 3.5 mg/100 ml. This wide variation has also been noted by Lau and Young, who used the same spectrophotometric method. Further experience is needed in the treatment of pneumonia due to *P. carinii* in patients with substantial renal insufficiency, in order to determine the optimal dosage regimen.

**References**


**Clicks due to Swan-Ganz Catheter**

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Nonejection systolic and diastolic clicks appeared when a Swan-Ganz catheter was positioned in the proximal portion of the right pulmonary artery. The clicks disappeared on inflation of the catheter's balloon. Initial impressions included secondary prolapse of the mitral leaflets, an accentuated third heart sound, and the exposure of an occult opening snap. These high-frequency sounds are thought to be generated by the forward and backward movement of the catheter against either the proximal portion of the pulmonary artery or the right ventricular outflow tract or by a whipping action of the catheter itself.

The use of the Swan-Ganz catheter has proved to be a boon to the bedside monitoring of the hemodynamic status of the critically ill patient. Recent literature has expounded the use of this catheter not only as a hemodynamic monitor, but also as a diagnostic aid in such disorders as a ruptured ventricular septum, acute valvular insufficiency, cardiac tamponade, pulmonary embolus, right ventricular infarction, and states of high and low cardiac output.

The list of causes for nonejection clicks is ever expanding and includes pacemaker-induced clicks, the syndrome of mitral leaflet prolapse, secondary mitral valvular prolapse, ventricular aneurysms, congenital aneurysm of the membranous ventricular septum, mediastinal emphysema, pleuropulmonary adhesions, atrial myxoma, congestive cardiomyopathy, Ebstein's anomaly, mitral commissurotomy, and pneumothorax. This report describes the appearance of and possible explanation for nonejection clicks in a critically ill patient in whom a Swan-Ganz catheter had been inserted.

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