Efficacy and Effects on Pulmonary Function Tests of Weekly 600 mg Aerosol Pentamidine as Prophylaxis against *Pneumocystis carinii* Pneumonia

**Summary:** A prospective study was designed to evaluate the efficacy and effects on pulmonary function tests of weekly 600 mg aerosolised pentamidine as prophylaxis against *Pneumocystis carinii* pneumonia (PCP) amongst two groups of patients infected with the human immunodeficiency virus. Group 1 (primary prophylaxis) consisted of patients with either diseases indicative of AIDS other than PCP or whose absolute CD4 positive lymphocyte count was below 200/mm³, and Group 2 (secondary prophylaxis) comprised patients with previous proven episodes of PCP. Fifty-five patients (30-Group 1, 25-Group 2) were studied over a period of 36 months, and no patients reached a study end point of either relapse or death due to PCP after a mean duration of treatment of 14.9 months (range 9–36 months). There were no significant differences between the pulmonary function tests performed at the start and end of the study on both groups of surviving patients. Ten patients (18%) reported coughing and eight patients (15%) were documented to have bronchoconstriction, which was found to be preventable by prior administration of disodiumcromoglycate. The results showed that weekly 600 mg aerosolised pentamidine is effective and well tolerated for primary and secondary prophylaxis against PCP without additional adverse effects. Further prospective randomized trials are needed to determine whether doses higher than the current recommended 300 mg monthly dosage of aerosolised pentamidine provide more efficacy before such an alternative prophylactic treatment is generally adopted for patients who cannot tolerate other systemic agents.

**Introduction**

*Pneumocystis carinii* pneumonia (PCP) is the most frequent cause of death in patients infected with the human immunodeficiency virus (HIV) [1,2]. It is also the most frequent life-threatening opportunistic infection leading to the diagnosis of the acquired immunodeficiency syndrome (AIDS). Trimethoprim-sulfamethoxazole has been shown to be effective in preventing PCP in other patients with HIV. However, it is not always tolerated by patients and has been associated with adverse effects, particularly in patients with renal impairment. Pentamidine in aerosol form is another option for prophylaxis against PCP, but it is also associated with adverse effects.

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The study was designed as a prospective evaluation of the efficacy and tolerance of weekly administration of 600 mg of whose absolute CD4 positive lymphocyte cell count was less than 200/μm³ showed the 300 mg dosage every four weeks to result in the fewest PCP episodes. However, 28 of the 139 (20%) participants in that arm of the study developed PCP after a median treatment of 212 days, suggesting that the 300 mg monthly dosage is not the optimal prophylactic treatment dosage and interval.

We report the results of a prospective open-labelled study evaluating the efficacy and effects on pulmonary function tests of 600 mg weekly aerosol pentamidine for primary and secondary prophylaxis against PCP in two groups of HIV-infected patients.

Patients and Methods

The study was designed as a prospective evaluation of the efficacy and tolerance of weekly administration of 600 mg of aerosol pentamidine isethionate as prophylaxis against PCP in two groups of patients. Group 1 (primary prophylaxis) comprised patients with either AIDS indicator diseases other than PCP or who had previous proven episodes of PCP. Participants were excluded if they had had severe asthma, an anaphylactic reaction to pentamidine or if they were currently using agents with known or likely efficacy against *P. carinii*.

Pentamidine isethionate was reconstituted in 6 ml of sterile water and administered for 35 to 40 min using a System 22 Antibiotic Tee-tube and Acorn nebuliser with an Optimist Master particle sizer (Medic-Aid Limited, Sussex, UK) acting as a baffle delivered at 8 l/min of pressurised oxygen. The generated aerosol droplets have a mass median aerodynamic diameter of 1.2 μm (Geometric Standard Deviation 2.9), with 93.6% of the particles below 5 μm as measured by a Malvern laser analyser. Each treatment was initially supervised by a doctor and physiotherapist who noted any immediate adverse effects and administered a bronchodilator if needed for severe coughing or bronchoconstriction. Each patient was taught about the setting up of the nebutising system and self-administration of the drug, and all patients were administering their own treatment by the third week. Each participant was followed from the first treatment on or about September 1987 until death or 31 December 1990. The study end point was either relapse due to PCP or death due to PCP that occurred during treatment for acute PCP. Concurrent medications, intercurrent illness and respiratory function tests (forced expiratory volume in the first second = FEV₁, forced vital capacity = FVC, carbon monoxide diffusion capacity = DLCO) and symptoms were documented at each two-monthly review. Independent and paired t-tests were used for statistical analysis.

Results

Sixty patients were recruited for the study. Five patients were excluded from the study; two due to non-compliance, one who elected to have the treatment fortnightly after having been treated weekly for 26 months, one who developed a skin rash following administration of the drug and another who was lost to follow-up. All five were excluded from the final analysis.

All but one participant were men. Their ages ranged from 24 to 56 years (mean 32.8). The HIV-related diagnoses of patients in Group 1 are shown in Table 1. Concurrent medications of both groups are shown in Table 2.

Nine patients (five from Group 1, four from Group 2) were intolerant of zidovudine because of recurrent anaemia and neutropenia. The mean dosage of zidovudine was 600 mg (range 500–1000 mg). Forty-five patients were on weekly 150 mg fluconazole for recurrent oral candidiasis. Eight patients were on maintenance intravenous trisodium phosphonoformate (Foscarnet) (120 mg/kg/day for six days of the week) for cytomegalovirus (CMV) retinitis. Monthly maintenance vincristin (2 mg) and bleomycin (30 mg) were given to three patients who had disseminated Kaposi's sarcoma.

Thirty-six months after the start of the study, all 55 patients completed the study without reaching a study end point. The mean duration of treatment for both groups was 14.9 months (range 9–36) (Table 3). However, there were eight and nine deaths in Groups 1 and 2 respectively.