Consent to treatment with zidovudine among HIV-infected patients

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■ Zidovudine delays the progression of disease in asymptomatic or mildly symptomatic patients infected with human immunodeficiency virus (HIV), but it can cause serious adverse reactions, a fact which makes zidovudine treatment undesirable to some patients. In this study, zidovudine was offered to HIV-infected patients with CD4 leukocyte counts between 200 and 500 cells/μL, and the acceptance or refusal of therapy was recorded over a 4-month period. Of 73 patients approached, 49 (67%) consented to the therapy (23 asymptomatic and 26 with AIDS-related complex). The high acceptance rate of zidovudine among both asymptomatic and mildly symptomatic HIV patients raises the question of finding additional financial resources and health care providers for close monitoring of side effects.

□ INDEX TERMS: ZIDOVUDINE; HIV INFECTIONS; TREATMENT REFUSED; PATIENT COMPLIANCE □ CLEVE CLIN J MED 1992; 59:45–47

ZIDOVUDINE (ZDV, formerly azidothymidine or AZT) decreases the mortality and frequency of opportunistic infections in selected patients with acquired immunodeficiency syndrome (AIDS) or AIDS-related complex (ARC).[1,2] However, treatment with ZDV has resulted in some serious adverse reactions, including bone marrow suppression, anemia, and neutropenia.[3]

In August 1989, the National Institute of Allergy and Infectious Diseases announced the results of two placebo-controlled studies conducted by the AIDS Clinical Trial Group (ACTG), which showed that ZDV delayed disease progression in patients infected with human immunodeficiency virus (HIV) who had fewer than 500 CD4 lymphocytes/μL and who were asymptomatic or mildly symptomatic. The results were subsequently published.[4,5]

It is estimated that more than 1 million people in the United States may be infected with HIV,[6] and that 500,000 of them may be asymptomatic and have CD4 leukocyte counts below 500 cells/μL. These people may benefit from early intervention with ZDV to slow the progression of HIV infection; however, because of the severe side effects of the drug, patients may be reluctant to undergo ZDV therapy. After the ACTG results were announced, we conducted a study at the HIV clinic at the University of Massachusetts Medical Center (UMMC) to determine the acceptance rate of ZDV among HIV-infected patients.

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This study was partially supported by the National Institute of Allergy and Infectious Diseases, Grant Number AI25831. This paper was originally presented as a poster session at the Sixth International Conference on AIDS, San Francisco, June 1990.

METHODS

Long before the ACTG trials, the FDA had approved the use of ZDV for HIV-infected patients with CD4 counts below 200 cells/μL. Consequently, all our patients with CD4 counts below 200 cells/μL had already been offered ZDV before this study was conducted. Therefore, HIV-infected patients with CD4

TABLE
ACCEPTANCE OF ZIDOVUDINE THERAPY

Category	Contacted	% of total	Accepted ZDV	Rate
Sex				
Male	46	63%	32/46	70%
Female	27	37%	17/27	64%
Race				
White	46	63%	31/46	67%
Hispanic	23	32%	17/23	74%
Black	4	5%	1/4	25%
Risk factors*				
Intravenous drug user	51	70%	32/51	63%
Homosexual	14	19%	9/14	64%
Other	11	15%	9/11	82%
Total	73	100%	49/73	67%

*Some patients had multiple risk factors.

cell counts between 200 and 500/μL who had been seen at the UMMC HIV clinic were contacted by mail or phone and given appointments for the purpose of initiating ZDV therapy (at a dose of 500 mg/day). Eligible new patients were offered ZDV therapy when their CD4 count dropped to 500 or lower. The interviews included detailed discussion of the results of the ACTG studies. The number of patients consenting to ZDV therapy was recorded over a 4-month period. During those 4 months, compliance was monitored for the group that had accepted ZDV therapy, and changes regarding acceptance or refusal of ZDV were followed among the patient cohort.

RESULTS

A total of 73 patients were offered ZDV treatment. The proportion of sex and risk groups reflect the demographic characteristics of HIV-infected patients presenting to the UMMC HIV clinic (*Table*). The distribution of risk factors was as follows: intravenous drug use, 67% of patients; homosexuality, 18%; other risk factors, 16%. The racial distribution was 64% white, 32% Hispanic, and 4% black. The ratio of males to females was 1.7 to 1. Of the 73 patients studied, 49 (67%) accepted treatment, 8 refused treatment, 6 failed to show for interview appointments, and 10 continued to consider whether they would accept treatment. Of the 49 patients who accepted treatment, 23 (47%) were asymptomatic and 26 (53%) had ARC. Of the 8 patients who refused ZDV, 3 were asymptomatic and 5 had ARC. Their reasons for refusal included active drug use which would interfere with compliance with the treatment regimen (3), feeling of well-being and fear of side effects (3), no interest in taking ZDV (1), and too much emotional stress from both dealing with the HIV infection and taking medicine (1). The cost of the treatment was a factor influencing acceptance of treatment: 4 of the 10 patients who were considering ZDV therapy applied for financial assistance through the Massachusetts HIV-Drug Reimbursement Plan. Without assistance they would not be able to afford treatment.

Over the next 4 months, 40 of the 49 patients who accepted ZDV continued with the medication. Four of these patients experienced nausea but continued to take ZDV. Of the 9 who discontinued its use, 4 had minor side effects (nausea, vomiting, agitation, and fatigue), 2 were noncompliant with the medication, and 3 failed to meet follow-up appointments and obtain refills of the medication). No hematologic toxicities were observed during this period.

Of the eight patients who initially refused ZDV, two eventually accepted treatment. Also, 7 of the 10 who were considering taking ZDV eventually accepted. Thus, the number of patients on ZDV therapy at the end of the study was the same as the number who accepted therapy initially.

Four of the six patients who failed to meet the initial appointment continued to avoid scheduled appointments, but two were seen subsequently: one patient's condition had progressed to AIDS, and one had a repeat CD4 count of 500 cells/μL. It was felt that the latter patient should be followed closely without ZDV.

CONCLUSION

At UMMC, 61% of all HIV patients were infected via intravenous drug use. Before ZDV was shown to be efficacious for asymptomatic and mildly symptomatic patients, the recruitment of intravenous drug users into AIDS clinical trials at this center was slow, and the dropout rate was high.[7] Intravenous drug users have been poorly represented in national drug trials. Among our patients, intravenous drug users and minority groups were equally likely to consent to ZDV treatment after it was shown to be effective in delaying the progression of HIV infection.

Our data suggest that the results of the ACTG trials might have persuaded our patients to begin ZDV treatment. In recruiting eligible patients into the ACTG trials, the patients were informed of the efficacy and side effects of ZDV. The latter were often cited by our patients to be a major stumbling block to initiation of ZDV therapy. In the recently published trials of ZDV[4,5] in the treatment of patients with asymptomatic and

mildly symptomatic HIV infection, and in other trials of ZDV[1–3] among patients with AIDS and ARC, adverse reactions among asymptomatic and mildly symptomatic patients occurred less frequently when compared with patients with more progressive illness. This fact might have helped allay the fears of our patients and promote ZDV acceptance among them.

ZDV has been used widely for prolongation of life in patients in the late stages of AIDS. Although our study population is small, it is evident that ZDV will be prescribed even more widely to delay progression of the disease in asymptomatic or mildly symptomatic patients, particularly since the Food and Drug Administration further expanded indications for its use in March 1990.

Intravenous drug use is the second most common risk behavior for acquiring HIV infection in the United States.[8,9] It accounts for more than 27% of all AIDS cases. Blacks and Hispanics constitute a disproportionate number of HIV-infected patients nationwide because of a relatively higher incidence of drug use among these groups than among whites, although this disproportion is not apparent in our study population.

Already HIV infection has overwhelmed the resources of black and Hispanic communities, particularly in the inner cites where intravenous drug use is prevalent. To effectively treat early asymptomatic or mildly symptomatic HIV infection within the intravenous-drug-using and minority populations, a national policy is needed which addresses the questions of finding the additional financial resources and health care providers which are necessary to accomplish early treatment of HIV disease, and to provide greater access to drug treatment programs and more systematic education and counselling in the prevention of HIV infection.

ACKNOWLEDGMENTS

The author thanks Ms. Karen Tolson and Ms. Kim Wojnowski for their assistance in the preparation of this manuscript.

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