PHARMACY PRACTICE

Pharmacists' Activities in Monitoring Zidovudine Therapy in an AIDS Clinic

Nimira Walji, Ann Beardsell and Glen Brown

INTRODUCTION

The Acquired Immunodeficiency Syndrome (AIDS) epidemic has a profound impact on society and the provision of health care due to the disease's associated morbidity, mortality, and expense. The economic impact of AIDS is significant secondary to the requirement of frequent hospitalizations and the use of new investigational drugs and/or large doses of conventional drugs. This was confirmed in an internal evaluation conducted at St. Paul's Hospital which revealed that drug costs for hospitalized AIDS patients were greater than that for non-AIDS patients. The epidemic has prompted an intensive program to develop and optimize therapy of human immunodeficiency virus (HIV) infections in an attempt to decrease overall morbidity and cost.

Zidovudine (Retrovir®, azidothymidine or AZT) is an anti-retroviral agent with activity against HIV and demonstrates benefit in prolonging survival, decreasing mortality and improving quality of life in AIDS and AIDS-related complex (ARC) patients.[1,2,3] Since zidovudine has only virustatic activity, lifelong therapy and ongoing monitoring is required for maintaining the most efficacious drug regimen with the least toxicity. Zidovudine was made available as an emergency release drug in 1987 by the manufacturer, Burroughs Wellcome, through an open trial designed to assess the long term safety of zidovudine therapy.[4] The outpatient Infectious Disease Clinic (IDC) at St. Paul's Hospital was one of the centres participating in this trial.

During the open trial, the IDC was the centralized distribution centre of zidovudine in the province of British Columbia. Enrolled patients were initially required to visit the clinic at weekly intervals prior to which they obtained specific laboratory tests. At the clinic, the patients were first examined by a study physician who documented their progress and indicated all necessary changes in therapy in each patient's medical chart and the manufacturer's monitoring form. Subsequently, the patients were interviewed by a pharmacist.

The initial interview was approximately 15-20 minutes in duration involving explanation of background information about the clinical trial, zidovudine, common side effects and their management. Subsequent visits were about 10-15 minutes long during which the pharmacist made an in-depth assessment of the patient's progress for signs and symptoms of efficacy and toxicity. Pharmacists at the clinic used data obtained from the patient and data from the chart to form their assessment of zidovudine therapy. This involved chart review of the physician's notes and laboratory data, questioning of the patient to assess clinical efficacy, toxicity and concurrent use of medications to obtain all necessary information.

The pharmacist intervened in response to any indication of suboptimal utilization of, or adverse effect to zidovudine. Any problems identified, and the pharmacist's proposed solutions, were discussed with the health care team. Examples of such problems would be adverse effects with current dose, interacting concurrent drug therapy (e.g. acetaminophen) or inability to manage side effects on current dose. When the interventions initiated resulted in a change in total daily dose, a new prescription was processed and the appropriate amount of zidovudine was dispensed. As patients became stabilized on their optimum dose, the interval between visits was gradually increased from one to four weeks at the pharmacists' discretion. Stable patients were required to attend the clinic once a month for continued monitoring and zidovudine refills. After each interview, the pharmacist recorded, in the patient's chart, the events of the interview, any interventions made, and the outcome.

The goal of this evaluation was

Nimira R. Walji, B.Sc. (Pharm.) is a Staff Pharmacist at St. Paul's Hospital in Vancouver, B.C.
Ann Beardsell, B.Sc. (Pharm) is Ambulatory Pharmacy Services Supervisor at St. Paul's Hospital in Vancouver, B.C.
Glen Brown, Pharm.D. is Assistant Director, Clinical Pharmacy Department at St. Paul's Hospital in Vancouver, B.C.
Address correspondence to: Nimira Walji, Pharmacy Department, St. Paul's Hospital, 1081 Burrard Street, Vancouver, B.C. V6Z 1Y6.

to document and characterize the types, frequency and acceptance by physician and/or patient of pharmacist-initiated interventions regarding zidovudine therapy in non-hospitalized AIDS and ARC patients.

PHARMACIST INTERVENTIONS

The types and frequency of pharmacist-initiated interventions were summarized through a retrospective chart review of 285 patients who visited the clinic during a five to seven day span in each of three consecutive months (September, October, and November 1989). The charts of all patients who visited the clinic on these randomly selected days were reviewed. A total of approximately 500 patients were enrolled in the open trial at the time of this evaluation. However, 285 (57%) of the population was used as the sample size and was thought to be an adequate representation of the total number of enrolled patients. Two consecutive visits were used to collect data for each patient: the first visit verified that monitoring parameters were being followed and identified the type and frequency of interventions, while the subsequent visit was used to identify the acceptance rate by the physician and/or patient of the pharmacists' recommendations. A form was developed to record information from each chart review (Appendix I).

Of the 285 patient charts reviewed, there were 75 interventions documented and 73 (97%) of these were accepted by either physician and/or patient (Table I). The two interventions rejected were requests to decrease dosage. In one case, the request was made due to increased toxicity to the patient, while in the other, the patient was also on concurrent chemotherapy.

Table I: Types, Number and Acceptance of Interventions made by Pharmacists during Zidovudine Therapy Monitoring

Type of Intervention	Sep/89	Oct/89	Nov/89	TOTAL	ACCEPTANCE
decrease dosage	11	4	3	18	16 (89%)
increase doage	0	4	0	4	4 (100%)
discontinue drug	1	3	0	4	4 (100%)
repeat lab work	0	4	1	5	5 (100%)
additional lab work	1	2	2	5	5 (100%)
extend time until next visit	5	8	0	13	13 (100%)
address non-compliance	1	1	1	3	3 (100%)
initiate adjunctive therapy	1	2	0	3	3 (100%)
adjust dosing schedule	3	0	0	3	3 (100%)
clarify potential adverse effects	0	5	3	8	8 (100%)
alternate adjunctive therapy	1	2	2	5	5 (100%)
miscellaneous	1	2	1	4	4 (100%)
Total no. of interventions:	25	37	13	75	73 (97%)
No. of patient charts reviewed:	85	121	79	285	

DISCUSSION

In recent years, the hospital pharmacists' role has developed to include participation in more clinical and patient-oriented activities. Pharmacists now have the opportunity to apply their knowledge and skill to the selection, monitoring, and discontinuation of drug therapy. The advent of hospital ambulatory care clinics has created a new avenue for pharmacists to participate in patient care.[5,6] The benefits of decreased hospitalization costs, and reduced morbidity, due to pharmacists' participation in drug therapy monitoring and patient education have been documented in warfarin anticoagulation clinics.[7,8,9] Using set protocols, pharmacists have also been shown to be effective providers of primary care for chronically ill patients with conditions such as hypertension and diabetes[10] and other conditions.[11,12] Pharmacists have also taken an active role in distributing, monitoring, documenting and evaluating investigational agents in clinical trials.[13]

This report describes an outpatient infectious disease clinic, where pharmacists are an integral part of patient care and the health care team. Pharmacists' routine monitoring of patient progress while receiving zidovudine resulted in frequent recommendations to alter drug therapy. The most frequent types of interventions made by pharmacists were to decrease the dose of zidovudine, extend time until the next clinic visit, clarify potential adverse effects of zidovudine, and initiate or recommend alternate adjunctive therapy. Since many of these interventions involved assessing for signs of toxicity, it is postulated that this close monitoring averted many adverse effects and improved quality of patient care. However, no attempt to assess the clinical or cost impact of the pharmacists' interventions on patient outcome was undertaken in this evaluation.

The number of interventions decreased over the time course of the evaluation reflecting a change in the prescribing of zidovudine. Based on FDA recommendations and an announcement by the Minister of Health in September 1989, the starting dose of zidovudine was decreased by one-half after unpublished clinical trials showed that a lower dose was as efficacious as the usual 1200 mg/day dose.[14] This resulted in improved tolerance and decreased need for subsequent changes in zidovudine therapy. Also, dideoxyinosine (DDI), another investigational agent, was being evaluated in clinical trials and many patients were switched from zidovudine to DDI due to low tolerance for zidovudine.

Pharmacy practice in the IDC is unique since pharmacists can dedicate time to conducting patient interviews in privacy without other

responsibilities of a typical drug store environment. This is similar to the "open pharmacy concept"[15] where the traditional barriers and interruptions are not present and where an informal setting allowed for an open, relaxed discussion of an individual's therapy and facilitated acceptance of recommendations.

The high acceptance rate (97%) by physician and/or patient of pharmacist-initiated interventions suggests that pharmacists' participation had significant effects on the provision of zidovudine therapy. Acceptance of recommendations by physicians was mostly due to pharmacists conducting prospective, close monitoring of the patients' therapy and their ability to support their reasons for intervening based on specific data. Interaction with the physician was increased due to their close proximity on the site and fostered the team approach to patient care. The ongoing sessions with pharmacists not only related to drug therapy and educating patients but inevitably included providing an emotional support for them. At times, pharmacists would refer patients to other care givers as required to provide support for the individual and the family.

In summary, we have highlighted some important points in the role of a pharmacist in an outpatient clinic. A pharmacist can have an impact on drug therapy when allowed to practice in an organized structure of service which includes time dedicated for a patient interview; a systematic approach to monitoring therapy; and privacy to allow for greater patient/pharmacist interaction. The high acceptance rate for interventions suggests that close monitoring of drug therapy by pharmacists can increase their ability to make recommendations in a prospective manner thus increasing the likelihood of these being accepted by either the health care team or the patient.

REFERENCES

1. Purdy BD, Plaisance KI. Infection with the human immunodeficiency virus: epidemiology, pathogenesis, transmission, diagnosis, and manifestations. *Am J Hosp Pharm* 1989; 46:1185-209.
2. Langtry HD, Campoli-Richards DM. Zidovudine: A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy. *Drugs* 1989; 37:408-50.
3. Fischl MA, Richman DD, Grieco MH, et al. The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex: a double-blind placebo-controlled trial. *N Engl J Med* 1987; 317:185-91.
4. Open trial of the long-term safety of retrovir. Burroughs Wellcome Inc., Canada. May 1987.
5. Wong RJ, Volberding PA. Providing clinical pharmacy services in an AIDS-oncology ambulatory-care clinic. *Am J Hosp Pharm* 1988; 45:2351-54.
6. Ratliff RW, Commander McGowan B. Impact of pharmacists in two ambulatory-care clinics in a veterans administration medical center. *Am J Hosp Pharm* 1989; 46:1417-19.
7. Gray DR, Garabedian-Ruffalo SM, Chretian SD. Cost justification of a clinical pharmacist-managed anticoagulation clinic. *Drug Intell Clin Pharm* 1985; 19:575-80.
8. Garabedian-Ruffalo SM, Gray DR, Sax MJ, Ruffalo RL. Retrospective evaluation of a pharmacist-warfarin anticoagulation clinic. *Am J Hosp Pharm* 1985; 42:304-8.
9. Conte RR, Kehoe WA, Nielson N, Lodhia H. Nine-year experience with a pharmacist-managed anticoagulation clinic. *Am J Hosp Pharm* 1986; 43:2460-64.
10. Tiggelaar JM. Protocols for the treatment of essential hypertension and type II diabetes mellitus by pharmacists in ambulatory clinics. *Drug Intell Clin Pharm* 1987; 21:521-29
11. Erickson SH. Primary care by a pharmacist in an outpatient clinic. *Am J Hosp Pharm* 1977; 34:1086-90.
12. Anderson PO, Taryle DA. Pharmacist management of ambulatory patients using formalized standards of care. *Am J Hosp Pharm* 1974; 31:254-57.
13. Bjornson DC, Meyer DE, Cambre JD, Hiner Jr. WO, Cammarata FA. Impact of HIV infection on pharmaceutical services at Walter Reed Army Medical Center. *Am J Hosp Pharm* 1989; 46:1170-75.
14. Personal communication Burroughs Wellcome.
15. Graubert JI. New VA pharmacy chief looks to the nineties. *Am J Hosp Pharm* 1988; 45:163-64.

Appendix I

IDENTIFICATION OF PHARMACIST INTERVENTION DURING ZIDOVUDINE MONITORING

Chart No. _____

Date AZT therapy begun: _____

Date of chart review: _____

Date of follow-up: _____

Current dose: _____

Initial dose: _____

PARAMETERS MONITORED BY PHARMACIST

LABORATORY DATA:
- platelets _____
- granulocytes _____
- white blood cell count _____
- hemoglobin _____
- reticulocyte count _____
- LDH _____
- AST _____
- other: _____

ADVERSE REACTIONS:
- headache _____
- insomnia _____
- myositis, myalgia _____
- nausea _____
- other: _____

PATIENT FACTORS:
- compliance _____
- appetite _____
- alcohol use _____
- energy level _____
- other: _____

PHARMACIST INTERVENTION:
- decrease dosage _____
- increase dosage _____
- discontinue drug _____
- restart drug _____
- reversal of MD plan _____
- repeat lab work _____
- recommend blood transfusion _____
- extend time until next visit _____
- specialist referral _____
  - specify: _____
- information for patient _____
  - specify: _____
- physician contacted _____

NO. OF PARAMETERS IDENTIFIED: _____

CONCURRENT MEDICATIONS:

Indication:
- megestrol acetate _____
- vitamins _____
- antibiotics _____
- aero. pentamidine _____
- acyclovir _____
- hypnotics/anxiolytics _____
- analgesics _____
- other: _____

Drug'drug interaction:
- acetaminophen/asa _____
- hepato/nephrotoxic _____
- chemotherapy _____
- myelosuppressive _____
- other: _____

CONCURRENT MEDICAL CONDITIONS
- pneumocystis carinii _____
- kaposi's sarcoma _____
- viral illness _____
- other: _____

FOLLOW-UP:

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

INTERVENTION ACCEPTED: Y _____ N _____