Medication Use Patterns in HIV-Positive Patients

R. Chow, T. Chin, I.W. Fong and R. Bendayan

ABSTRACT

Patients with HIV infection or AIDS often receive several medications for treatment or prevention of their primary disease and/or associated complications. The objective of this study was to document patterns of drug use in an HIV-positive, outpatient population. Data were collected via one-on-one interviews with 26 HIV-positive patients; prescription and non-prescription drug use, adverse drug reactions and drug allergies were recorded. Anti-retroviral therapy was received by over 90% of the patients. Over 90% of patients were on anti-infective agents, commonly cotrimoxazole or dapsone, while 27% received acyclovir. At least 70% of patients used three or more prescription medications concurrently. Every patient reported self-medicating with at least one over-the-counter (OTC) product and over half used three or more OTC products concurrently. Adverse reactions, mainly attributable to zidovudine, were reported by over 80% of patients. Non-compliance was a common drug-related issue; over 70% of patients omitted drug doses. In conclusion, the use of multiple medications in the ambulatory HIV-positive patients presents the health care team with potential drug-related problems that may ultimately affect the efficacy and toxicity of therapy. Thus pharmacists may play an active role in the provision of direct care to these patients.

Key Words: *compliance, HIV/AIDS patients, medication usage, polypharmacy*

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RÉSUMÉ

On prescrit souvent plusieurs médicaments aux malades séropositifs ou atteints du SIDA pour traiter ou prévenir l'atteinte initiale et(ou) les complications associées. La présente étude vise à examiner le profil d'utilisation des médicaments au sein d'une population de patients ambulatoires séropositifs. On a collecté les données sur l'utilisation des médicaments d'ordonnance et des médicaments en vente libre, les réactions indésirables et les allergies aux médicaments lors d'entretiens individuels avec 26 patients séropositifs. Plus de 90 p. 100 suivent un traitement anti-rétroviral. Plus de 90 p. 100 prennent des anti-infectieux, habituellement le cotrimoxazole ou la dapsone, tandis que 27 p. 100 reçoivent de l'acyclovir. Au moins 70 p. 100 prennent simultanément trois médicaments d'ordonnance ou plus. Tous indiquent qu'ils prennent au moins un médicament en vente libre en guise d'auto-médication; plus de la moitié utilisent simultanément trois de ces produits ou plus. Plus de 80 p. 100 mentionnent des réactions indésirables, principalement attribuables à la zidovudine. Les écarts au régime thérapeutique sont courants; plus de 70 p. 100 omettent de prendre certaines doses de médicaments. En conclusion, la prescription de plusieurs médicaments aux patients ambulatoires séropositifs risque de poser à l'équipe de soins des problèmes d'ordre pharmacologique susceptibles d'avoir des répercussions sur l'efficacité et la toxicité du traitement. Les pharmaciens pourraient donc intervenir activement en fournissant des soins directs à ces patients.

Mots clés: *Observation des prescriptions, patients séropositifs/atteints du SIDA, polypharmacie, utilisation des médicaments*

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INTRODUCTION

Patients with human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS) often receive several medications for prevention or treatment of their primary disease and/or associated complications. Polypharmacy is not uncommon in this patient population. The high number of drugs used may increase the risk of adverse effects and the potential for significant drug-drug interactions.[1,2] In a study of prescription drug use patterns in HIV patients, Bjornson et al found that patients on zidovudine (azidothymidine or AZT) were often prescribed anti-infectives, central nervous system agents, and skin and mucous membrane agents concomitantly.[2] In addition, therapeutic agents, regimens, and doses change so quickly with new discoveries that optimal medication utilization may be complex and confusing. The pattern of drug usage in this patient

population has not been well-defined; however, important problems of polypharmacy and drug non-compliance have been reported.[1,2]

The objective of this study was to document the patterns of drug usage in an HIV-positive, ambulatory patient population at St. Michael's Hospital in Toronto, Canada.

In Metropolitan Toronto, there are six hospital-based outpatient HIV clinics currently in operation. These clinics are located at: The Hospital For Sick Children, Mount Sinai Hospital, St. Michael's Hospital, Sunnybrook Health Science Centre, The Toronto Hospital (General Division) and The Toronto Hospital (Western Division). At the time of this study, the Ambulatory HIV Clinic at St. Michael's Hospital operated three half-days per week and provided services for about 150 to 200 patients. The multidisciplinary HIV Clinic team consisted of physicians, nurses, a psychiatrist, a psychologist, a dietician, a social worker, and an art therapist. This project represented the first involvement of a pharmacist with the HIV Clinic team.

METHODS

The project was undertaken at the Ambulatory HIV Clinic, St. Michael's Hospital, Toronto, from January 1991 to April 1991. The nursing staff identified and referred patients to this study. Patients were referred if they were receiving medications, were willing and had time to participate, and were fluent in the English language.

A questionnaire was prepared in order to document demographic data, patients' prescription and non-prescription drug use, adverse drug reactions, drug allergies, and social histories. The primary investigator conducted all interviews. These interviews averaged 15 to 30 minutes in length. Prior to each interview, an information sheet about the project was reviewed with the

patient. During the interview, the investigator posed pre-written, non-leading, open questions to the patient. However, some patients did not understand terms, such as "adverse effects", and as a result, examples were given for clarification. The questions in the questionnaire were asked and answered verbally. After the interviews, patients' charts were reviewed, if available, and information obtained during the interview was verified; especially in cases where the patient appeared confused or uncertain, the chart reviews were extremely helpful. The investigator was able to review the charts of all but one patient. As well, patients' personal histories and any pertinent information the patient could not provide during the

interview, such as drug doses or regimens, were obtained from the patients' charts.

Patient confidentiality was maintained by assigning a number code to each patient; a written consent form was deemed unnecessary by the hospital ethics committee.

RESULTS

A total of 26 participants were interviewed over a period of four months. All patients were male with a mean age of 37.7 ± 9.6 years (range: 25-62), with different levels of education, the majority of whom were employed (Table I). Over 80% of the patients were homosexual; two of the patients (8%) reported to have used recreational drugs intravenously in the past (Table II). Over 60% of our pa-

Table I: Demographic Information of the HIV-Positive Ambulatory Patient Population (n=26)

Age (years):	37.7 ± 9.6* (25-62)**	
Age at diagnosis (years):	35.0 ± 10.4* (19-61)**	
Education:	University Degree	34.6%
	College Degree	7.7%
	High School Degree	30.8%
	Elementary	26.9%
Employment:	Employed:	61.5%
	Unemployed:	38.5%

*   mean ± standard deviation
** range

Table II: Risk Factors and Substance Abuse History of HIV-Positive Ambulatory Patient Population (n=26)

Risk Factors*:	Homosexuality**	88.5%
	I.V. Drugs Use	7.7%
	Blood Transfusion	3.8%
	Hemophilia	3.8%
Illegal Drug Use:	No Use	69.3%
	Past Use	26.9%
	Current Use	3.8%
Alcohol Use:	40 drinks/month	7.7%
	30 drinks/month	19.2%
	< 10 drinks/month	38.5%
	No Use	34.6%
Use of Tobacco/Cigarettes:	2 packages/day	7.7%
	1 package/day	7.7%
	< 1 package/day	15.4%
	No Use	69.2%

*   For surveillance purposes, cases of AIDS are classified into mutually exclusive hierarchical risk or transmission groups, of which predictions are made by a mathematical projection of already-reported cases.
** One homosexual patient was also an IV drug user.

tients consumed alcohol to varying degrees, while approximately 30% used some form of tobacco (Table II). In these respects, our population was similar to other populations of HIV-positive patients.[3]

Over 90% of those patients using prescription drugs were receiving anti-retroviral drug therapy, primarily zidovudine (Figure 1). A total of four patients or approximately 15% were receiving "other anti-retrovirals" (Figure 1), which at the time, were investigational medications with possible anti-retroviral activity; of these four patients, two were receiving zidovudine concurrently. Two patients were not receiving anti-retroviral therapy; one was undergoing chemotherapy for non-Hodgkin's lymphoma, while the other was being treated for *Mycobacterium avium intracellulare*. Anti-infective drugs were taken by over 90% of the patients; among these, 80% were taking cotrimoxazole, dapsone, or pentamidine inhalation for *Pneumocystis carinii pneumonia* (PCP) prophylaxis. Acyclovir was taken by slightly over 25% of the patients for the treatment or suppression of *Herpes simplex* and *Varicella zoster* infections; none of the patients was using acyclovir for its proposed synergistic effects with zidovudine.[4] Over 70% of the patients were taking three or more prescription medications concurrently.

In addition to the vast array of prescription medications, our patients also used a variety of over-the-counter (OTC) medications (Table III). Each of the patients reported self-medicating with at least one OTC product, often without the knowledge of their physician. Fifty percent of the patients were using both OTC medications recommended by physicians and OTC medications that were self-initiated. Approximately 35% of the patients were using OTC medications that were self-initiated,
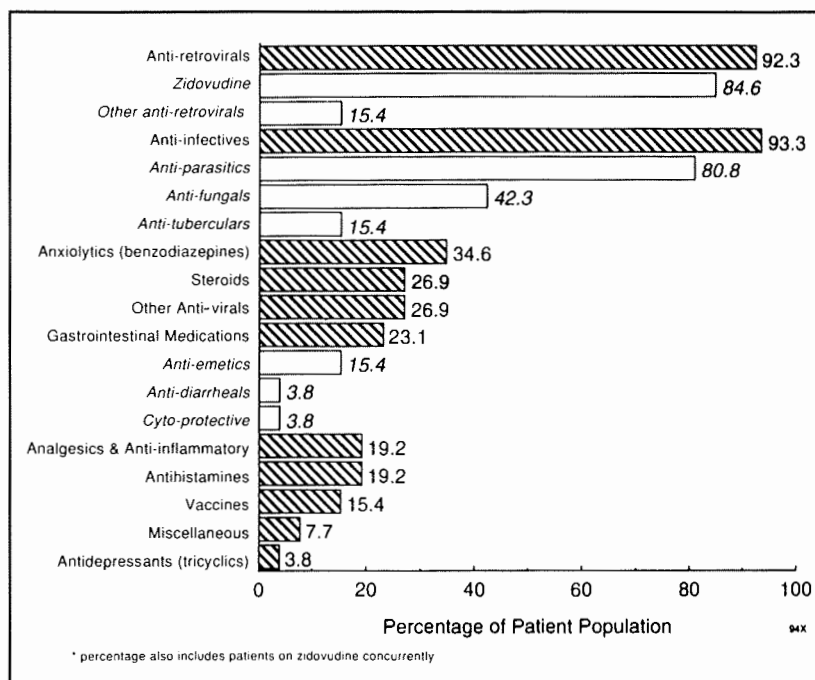

Figure 1. Prescription Medications Used in the HIV-Positive Ambulatory Patient Population (n=26).

Table III: Over-the-Counter (OTC) Medications Use in the HIV-Positive Ambulatory Population (n=26)

Medications	Percentage of Patient Population	Purpose
Anti-virals*	11.5%	• anti-viral activity against the HIV organism (but no recognized therapeutic use)
Vitamins	57.7%	• for overall good health • to help immune system
Other Supplements	23.1%	• to supplement meals and help immune system
Antihistamines	3.8%	• to relieve rashes induced by dapsone, cotrimoxazole, zidovudine • to relieve allergy symptoms
Analgesics	57.7%	• to relieve headaches and myalgias
Gastrointestinal Medications	26.9%	• to relieve nausea, vomiting and/or diarrhea due to medications and/or disease
Cough and Cold Products	23.1%	• to relieve symptoms of the common cold
Miscellaneous	15.4%	• to relieve dermatological, gastrointestinal and sleep problems

* Excluding anti-retroviral agents.

while 15% of the patients were using OTC medications recommended by physicians. Over 50% of the patients consumed vitamins on a regular basis. Analgesics and anti-inflammatory agents were used by over 55% of the patients for headaches, myalgias and arthralgias. Over 50% of the patients used three or more OTC medications concurrently.

Three patients were using unorthodox agents presumed to have anti-retroviral activity, such as hypericin, and herbal Chinese remedy containing compound Q (trichosanthin), and pentosan, a sulphated polysaccharide similar to dextran sulphate.[5] Over 30% reported using medications that had been prescribed for friends, while 15% reported lending their prescription medications to friends.

Patients' drug regimens included agents with both short (every four to six hours with AZT) and long (every Monday, Wednesday and Friday with cotrimoxazole compound) dosing intervals. Over 70% of our patients reported omitting drug doses for personal convenience or due to forgetfulness (Figure 2). Some patients intentionally missed doses in order to avoid adverse effects.

Patients reported experiencing various adverse reactions to their medications. Over 80% of the patients reported experiencing adverse effects with zidovudine, mainly related to the gastrointestinal (65%), central nervous (26%) and haematological (13%) systems. As well, 57% of the patients reported experiencing adverse effects i.e., rashes and high fever with cotrimoxazole and three patients reported adverse effects with dapsone.

DISCUSSION

The patient population in this study was similar to other AIDS patient populations surveyed[3] in that most
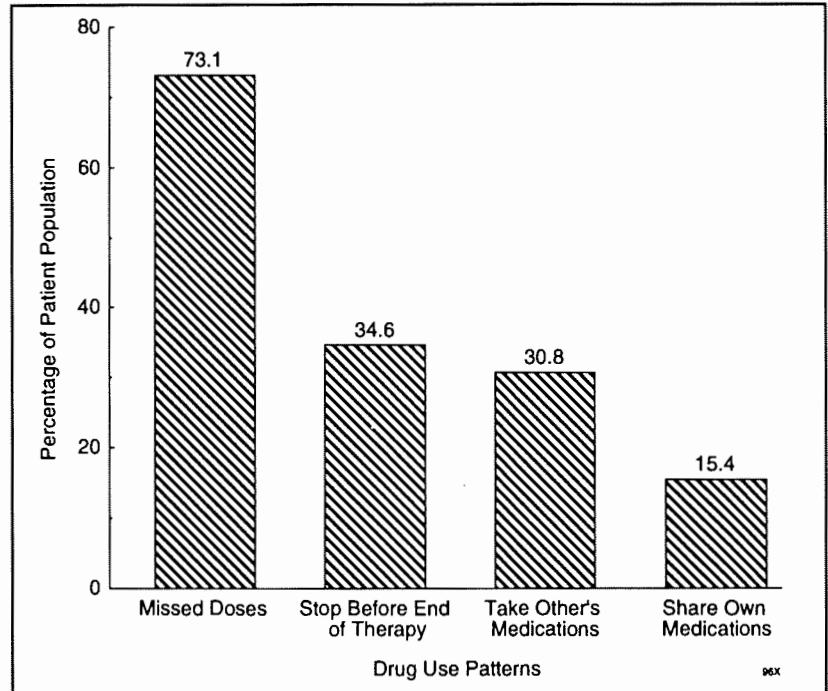

Figure 2. Patterns of Drug Use in the HIV-Positive Ambulatory Population (n=26).

were relatively well-educated, homosexual men between 30 to 40 years of age. Polypharmacy was evident in over 50% of our patients, with the majority receiving three or more prescription and/or OTC medications concurrently. The most common medications taken were anti-retrovirals, systemic anti-fungals, anti-virals, analgesics, and anti-inflammatory agents. Polypharmacy has been documented in other AIDS patients.[1,2] In a study by Greenblatt et al, the mean number of prescription medications used by 96% of the HIV-positive patients was approximately five and the greater use of prescription medications correlated with a more advanced stage of illness.[1]

OTC medications, mainly vitamins, analgesics and anti-inflammatory agents, were used by patients either on the recommendation of a physician or of their own accord (self-initiated). The OTC medications were mainly used to alleviate adverse effects such as headaches, myalgias, nausea, vomiting, diarrhea, and rashes largely

attributed to zidovudine. The patients' reasons for using vitamins and supplements were to maintain overall good health and to help their immune systems.

In our study, patients reported that physicians usually recommended nonsteroidal anti-inflammatory drugs (NSAIDs) as pain relievers due to the association of an increased frequency of marrow suppression with concomitant use of acetaminophen and zidovudine.[5,6] It was once thought that the mechanism of this interaction occurred at the level of hepatic glucuronidation. However, recent studies show that acetaminophen does not competitively inhibit the glucuronidation of zidovudine.[7,8,9] Instead, concomitant administration of some NSAIDs, notably indomethacin, naproxen, and acetylsalicylic acid, was found to have an inhibitory effect on the glucuronidation of zidovudine.[9] Based on these recent studies, investigators suggest that it would be reasonable not to limit the use of acetaminophen in patients taking zidovudine.

The two patients who used unorthodox therapies were well-educated. Interestingly, Greenblatt et al identified an association between greater educational attainment and the use of unorthodox therapies.[1] These two patients reported that their physicians were aware of their use of these agents.

Drug compliance may also pose a problem in this population, since patients take multiple medications with different regimens. The likelihood of adverse drug reactions increases with the use of multiple medications; as a result, patients may be more likely to omit doses to "avoid" adverse effects. Another factor which may reduce compliance is confusion and memory loss associated with the progression of HIV disease. In a recent study, Morse et al examined the determinants of subject compliance within a double-blind, placebo-controlled protocol designed to evaluate the potential value of zidovudine in asymptomatic, HIV-positive patients.[10] No conclusions were made regarding the incidence of drug compliance in this patient population. However, part of the study involved nurses' reports and patients' self-reports on the frequency of missing pills. On a 5-point scale, the mean frequency of missing pills was found to be 2.4 (baseline, n=40) and 2.6 (6 months later, n=34) by the nurses, and 2.9 (baseline, n=40) and 3.1 (6 months later, n=34) by the patients.[10] These data suggest that the frequency of missing pills for HIV-positive patients is 50% or higher.

Another aspect of compliance with respect to HIV-positive patients was studied by Carlson et al.[11] In this study, HIV-positive psychiatric patients were found noncompliant because they continued unsafe sexual practices when discharged from the hospital. Currently, there are no published drug compliance data specific to the HIV-positive patient population. A study of patients on long-term anti-hypertensive drug therapy reported that drug compliance may be as low as 50%.[12] Given the potential for low drug compliance in the HIV-positive patient population, further studies are warranted.

As medications are developed to prolong the HIV-positive patient's survival, patient care will focus on chronic drug therapy,[13,14] and it will be an ever-increasing challenge to identify, resolve and prevent drug-related problems. Zidovudine dosage is often limited by toxicity and adverse effects. In this patient population, over 80% reported to have experienced adverse effects with zidovudine.

The findings from this study suggest a role for the pharmacist in the HIV clinic team. Our observations regarding the frequency of polypharmacy, adverse drug effects, and non-compliance, and the potential for educating the multidisciplinary clinic team with respect to new therapeutic developments prescribing habits, may serve to justify the implementation of pharmacy services in the HIV clinic. In a recent study by Walji et al, 73 of 75 interventions made by pharmacists monitoring zidovudine therapy in an outpatient AIDS clinic were accepted by physicians.[15] It is vital that the pharmacist be pro-active and assume responsibility by providing pharmaceutical care to the HIV-positive patient. ⌨

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