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Adverse events relating to antiretroviral prophylaxis for occupational accidents

ABSTRACT

The objective of the study was to describe adverse events detected clinically or in the laboratory that were secondary to the use of antiretroviral agents among individuals undergoing antiretroviral prophylaxis. Evaluations were performed on 37 teaching hospital employees who underwent prophylaxis using four regimens of antiretroviral medication following occupational exposition to contaminated fluids from patients with human immunodeficiency virus infection. Thirty-two (86.5%) developed adverse events detected clinically or in the laboratory. The prophylaxis administered to two professionals (5.4%) had to be suspended because of the reactions that occurred. Adverse events relating to prophylaxis for HIV infection in health care workers who were victims of occupational accidents were frequent. However, it was rarely necessary to withdraw the antiretroviral medication.

KEYWORDS: Occupational exposure, prevention & control. Exposure to biological agents, prevention & control. Anti-HIV agents, adverse effects.

INTRODUCTION

Accidents involving needlesticks, sharp injuries or mucosal contact with biological material such as blood, tissue or other potentially infected material have been correlated with the transmission of viral pathogens such as the human immunodeficiency virus (HIV) or hepatitis B or C.[4]

The risks of HIV transmission by means of perforating-cutting accident or mucosal exposure are known and have been measured, respectively, as 0.3%[2] and 0.1%.[5]

The risk factors that seem to be associated with higher HIV transmission rates in occupational exposure are deep wounds, blood visible on the device involved in the accident, procedures involving needles used in arteries or veins, and source patients with advanced stages of HIV. However, such transmission can be reduced by 81%, through the preventive use of antiretroviral medication such as zidovudine (AZT).[3]

Adherence to the regimen is very important for treatment success, and is influenced by the complexity of the regimen indicated. High rates of prophylaxis suspension have been observed among individuals who suffered occupational exposure involving HIV, because of the occurrence of adverse events during antiretroviral prophylaxis.[1]

The present study had the objective of evaluating adverse events detected clinically and in the laboratory that were secondary to the use of antiretroviral agents for employees undergoing prophylaxis.

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METHODS

This study was conducted in a teaching hospital that has a specialized outpatient clinic for attending to employees who have been victims of occupational accidents involving biological material. When notified about an accident, the Hospital Infection Control Committee team assesses whether prophylactic measures and outpatient follow-up are needed or not, in relation to accidents with the risk of HIV or hepatitis B or C transmission. Between September 2003 and September 2005, 751 accidents involving material potentially presenting risks were recorded. These were attended to and catalogued in a database. Among these accidents notified, the use of antiretrovirals was indicated in the cases of 38 individuals (5.1%), of whom one refused the prophylaxis. This group of 37 individuals underwent chemical prophylaxis using antiretrovirals when there was a risk of acquiring HIV. Of these, 32 (86.4%) presented some type of adverse reaction to the regimen, detected either clinically or in the laboratory.

In cases of positive results from rapid tests or when the source patients presented a previous diagnosis of HIV infection, prophylaxis with antiretrovirals was started in accordance with the health professional's type of exposure, with outpatient clinical follow-up for the employee every 14 days for 28 days. A mobile telephone number was made available for the employee to contact a doctor specializing in infectious diseases, if necessary. At each consultation, the occurrence and severity of any adverse events and abnormalities in laboratory tests were evaluated. Following this period, the professionals were followed up for six to 12 months to identify possible transmission of infection relating to the occupational exposure.

Among the clinical events correlated with the use of these medications, some symptoms were grouped into syndromes. Gastrointestinal syndrome was characterized by nausea, vomiting, abdominal discomfort or diarrhea; neurological syndrome included symptoms like headache or dizziness; and general feelings of unwellness included nonspecific indisposition, lethargy or irritability.

Four combinations of antiretrovirals were used. The simplest regimen in terms of composition was an association of lamivudine with zidovudine, which was used for three patients whose exposure was considered to present low transmission risk. Another regimen used was an association of zidovudine, lamivudine and nelfinavir, for 31 patients. An association of zidovudine, lamivudine and indinavir was used for two employees. Finally, an association of lamivudine, zidovudine and atazanavir was used for an employee who had dyslipidemia who was undergoing dietary treatment. The indications for antiretroviral use followed the recommendations from the Brazilian Ministry of Health. The present study was approved by the Ethics Committee of Hospital São Paulo, Federal University of São Paulo.

RESULTS

Among the patients treated with the association of lamivudine and zidovudine (N=3), two reported gastrointestinal symptoms, one reported a neurological event and nonspecific feelings of unwellness were reported by one patient. Laboratory tests were performed in the case of one of these patients and did not present any abnormalities. In this group, the adverse events did not imply changing or suspending the regimen.

It was observed that 18 (58%) of the patients treated with the association of zidovudine, lamivudine and nelfinavir (N=31) presented gastrointestinal events, 13 patients (41.9%) did not feel well, eight (25.8%) had neurological events, four (13%) had muscle pains, two (6%) had pruritus, two (6%) had skin rash and one (3%) had weight loss (4 kg). Four employees (13%) using this prophylaxis did not complain of any adverse clinical event.

Also in relation to the use of this association, periodic follow-up was possible for 24 patients (77%), of whom 11 presented adverse events in laboratory tests. Among the events observed, the most frequent were elevations in liver enzymes such as transaminases, alkaline phosphatase or gamma glutamyltransferase, which were observed in seven of the 24 patients (29%). Hematological alterations (cytopenia) occurred in five patients (20%). Other events like hyperamylasemia, elevated creatine kinase (CK) and creatinine occurred rarely. Changing the regimen was necessary for five patients in this group (16%) and total withdrawal of the prophylaxis for two patients (6%).

Among the patients with the association of zidovudine, lamivudine and indinavir (N=2), gastrointestinal events occurred in one patient and complaints of dryness of the mucosa in the other. Routine laboratory tests were performed on one patient, which showed elevated liver enzymes. For one patient, it was necessary to change the regimen, from indinavir to nelfinavir, but it was not necessary to suspend the prophylaxis.

With the association of lamivudine, zidovudine and atazanavir (N=1), the only adverse clinical event was menstrual (increased number of days with flow). Laboratory tests showed a slight increase in creatinine. There was no need for change or suspension relating to this regimen.

There was no seroconversion among the employees who underwent antiretroviral prophylaxis.

DISCUSSION

With the clinical and laboratory follow-ups after two and four weeks, and assistance via mobile telephone, it was possible to achieve early identification of some adverse events relating to antiretrovirals and minimize them.

Despite the substantial rate of adverse effects, it was only necessary to suspend the prophylaxis in two cases (5.4%) and to replace it with another regimen for six of the 37 employees (16.2%), as a result of these events. The principal adverse events relating to the use of antiretrovirals were gastrointestinal alterations, neurological events and nonspecific feelings of unwellness. Only 27 patients could be assessed by means of laboratory tests, and the most prevalent alterations among these patients were in liver enzymes, bilirubins, alkaline phosphatase, gamma glutamyltransferase and hematological factors.

No seroconversion was observed among the employees who underwent prophylaxis. Although this is an important finding, the sample of the present study was too small to be able to affirm that the antiretroviral medication prevented HIV infection, in the way that was shown in the study by Cardo et al.[3]

The occurrence of adverse events can be minimized through the use of less powerful regimens. Subtraction of the protease inhibitor reduces the incidence of such events and increases the employees' adherence to treatment.[1] This is a practical strategy, but it may reduce the power of the regimen, with an increased risk that the prophylaxis may fail.

Among the strategies for managing adverse events relating to antiretroviral use, medications for treating symptoms can be used, or one drug can be subtracted from the regimen (the protease inhibitor). Moreover, it is better to complete the stipulated time period using a diminished regimen than to insist on a regimen that the patient finds difficult to tolerate, because such regimens may result in irregular adherence and serious discomfort for the patient.

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