Side effects of AZT prophylaxis after occupational exposure to HIV-infected blood

Summary  It was the objective of this study to document and evaluate AZT-induced short-term toxicity in healthy individuals. The study was designed as a longitudinal monocentric side-effect monitoring study with prospective data collection. It was carried out at the Cologne University Hospital. The study population comprised health care workers who were taking AZT prophylaxis after accidental exposure to HIV-infected blood. Fourteen individuals were included into the study; seven of them discontinued treatment prematurely, five due to severe subjective symptoms. In case of one worker AZT had to be stopped due to severe neutropenia (800 cells/μl) with signs of upper respiratory tract infection. Four of 11 individuals taking AZT for at least 4 weeks developed neutropenia (2 WHO I, 1 WHO II, 1 WHO III). All other laboratory parameters stayed within normal range. In particular, no anemia was observed. In conclusion: Compared with other studies more neutropenias are observed. Due to side effects 50% of the workers discontinued AZT administration prematurely. The data presented herein show that AZT causes considerable side effects which must be weighed against the potential protective antiviral effect.

Key words  AZT prophylaxis · Side effects · Occupational exposure · Neutropenia

Introduction

Prophylactic administration of azidothymidine (AZT) after occupational exposure to HIV-infected material is an approach being increasingly applied, although its therapeutic efficacy has not yet been proven. Therefore, thorough recording and evaluation of therapy-induced side effects is of particular importance. The individuals who take AZT prophylactically offer the unique opportunity to study AZT-induced hematotoxicity in healthy individuals. AZT effects on human hematopoiesis have been well characterized for AIDS and AIDS-related complex (ARC) patients [2, 6]. Anemia and neutropenia have been observed. However, as reviewed by Scadden et al., hematological changes observed in AIDS are caused by a multifactorial process, which makes it difficult to discriminate between AZT-induced changes and other possible factors involved [8]. Thus, the study of healthy individuals receiving AZT as prophylaxis after occupational exposure to HIV-infected blood is particularly useful, because hematological changes observed in this group are most likely due to the AZT medication.

Starting in June 1991, health-care workers (HCW) at the University Hospital of Cologne were offered prophylactic administration of 3′-azido-3′-deoxythymidine (AZT) after occupational percutaneous exposure with HIV-infected blood. If, after thorough information and counseling, they decided to take AZT, a daily dose of 1000 mg was recommended for a period of 42 days. The subjective and organ-related side effects were carefully documented in a concomitant study. The results of this study are reported here.

Method

Based on an official statement of the board of directors of the University Hospital of Cologne, AZT prophylaxis is recommended after percutaneous penetration or after mucosal contamination with known HIV-infected blood.

Inclusion criteria

Only individuals meeting the following criteria were included into the study:

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Table 1. Laboratory parameters monitored
- Hb, Hct, RBC, reticulocytes, WBC, lymphocytes, granulocytes, platelets, iron, transferrin, haptoglobin, MCH, MCHC, MCV
- Serum electrolytes, serum proteins
- AST, ALT, AP, gamma-GT, bilirubin

- HIV antibody negative before initiation of AZT and 4 months thereafter
- No prior renal, hepatic, hematological or immunological disease
- Age > 18 years
- Informed consent

Drug administration
The treatment schedule of AZT prophylaxis was 1000 mg AZT daily p.o. for a period of 6 weeks. It was strongly recommended to start AZT prophylaxis as soon as possible after exposure to AIDS-infected blood (within 2 h).

Side-effect monitoring
Peripheral blood was drawn before initiation of AZT therapy and biweekly during the treatment course. A list of the laboratory parameters monitored is shown in Table 1. HIV antibodies were determined before, as well as 6 weeks and 4 and 12 months after exposure. In case of changes from normal a follow-up until normalization of parameters was conducted. During each visit the participants were interviewed for subjective side effects. Organ-related side effects were graded according to the WHO toxicity scale. Subjective side effects were graded as follows: Mild means that the participants described the side effects as mild, well tolerable, and not disturbing everyday life and work; severe side effects were described as strong, sometimes leading to the administration of symptomatic drugs, and strongly interfering with everyday life and work.

Toxicity was evaluated according to the WHO grading system. Concerning the neutrophil count, WHO grades are defined as follows: grade 0: > 2.0/mm³, grade I: 1.5–1.9/mm³, grade II: 1.0–1.4/mm³, grade III: 0.5–0.9/mm³, grade IV: < 0.5/mm³.

Results
Participant characteristics
From August 1991 until May 1993, 14 individuals entered the study. The median age was 30.6 years. The female-to-male ratio was 11/3. The professional distribution was as follows: six medical doctors, five nursing staff members, and three students (Table 2). All patients were HIV-Ab negative before therapy and no seroconversion occurred until March 1994. No concomitant medication was taken.

Duration of therapy
Median duration of therapy was 30 days (average 33). Seven of 14 individuals (50%) completed the full course of AZT prophylaxis (6 weeks). Of the seven participants who discontinued therapy prematurely, five did so due to severe subjective side effects, one due to neutropenia and upper respiratory tract infection, and one for unknown reasons (Table 3).

Subjective side effects
Nine of 14 participants (64.2%) reported subjective side effects. Three individuals (21.4%) experienced mild side effects as defined before. Another six individuals (42.8%) reported severe side effects. Due to these side effects five of them discontinued AZT prophylaxis prematurely, three individuals after 4 weeks, one after 10 days, and one after 2 days (Table 4). Side effects reported included headache, fatigue, nausea, exhaustion, myalgia, arthralgia, and flu-like symptoms.

Organ-specific side effects
Renal, hepatic, and metabolic parameters, and electrolytes and serum proteins from all participants were found within the normal range before AZT treatment. No toxicities with regard to these parameters were observed in any one participant during therapy. The follow-up period for each individual ranges between 7 and 30 months.

Eleven individuals received AZT for at least 4 weeks. Hematological parameters of every one of them were within the normal range before AZT. During treatment, four participants showed hematological side effects with regard to blood neutrophil count. Two developed neutropenia of WHO grade I, one individual neutropenia of WHO grade II, and one individual neutropenia of WHO grade III. No anemia was observed. Table 5 shows the nadir of the neutrophil counts of these individuals. Participant 6 was advised to discontinue AZT therapy after 4 weeks because of the develop-