Human immunodeficiency virus infection and nutritional status in female drug addicts undergoing detoxification: anthropometric and immunologic assessments

Pilar Varela, Ascensión Marcos, Irene Santacruz, Sidonia Ripoll, and Ana M Requejo

ABSTRACT To clarify the interrelations among drug abuse, malnutrition, and immunosuppression, the effects of human immunodeficiency virus (HIV) infection on the nutritional status of 17 noninfected and 19 HIV-infected asymptomatic female drug addicts undergoing detoxification were evaluated by measuring anthropometric and immunologic indexes. Anthropometric measurements were normal in both groups as a result of weight gain (10 kg) in every patient after the detoxification period. Leukocyte and lymphocyte values and CD2 lymphocyte subset counts were also similar in both groups. CD4 counts (P = 0.04) and the ratio of CD4 to CD8 cells (P = 0.6 \times 10^{-2}) were lower whereas CD8 counts (P = 0.003) were higher in the HIV-infected than in the noninfected group. Responses to a delayed-hypersensitivity skin test were below normal in both groups but significantly more so in the HIV-positive group (P = 0.05). CD19 counts were lower (P = 0.02) and values for serum immunoglobulins G and M were higher (51% and 37%, respectively) in the HIV-infected females than in the noninfected women. These results may suggest that despite anthropometric recovery, the HIV-infected women had depleted immune function, resulting not only from HIV infection but also from the subclinical malnutrition triggered by previous drug addiction. *Am J Clin Nutr* 1997;66:504S–8S.

KEY WORDS Women, drug addict, nutritional status, malnutrition, HIV infection, human immunodeficiency virus, cell-mediated immunity, humoral immunity, innate immunity, immunocompetence, weight recovery

INTRODUCTION

Drug abusers are prone to developing chronic diseases such as chronic hepatitis or human immunodeficiency virus (HIV) infection (1, 2). Moreover, it is well documented that the use of addictive drugs such as heroin, cocaine, and marijuana affects food and liquid intake behavior and taste preference (3). These alterations often lead to severe weight loss, which results in deterioration of the body and contributes to the development of malignant or infectious complications (4). Altés et al (5) found a prevalence of protein-energy malnutrition in drug addicts who had been taking heroin until a few hours before their hospital admission for detoxification. These nutritional deficiencies can impair immunity and, thus, influence susceptibility to infectious agents, including HIV (6).

In this sense, nutritional status has been identified as a major factor associated with poor prognosis for patients with HIV infection and AIDS (acquired immunodeficiency syndrome) (7). This association is due to the synergistic relation that exists between nutrition and immune response: nutritional status affects a host’s immune function and vice versa. The existence of an infectious process, acute or chronic, has an adverse effect on nutritional status (8, 9). Thus, immunocompetence is a sensitive and functional measurement of nutritional status because it has the unique quality of being altered even before the onset of clinical symptoms of malnutrition (10).

Moreover, administration of opiates and opioid peptides has been reported to affect a wide range of immunologic changes (11). For example, a subcutaneous implant of morphine, which is commonly used, produces sustained atrophy of the spleen and thymus (12). This atrophy is manifest within 24 h of implantation and is accompanied by a decrease in lymphocyte contents in spleen and thymus (13), inhibition of mitogen-stimulated T and B cell responses (14), and altered antigen-specific antibody production (15).

The amount of information available related to nutritional status in HIV-infected patients, ranging from asymptomatic to developed AIDS, has progressively increased throughout the past decade (16). However, information about the nutritional disturbances associated with drug abuse, especially in females, is scarce in the literature, possibly because of the higher incidence (82.5%) of AIDS in male patients, according to Spanish data (17). Therefore, the aim of this work was to assess, through use of anthropometric and immunologic evaluation, the effect of HIV infection on the nutritional status of female heroin addicts undergoing detoxification.

SUBJECTS AND METHODS

Thirty-six females (ranging in age from 21 to 28 y) who used illegal drugs intravenously (principally heroin) and who were assigned to the Proyecto Hombre Institution in Madrid were
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included in this study. The subjects were divided into two
groups depending on HIV infection: 17 patients were not
infected (HIV-negative group) and 19 patients were HIV
infected but were asymptomatic (18) (HIV-positive group).
Patients had voluntarily sought detoxification therapy and were
recruited for this study in the interval between 1 and 12 mo of
the first medical intervention. During the first 2 mo of the
detoxification period most patients recovered their appropriate
body weights.

All subjects tested, as well as the medical staff, gave their
informed consent once the purpose and nature of the study had
been explained. The procedures followed were in accordance
with the Helsinki Declaration as updated in Tokyo in 1975 and
as revised in 1983.

In all patients, a venous blood sample was obtained for the
detection of antibody to HIV. This detection was carried out by
the double-enzyme immunoassay method with use of a double
well in a solid phase (19) and a detection system in which
beads were coated with HIV-1 core and env antigens derived from
recombinant DNA (20). To ensure that drug addicts
complied during the detoxification phase, urine samples were
tested for opiates, amphetamines, and barbiturates by use
of enzyme immunoassay, as well as for cocaine, cannabinoid,
benzodiazepine, and alcohol by use of spectrofluorometry (21).

The assessment of patients who tested negative for the above
substances included the following anthropometric measure-
ments: age, height, body weight, ideal body weight (IBW) (22),
body mass index (BMI; in kg/m²), and weight gain. All the
indexes related to weight were measured just before the start of
the detoxification period (minimum value) and during the study
(actual value) by standard methods.

Blood samples (2 mL) were drawn from the antecubital vein
of patients after they had fasted for 12–15 h. Samples were
collected in EDTA-coated evacuated tubes (Becton Dickinson,
Sunnyvale, CA) and were analyzed within 4 h. Peripheral
blood leukocyte and lymphocyte counts were determined by
standardized clinical laboratory procedures (Coulter Counter,
Hialeah, FL).

To assess lymphocyte subpopulations, whole-blood samples
(100 µL) were incubated with 10 µL of appropriate concen-
trations of monoclonal antibodies (Coulter Clone, Coulter
Corporation) at 4 °C for 10 min. The following lymphocyte subsets
were evaluated by flow cytometry: CD2 (pan T cells), CD4
(helper T cells), CD8 (cytotoxic-suppressor T cells), and CD19
(B lymphocytes). Each sample was processed by the Immuno-
prep EPICS lymphocyte preparation system. The Immunoprep
reagents include a lysing agent for elimination of erythrocytes,
a stabilizer for the leukocytes, and a fixative to maintain
sample integrity (23). The control samples were incubated with
purified phycoerythrin-labeled mouse and fluorescein isothio-
cyanate–labeled mouse immunoglobulin G1. The fluorescence
of the subsets was analyzed with a Facstar Plus dual-laser
cytometer (Becton Dickinson). Forward light-scatter intensity
combined with ring-angle scatter was analyzed with the appro-
priate software (Becton Dickinson).

Cell immune function was evaluated by delayed-hypersen-
sitivity dermal response to seven recall antigens with use of a
skin test antigen applicator (Multitest CMI; Merieux Institute
Inc. Miami) (24). The seven antigens administered simulta-
neously by this applicator were tetanus, diphtheria, streptococ-
cus, tuberculin, candida, proteus, and trichophyton, as well as
a control (glycerin) injection. Reactions were assessed 48 ±
2 h after injection by measuring mean induration diameter (in
mm). Induration of ≥ 2 mm was considered a positive reaction.
“Score” is defined as the sum of inductions for positive
responses. Normal response was defined according to the cri-
teria of Jaurrieta et al (25) for Spanish females. Serum immu-
oglobulins and complement factors were determined by single
radial immunodiffusion (26).

All results are expressed as means with SDs. The effect of
HIV in drug addicts was assessed by unpaired Student’s t tests
(two-tailed). P < 0.05 was considered to be significantly
different. The association between two continuous variables
was determined by the Pearson coefficient of correlation.
Statistical analysis was performed by using the SAS/STaRT
computer program (SAS Institute Inc, Cary, NC) (27).

RESULTS

The anthropometric measurements tested are summarized in
Table 1. When the noninfected females were compared with
the HIV-infected group, no significant differences were ob-
erved in height, actual or minimum weight, actual or mini-
imum IBW, actual or minimum BMI, weight gain, or length of
detoxification period. Nevertheless, age and addiction time
were significantly higher in HIV-positive than in HIV-negative
females (P = 0.0005 and P = 0.0002, respectively).

Data obtained for leukocyte and lymphocyte values as well as
for lymphocyte subpopulations related to cellular immunity
are shown in Table 2. Leukocyte and lymphocyte counts and
lymphocyte percentages were similar in both groups. Periph-
eral blood lymphocyte subsets, however, were significantly
different between HIV-negative and HIV-positive drug addicts.
Percentages of both the CD2 and CD8 subsets were higher
(P = 0.04 and P = 0.1 × 10⁻², respectively) whereas the
percentage of the CD4 subset (P = 0.02) and the ratio of CD4
to CD8 cells (CD4:CD8) (P = 0.67 × 10⁻¹) were lower in
HIV-infected than in noninfected women. When data were
expressed in absolute values, CD4 cell counts were depressed

TABLE 1

Effects of human immunodeficiency virus (HIV) infection on
anthropometric measurements in female drug addicts undergoing
detoxification therapy

<table>
<thead>
<tr>
<th></th>
<th>HIV negative</th>
<th>HIV positive</th>
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<tbody>
<tr>
<td></td>
<td>(n = 17)</td>
<td>(n = 19)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>21.47 ± 4.25</td>
<td>26.42 ± 4.26</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.82 ± 5.08</td>
<td>160.34 ± 6.12</td>
</tr>
<tr>
<td>Actual weight (kg)</td>
<td>55.11 ± 7.01</td>
<td>55.62 ± 6.65</td>
</tr>
<tr>
<td>Minimum weight (kg)</td>
<td>45.29 ± 6.57</td>
<td>44.77 ± 7.15</td>
</tr>
<tr>
<td>Actual IBW (%IBW)</td>
<td>101.15 ± 11.60</td>
<td>102.09 ± 19.92</td>
</tr>
<tr>
<td>Minimum IBW (%IBW)</td>
<td>83.13 ± 9.17</td>
<td>82.17 ± 10.50</td>
</tr>
<tr>
<td>Actual BMI (kg/m²)</td>
<td>21.45 ± 2.61</td>
<td>21.56 ± 1.99</td>
</tr>
<tr>
<td>Minimum BMI (kg/m²)</td>
<td>17.42 ± 2.24</td>
<td>17.12 ± 2.15</td>
</tr>
<tr>
<td>Weight gain (kg)</td>
<td>9.45 ± 4.80</td>
<td>11.45 ± 5.55</td>
</tr>
<tr>
<td>(%IBW)</td>
<td>22.10 ± 13.98</td>
<td>27.32 ± 14.75</td>
</tr>
<tr>
<td>Addiction time (y)</td>
<td>3.73 ± 1.90</td>
<td>7.46 ± 3.31</td>
</tr>
<tr>
<td>Detoxification period (mo)</td>
<td>5.69 ± 6.09</td>
<td>6.85 ± 8.33</td>
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1 f ± SD.

2 Significantly different from HIV negative, P ≤ 0.05.
(P = 0.04) whereas the CD8 subset (P = 0.003) was elevated in the HIV-positive group; CD2 cells were similar in both groups.

When cell-mediated immune function (Table 2) was evaluated by a delayed-hypersensitivity skin test, a reduced response was found in all females studied. The depleted response was significantly more important in HIV-infected patients. The number of positive responses to seven antigens was 2.88 ± 1.36 (± SD) in the HIV-negative group compared with 1.89 ± 1.41 in the HIV-positive group (P = 0.04). Moreover, scores in noninfected and infected women were 8.28 ± 5.20 and 5.23 ± 4.10, respectively (P = 0.05).

Regarding humoral immunity (Table 3), B lymphocyte counts appeared to be lower in the HIV-positive group (P = 0.02), whereas the CD19 subset percentage was similar in both groups. In infected female addicts, only the CD19 subset count showed a negative and significant correlation with weight gain (in kg) (r = −0.42; P = 0.04); no significant correlation was found between anthropometric and immunologic indexes in the noninfected group. Serum immunoglobulin G and M concentrations were higher in the HIV-infected group (P = 0.4 × 10⁻⁹ and P = 0.004, respectively). HIV infection did not modify innate immunity as determined by complement factors (C3 and C4) in the patients tested.

### DISCUSSION

The longer addiction time in HIV-positive patients might be a result of the higher age of this group or vice versa. We detected a similar relation between age and time of addiction in infected and noninfected males who voluntarily sought detoxification therapy (28). This outcome might suggest that female drug addicts voluntarily seek detoxification at a younger age than do male drug addicts.

Anthropometric indexes showed no signs of malnutrition in either noninfected or HIV-infected females. Height and actual weight, IBW, and BMI values for both groups were within the normal range for age according to the standard Spanish tables (22). However, malnutrition was shown for all heroin addicts before they gave up the drug. Minimum weight, IBW, and BMI values in both groups were below normal. IBW values (%) were 18% lower than normal values. Low BMIs may increase the risk of morbidity according to Rhoads and Kagan (29), who reported a morbidity risk when BMI values were < 19. Protein-energy malnutrition has been reported in drug addicts taking intravenous heroin until a few hours before admission for detoxification (5). In the present study, HIV infection did not affect weight recovery because all females were able to gain similar amounts of weight (22% and 27% for HIV-negative and HIV-positive groups, respectively) during the detoxification period.

Leukocyte and lymphocyte values were similar in both groups of drug addicts and were also within normal values on the basis of criteria established by Isbister (30). However, lower peripheral lymphocyte values have been described previously in HIV-infected patients (31).

Cell-mediated immunity, evaluated by lymphocyte subsets and a delayed-hypersensitivity skin test, was impaired in all female drug addicts tested but more so in the HIV-positive group. A higher CD2 percentage was observed in the HIV-positive group, however; thus, CD2 count was not affected by HIV status. CD2 percentages in noninfected females were lower than normal values (32). This outcome is in accordance with results found by Chandra (33) under conditions of malnutrition.

CD4 lymphocyte subsets appeared to be depressed by HIV infection; percentages and absolute values of this subset were 44% and 18% lower, respectively, in HIV-infected females in relation to the noninfected group. It is well known that CD4 cell counts are lower in HIV-infected subjects (18). Moreover, malnutrition also negatively affects the CD4 lymphocyte subset (10). Gougeon et al (34) reported that one of the difficulties in understanding the complex pathology of HIV infection is explaining the progressive depletion of the CD4 cell population and consequently the destruction of the immune system. Although cytopathic effects of HIV are observed in vitro, they cannot be accounted for in vivo for CD4 T cell depletion.

### TABLE 2

Effects of human immunodeficiency virus (HIV) infection on leukocyte and lymphocyte values and cell-mediated immunity in female drug addicts undergoing detoxification therapy

<table>
<thead>
<tr>
<th>HIV negative (n = 17)</th>
<th>HIV positive (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocytes (× 10⁹/L)</td>
<td>7.18 ± 1.32</td>
</tr>
<tr>
<td>Lymphocytes (× 10⁹/L)</td>
<td>2.59 ± 0.72</td>
</tr>
<tr>
<td>(%)</td>
<td>36 ± 8</td>
</tr>
<tr>
<td>CD2 (× 10⁹/L)</td>
<td>1.49 ± 0.47</td>
</tr>
<tr>
<td>(%)</td>
<td>56 ± 12</td>
</tr>
<tr>
<td>CD4 (× 10⁹/L)</td>
<td>0.98 ± 0.32</td>
</tr>
<tr>
<td>(%)</td>
<td>38 ± 8</td>
</tr>
<tr>
<td>CD8 (× 10⁹/L)</td>
<td>0.66 ± 0.21</td>
</tr>
<tr>
<td>(%)</td>
<td>25 ± 5</td>
</tr>
<tr>
<td>Number of positive responses to 7 antigens</td>
<td>2.88 ± 1.36</td>
</tr>
<tr>
<td>Score (mm)³</td>
<td>8.28 ± 5.20</td>
</tr>
</tbody>
</table>

1 ± SD.

2 Significantly different from HIV negative, P < 0.05.

### TABLE 3

Effects of human immunodeficiency virus (HIV) infection on humoral and innate immunity in female drug addicts undergoing detoxification therapy

<table>
<thead>
<tr>
<th>HIV negative</th>
<th>HIV positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD19 (× 10⁹/L)</td>
<td>0.22 ± 0.13</td>
</tr>
<tr>
<td>(%)</td>
<td>9 ± 4</td>
</tr>
<tr>
<td>Immunoglobulin G (g/L)</td>
<td>11.72 ± 3.96</td>
</tr>
<tr>
<td>Immunoglobulin A (g/L)</td>
<td>1.59 ± 0.59</td>
</tr>
<tr>
<td>Immunoglobulin M (g/L)</td>
<td>2.34 ± 0.91</td>
</tr>
<tr>
<td>C3 (g/L)</td>
<td>1.38 ± 0.10</td>
</tr>
<tr>
<td>C4 (g/L)</td>
<td>0.30 ± 0.10</td>
</tr>
</tbody>
</table>

1 ± SD.

² Significantly different from HIV negative, P < 0.05.
because relatively few cells are productively infected. In this sense, the effects of malnutrition must be considered. The synergistic effects of malnutrition and infection have a dramatic effect on the population studied (35). This fact is clearly shown by the CD4 values in the noninfected female heroin addicts.

CD8 cell data in the present study were similar to values observed under conditions of malnutrition (36). The presence of HIV led to a higher CD8 percentage (43%) and count (32%). This outcome differs from that observed previously by us in male drug addicts undergoing detoxification, in whom HIV infection did not modify the CD8 count (37). It is important to consider that the noninfected female group had a normal CD8 count, whereas the infected group had values much higher than those considered normal (32).

Modifications in CD4 and CD8 numbers lead to a depressed CD4:CD8 in infected females. A low CD4:CD8 is considered to be an index of subclinical malnutrition or immunodeficiency (38). We previously observed a lowered CD4:CD8 in a male drug addict group undergoing detoxification therapy lasting between 3 and 6 mo. This low value was due both to the HIV infection effect (107%) (non-HIV-infected compared with HIV-infected males) and to previous drug abuse (31%) (non-HIV-infected males compared with healthy males) (37).

Cell-mediated immunity evaluated in vivo by a delayed-hypersensitivity skin test was lower in all drug addicts, being impaired in seropositive HIV patients. None of the women tested had normal responses. Similarly, neither the number of positive responses to the seven antigens nor the scores reached normal values for an average Spanish female population (25). These observations suggest that addiction may lead to deterioration of nutritional status, which is aggravated by the viral infection in HIV drug addicts. Similar results have been reported in malnourished and infected subjects, in whom depleted nutritional status enhanced susceptibility to infectious diseases (39, 40).

No changes were shown in B lymphocyte (CD19 subset) percentages, but the CD19 count was depressed in HIV-infected females. The negative correlation observed in the HIV-infected female group between the CD19 lymphocyte subpopulation and weight gain suggests that the higher the weight gain, the lower the CD19 cell number. In contrast, both immunoglobulins G and M were increased in the HIV-positive group compared with the HIV-negative group. It has been reported that serum immunoglobulin concentrations are unmodified or slightly increased in malnourished individuals to maintain B lymphocyte functionality (41). Nevertheless, immunoglobulin values can be increased when an infection process is present in response to an infectious agent (42).

Innate immunity evaluated by serum complement factors C3 and C4 was shown to be unmodified by HIV effect. All values observed were within the normal range (32). This outcome could mean that in our patients neither complement factor was affected by drug effect or HIV infection.

We conclude that anthropometric assessment showed an adequate recovery of nutritional status in female drug addicts after ~6 mo of detoxification. However, the changes in immunologic indexes found in these subjects either in the presence or absence of HIV infection suggest that the abnormalities triggered by drug abuse may remain for a long time and at a subclinical level. Therefore, nutritional status and clinical history should be assessed in both HIV-positive and HIV-negative drug addicts as early as possible. Each patient should be given nutritional education and therapy to improve their nutritional status, thereby delaying disease progression, principally in those who are HIV-infected, which will help them to get out of the drug habit and contribute significantly to an improved quality of life.

We are grateful to A Tejedor for her invaluable help in recruiting drug addicts. Our deepest gratitude is given to the Proyecto Hombre Institution for remarkable cooperation throughout the study. We also thank the Flow Cytometry Centre at the Universidad Complutense of Madrid and especially A Alvarez for his assistance in determining lymphocyte subsets by flow cytometry.

REFERENCES