Therapeutic prospects of natural alpha interferon from normal human leucocytes in the treatment of genital condylomata in HIV positive women

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Summary: Various Authors underline that HIV positive women have a higher CIN incidence and a higher prevalence of HPV.

HIV could act as cofactor in the proliferation of HPV manifestation, because of a hypothetical deficit of local immunity.

5 HIV positive patients have been examined:
3 of them presenting vulvocondylomas and/or VIN were treated with 1.000.000 IU αIFNn three times a week for three weeks.
2 of them presenting CIN and/or HPV were treated with a two-phase therapy:
A) Induction therapy: 3.000.000 IU 3 times a week for three cycles.
B) Maintenance therapy: 1.000.000 IU 3 times a week for three months.

IFN was the primary treatment for viral lesions, even though an improvement of prognostic indices (CD4, CD4/CDB, 2M), has shown its usefulness in association or in alternative to AZT.

Key words: HPV; HIV; Interferon.

INTRODUCTION

The latests statistics on AIDS cases in Italy show a progressive increase of heterosexuals (Table 1) 20% of AIDS cases among females and 4% among males are transmitted by heterosexual intercourse.

In Europe, heterosexual contagion represents 12% of the total figure, and 33% among AIDS affected females.

A slight decrease of AIDS cases has been recorded due to hemophilia, transfusions and drug addiction.

In 34% of AIDS pediatric cases, the mother contracted infection through sexual contagion (Table 3).

By defining as "AIDS" other pathologies such as cervical cancer a higher number of women will be affected by the disease.

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Table 1. – *AIDS: cases in Italy.*

31-03-1989		30-09-1992
16.6%	homosexual	15%
68.2%	drug addict	66.8%
3.0%	homosex. and drug add.	2.5%
1.8%	haemophilia	1.1%
1.5%	transfusion	1.4%
5.9%	heterosexual intercourse	7.1%
3.0%	uncertain factors	6.1%

(CDC Atlanta has also proposed to include pulmonic TBC and some forms of virus Pneumonia).

Considering that the transmission mechanism male > female is more relevant than the opposite one, in future, a higher presence of females among AIDS cases is forseen which can be attributed to heterosexual transmission.

The ratio male > female among HIV carriers will tend to parity.

MATERIALS AND METHODS

The research was carried out on 18 HIV positive women aged between 18 and 37.

On the grounds of CDC standards 2 patients presented the disease at the third stage and 16 patients presented it at the second stage.

Seropositivity ranged from 1 to 8 years.

Seven patients were drug addicts, 3 were patients at risk, and 6 had sexual intercourse at risk.

Three patients presented vulvocondylomas and one of them presented vulvocondylomas associated to VIN I, two of them presented CIN I-II and/or VCE (virus cytophatic effect).

In accordance with the standards of other research centers, patients presenting viral pathology and/or neoplastic pathology of the lower genital tract have been examined.

At the beginning the patients presented:

CD4 > 400 cells/mm^3 (n.v. 800/1200 mm^3);

WBC > 6000 cells/mm^3;

HB > 13 gr %;

Bet. 2 microglobulin < 4 mg %;

Hepatic functionality indices were within normal limits (Table 4).

Three patients had been treated with Zidovundine (AZT) at a dosage of 500 mg/die twice a day.

Natural alpha Interferon from normal human leukocytes (Alfaferone - Alfa Wassermann) therapy was carried out on 5 patients, 1 IU three times a week for three months in patients presenting vulvar HPV and/or VIN, and by using a two-phase therapy in patients presenting CIN and/or HPV (Table 5) as follows: induction therapy: 1.000.000 three times a week for 3 cycles maintenance therapy: 1 IU three times a week for 3 months.

The therapeutic effectiveness has been classified thus:

CR: complete response (complete remission of lesions);

PR: partial response (decrease of more than 50% of surface and/or number of lesions) (Table 5);

Table 2. – *AIDS: difference between males and females up to 31-10-1991 in Italy.*

	Males	Females
Drug addiction	5839 (66.32%)	1421 (72.05%)
Sexual intercourse	1129 (12.83%)	
Bisexual intercourse	510 (5.80%)	
Heterosexual intercourse	345 (3.92%)	390 (19.78%)
Uncertain risk	342 (3.88%)	93 (4.72%)
Drug add.+homosex.	144 (1.63%)	
drug. add.+bisex.	140 (1.60%)	
Prostitution	137 (1.55%)	5 (0.26%)
Hemophilia	125 (1.41%)	1 (0.05%)
Transfusions	94 (1.06%)	62 (3.13%)
	8805 (100%)	1972 (100%)

Table 3. – *AIDS: cases of children in Italy up to 23-01-1992.*

• Children at risk of perinatal infection:	1987
• Children at transfusional risk:	
thalassaemic	43
haemophilic	50
occasional transfusion	22
• Uncertain factors:	4

Table 4. – *Initial prognostic and diagnostic aspects.*

	Age	Diagnosis	CD4	CD4/CDB	β_2-Microglobulin
1)	20	HPV vulvar	440	0.61	3.48
2)	24	HPV vulvar	480	0.58	3.27
3)	29	HPV vulvar + VIN 1	500	0.63	3.50
4)	27	CIN 1-HPV (6-11)	407	0.58	3.60
5)	25	CIN 2-HPV (6-11)	443	0.58	3.60
		Average	454	0.60	3.37

Table 5. – *Therapeutical schemes.*

Vulvocondylomas: 1×10 IU three times a week for three months.

Cervicocondylomas: disphasic therapy:

a) induction 3×10 IU three times a week for three cycles;

b) maintenance 1×10 IU three times a week for three months.

AR: absence of response (no volumetric and/or numerical variation of lesions).

Diagnosis and therapeutic response have been carried out through biopsy, colposcopy and "in situ" hybridization on cervical smears.

RESULTS

The main target was the evaluation of gynaecologic lesions.

Even though an improvement of prognostic indices was recorded, the results cannot be compared because three patients had been treated, simultaneously with AZT (Table 6).

In all three patients presenting vulvar lesions complete regression was recorded after 3 months of treatment.

In one patient presenting florid condylomas, physical therapy was added.

Patients presenting cervical lesions gave complete response after 3 months and the successive check-ups have confirmed the above mentioned response (average follow-up 50 weeks).

Slight collateral effects such as fever, and debility were recorded; however, they disappeared spontaneously.

No relevant hematic alterations were found during the follow-up.

DISCUSSION

HIV positive females showed a higher HPV and/or CIN and/or VIN incidence due to a hypothetical immunodeficiency.

(Some histochemical research showed an increase of Langherans cells and helper T Lymphocytes after an IFN was therapy).

AZT the most effective antiviral drug for delaying the proliferation and allowing a longer survival.

αIFNn was used, in our research, in the treatment of HPV viral lesions.

Antiviral, antiproliferous and immunomodulating actions were attributed to natural alpha Interferon.

Antiviral action was carried out by blocking virus manifestation and its proliferation (replication) in safe (undamaged) cells.

Antiproliferous action was carried out by cell inhibition and by acting on DNA synthesis and by derratation of messenger RNA.

Immunomodulating action was carried out by activating of natural-k cells, of cytotoxic Helper T Lymphocytes, macrophages, and the release of Interleukina 2.

All these actions can be used to reduce the replication of HIV, increase the num-

Table 6. – *Immunological aspects during the follow-up of the patients treated with α IFNn.*

	Beginning	3rd. month	6th. month
CD4	45	491	521
CD4/CD8	0.60	0.64	0.64
β_2 M.	3.37	3.34	2.81

ber of Helper T Lymphocytes and consequently to delay AIDS manifestation.

On the other hand, AZT therapy could not be used on patients presenting collateral effects such as leucopenia, anemia, plateletpenia which depend on dosage and on donation of therapy or because there were some counterindications such as anemia, plateletpenia high level of transaminase, use of methadone, poor general conditions or because they refused to be treated with such therapy.

However, it is advisable to use alternative drugs which have a bioinhibiting effect, while waiting for a vaccine.

Research carried out among patients who have been treated with AZT in addition to IFNn, is very reassuring because significant improvements have resulted especially if the two therapies are associated.

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