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A short-term intervention trial on HIV positive patients using a Sri Lankan classical rasayana drug – *Ranahamsa Rasayanaya*

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Abstract

Rational use of *Rasayana* therapy, in the management of HIV infected individuals, could potentially stabilize the destructive control mechanisms, by modulating the psycho-neuro-endocrine-immune axis. The objective of the present study has been to determine the short-term effects of *Ranahamsa Rasayanaya* (RR) in HIV infected patients. A total of 27 patients with documented HIV infection were randomly assigned to two groups, Group A – 5 g of RR twice daily with cow's milk and sugar. Group B – Only routine modern therapy was continued, if any they were taking, including highly active anti-retroviral therapy (HAART). Absolute $CD4^+$ T-cell and total lymphocyte counts were measured in these patients, registered under Group A. Only 21 participants completed the study protocol (In Group A, 15 patients and in Group B, 6 patients). Initial mean $CD4^+$ T-cell count was 304.50 ± 43.36 cells/microliter, which increased to 430.44 ± 66.01 cells/microliter by 41.36% ($P<0.05$), measured among 9 patients out of 15, who received RR in Group A. The RR seemed to be a safer adjuvant in people with HIV infection with respect to absolute $CD4^+$ T-cell count over a 90 days treatment.

Key words: $CD4^+$ T-cells, HIV/AIDS, psycho-neuro-endocrine-immune modulation, *Rasayana* therapy, *Ranahamsa* rasayanaya.

Introduction

AIDS-related wasting syndrome[1] is a pre-terminal manifestation of the advanced HIV disease,[2] which is resulted from the destructive control mechanisms.[3] Such hyper-catabolic state of the body could be viewed under the ayurvedic concepts of jara[4] or aadana[5] in sharira.[6] Therefore, it is reasonable to postulate that, such imbalance of body-mass homeostasis could be disrupted by *Rasayana* (rejuvenating) therapy, because of its capability to reestablish[7]

Navayauvana or visarga[8] in *Deha*[9] or nourishment with an anabolic effect in the management of various illnesses including aging at the advent of ayurveda.[10] Comparably, *Ranahamsa Rasayanaya* (RR), a Sri Lankan classical *Rasayana* drug is being used in the treatment for similar conditions[11,12] by the traditional physicians (deya vaidya). Thus, the same medicament has been adapted to treat HIV infected patients in the present study, aiming to counteract the associated destructive control mechanisms in the HIV infection, by modulating the psycho-neuro-endocrine-immune (PNI) axis. The current study has been encouraged by the following facts, the majority of people living with HIV/AIDS are presently using complementary medicine,[13] CCRAS, India promoting the *Ayurveda* and Siddha clinical researches on HIV/AIDS[14] and the United Nations proposed "Combat HIV/AIDS, Malaria and other diseases." as the 6th development goal among the millennium development goals (UNMDG).[15]

Aims and objectives

The clinical study has been planned and carried out with the following aims and objectives.

1. To understand the process of etiopathogenesis of HIV/AIDS according to ayurvedic point of view.
2. To evaluate the efficacy of Ranahamsa Rasayanaya on HIV positive patients by assessing the overall improvement in signs and symptoms and mental health of the patient.

Materials and Methods

The study was conducted in collaboration with M.P. Shah Medical College and G.G. Hospital, Jamnagar.

Patients attending the following institutions O.P.D. and I.P.D.

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were selected:

1. Pt. Dinadayal Upadhyay Medical College and Hospital, Rajkot,
2. Infectious disease ward at M.P. Shah Medical College and G.G. Hospital, Jamnagar,
3. Reliance Community Health Care Center, Moti Khavdi, and
4. Kayachikitsa Department in I.P.G.T. and R.A. Hospital, Jamnagar,

Those fulfilling the criteria of selection were registered under the present clinical study irrespective of age, sex, caste, religion, etc.

Criteria of selection

Patients were selected for the present study, if they satisfy the following basic requirements:

1 They must be diagnosed as HIV positive (seropositive for HIV) by all the three tests (i.e., ELISA, Tridot and Western blot tests), carried out in an Integrated Counselling and Testing Center (ICTC) or Voluntary Counselling and Testing Center (VCTC) or any other such institutes.

2 They must provide a laboratory result form duly signed and issued from such an establishment, declaring the HIV status (i.e., seropositive for HIV) of the patient, and

3 They must fulfill the inclusion criteria.

Inclusion criteria

1. Documented HIV positive (seroreactivity) status tested with ELISA, Tridot and Western blot tests.
2. Absolute $CD4^+$ T-cell count may be done, if patient could afford it.

Exclusion criteria

1. Selected HIV seroreactive patients should not show more than one major-sign or minor-sign of the World Health Organization (WHO) case definition for AIDS surveillance.[16]
   Major signs of WHO case definition for AIDS surveillance: Weight loss more than or equal to 10% of body weight, chronic diarrhea for more than one month, prolonged fever for more than one month (intermittent or constant). Minor signs of WHO case definition for AIDS surveillance: Persistent cough for more than one month, oropharyngeal candidiasis, generalized pruritic dermatitis, generalized lymphadenopathy, history of herpes zoster, chronic progressive or disseminated herpes simplex infection.
2. They should not be suffered from any major concurrent illness, which affects one or more systems of the body. E.g.: Ischemic heart disease (IHD), diabetes mellitus (DM), tuberculosis (TB), malignant tumors, etc.

The study design: The patients were selected randomly, divided into two groups, *namely* treatment (Group A) and control group (Group B) and interrogated and examined clinically along with laboratory investigations. All the clinical findings of a particular patient was thoroughly documented in a research pro-forma along with an O.P.D. case form and registered in the departmental O.P.D. register. The study design was approved by Institutional Ethical Committee,IPGT & RA,Jamnagar.

In the C treatment group, all the patients were given Chitrakadi tablets twice daily after lunch and dinner for ama pachanartha (to digest morbid chyme) and agni dipanartha(to stimulate gastric fire) for five to seven days period and Eranda bhrishta Haritaki powder 6 g with luke warm water, once daily at the bed time for koshtha shuddhi for five to seven days period before starting the treatment.

1. Group A (treatment – RR)

The test drug:	*Ranahamsa Rasayanaya* (RR)
Dose:	5 g twice daily
Period of treatment:	90 days*
Anupna (vehicle):	Cow's milk and sugar

*During the course of the treatment, patients were allowed to continue modern medicine, if they were taking any.

2. Group B (control)
No specific ayurvedic medicine was given. They were allowed to take routine modern therapy, if they were taking any, including the highly active anti-retroviral therapy (HAART).

Pathya – apathya: Advised to all the participants regardless of the group, they were assigned to take hygienic food, milk and milk products, to have a cup of buttermilk after a meal and have a bath everyday and to reduce highly seasoned foods with salty and sour tastes.

Criteria of assessment: A specially prepared pro-forma was utilized to report and record the necessary clinical findings. A scoring pattern was used to document the subjective as well as objective signs, in the pro-forma. The efficacy of the trial drug was evaluated by the improvement of signs and symptoms along with the laboratory investigations, especially absolute $CD4^+$ T-cell count, $CD4^+$ T-cell percentage and total lymphocyte count.

Objective criteria: 1. Absolute $CD4^+$ T-cell count was carried out, once the patient could afford it.

1 Body weight along with body mass index (BMI).

2 Routine hematological investigations were performed.

Subjective criteria: 1. Efficacy of the test drug was evaluated through symptomatic relief, physical well being, as per ayurvedic parameters for *dhatukshaya*, *Ojakshaya* and *Rajayakshma lakshana*, etc. 2. Mental health of the patient was also evaluated with the established and acclaimed psychological parameters, as per ayurvedic parameters as well.

3. Routine hematological, biochemical, urine, stool and radiographic investigations were carried out before and after the treatment.

Overall effect of the test drug: The improvement of the course of HIV disease is categorized according to the cumulative percentage of the relief from the reported symptoms and signs.

Completely cured: 100% (Patient must become HIV negative (seroreversion[17]), after the treatment); Marked improvement: 75 - 99%; Moderate improvement: 51 - 74%, Mild improvement: 25 - 50%; Unchanged: < 25%

Statistical analysis

Evaluation of the data through statistical estimations within the group and comparison between the groups after treatment (AT) were assessed by using paired and unpaired Student's *t*

tests respectively. Being number of observations (n) in each group below 30, Student's *t* test was employed for the purpose. The statistical estimations particularly sample mean, standard deviation (SD), standard error of mean (SEM), calculated *t* value and probability (*P*) value were obtained by applying the standard formulae. Probability (*P*) values of *t* are tabulated for various degrees of freedom (df) according to the number of observations. *P* value less than 0.05, is considered as statistically significant.

Observations and Results

Maximum patients (88.9%) were reported to be in the age group of 20-49 years. Majority of patients (70.4%) were males. Over 85% patients had either primary or secondary education. All the patients (100%) belonged to urban setting.

More than 70% reported that they participated in high risk activities. Although, higher number of patients reported that, they participated in the high risk activities, but no patient was found to use intravenous drug use (IDU), which is considered as a high risk activity[18] as well as a transmission route of HIV.[19] More than half of the patients (55.6%) believed that, they acquired HIV infection through unprotected homosexual contact, while 37.0% patients believed that, they got infected with HIV through unprotected heterosexual contact, and an isolated case reported (a minor) that, the transmission of HIV might be due to unsafe injections. Strangely, another solitary patient reported the acquisition of the disease not known. All patients (100%), registered under the clinical study reported that, they had a positive past history of exposure to injections. Around 85% patients admitted to having casual sexual encounters with someone other than their regular partner or spouse. No patient had traveled abroad. Surprisingly, small number of patients found to have a past history of sexually transmitted infections (STI), which is also a risk factor[20,21] for acquiring the infection. Men having sex with men (MSMs)[22] were found to be 85.2%, because large number of participants were referred to the present study by Lakshya trust and Nokhum ayakhum, Rajkot, a non-governmental organization (NGO) working for the welfare of gay community. A large number of patients (88.9%) have had sex with multiple partners. Regular use of condoms while engage in sexual activities found to be a common practice among the patients (74.1%). Majority of the patients engage in vaginal intercourse (85.2%), followed by oral sex (70.4%) and anal sex (59.3%). Many patients (77.8%) reported that, negative family history for HIV infection.

Most of the participants (92.6%) were infected with HIV-1,[23,24] except 2 patients, in whom the strain of HIV was not specified in their laboratory result form. No patient was reported, under the clinical stage 4 of the WHO Classification System for HIV infection,[25] while many (74.1%) were found to belong to the clinical stage 2, followed by clinical stage 1 (18.5%) and clinical stage 3 (7.4%). But, according to the 1993 revised CDC classification system for HIV infection and expanded AIDS surveillance case definition for adolescents and adults,[26] one third of the patients (33.3%) initially had an absolute $CD4^+$ T-cell count below than 200 cells per microliter; therefore, they all come under having AIDS. Chronicity of the HIV disease was observed to be more than one year among higher number of patients (40.7%), which is calculated from the date of laboratory result form issued by an ICTC or VCTC to the date of the registration under the present study.

Scoring pattern

No.	Parameters	Score
1.	Major symptoms	12
2.	Minor symptoms	16
3.	Nonspecific constitutional symptoms	35
4.	Symptoms of *Ojas* disorders	27
5.	The 7-item Hamilton scale for depression (HAMD-7)	33
6.	Total	123

Patients' distribution among the groups

Group	Total number of patients registered	Number of patients discontinued	Number of patients completed
Group A (RR)	21	06	15
Group B (control)	06	00	06
Total number	27	06	21

Effect of the therapy

Effect of Ranahamsa Rasayanaya on major and minor signs

The test drug had a statistically significant ($P<0.05$) reduction in diarrhea (100.0%) and cough (71.43%) in the treatment group. Remaining symptoms were unaffected by the test drug, except fever. Not any patient complained of fever within the treatment group.

Effect of Ranahamsa Rasayanaya on nonspecific constitutional symptoms

It was found to give statistically significant ($P<0.05$) results in reducing debility (by 41.18%), headache (by 75.00%), muscular aches and pains (by 66.67%) and loss of appetite (by 44.44%).

Following nonspecific constitutional symptoms were found to be reduced markedly, but without being statistically significant, such as reduced digestive fire and insomnia.

The test drug is statistically significant in producing an apparent increment in the ingestive capacity of the patients. But it was failed to achieve statistically significant results in increasing the digestive capacity of the patients.

Effect of Ranahamsa Rasayanaya on the 7-item Hamilton scale for depression

Evaluation of the test rug effect on 7-item Hamilton scale for depression (HAMD-7) revealed that, it produced statistically significant ($P<0.05$) results in reducing following symptoms such as interest, pleasure, level of activities (by 37.50%), tension, nervousness (by 16.67%), reduced energy level (by 33.33%) and total HAMD-7 (by 18.09%). Other symptoms were unaffected, except for suicidal thoughts. Suicidal thoughts were reduced, but not in a statistically significant manner.

Effect of Ranahamsa Rasayanaya on hematological parameters

After treatment with the test drug, it was found that, absolute $CD4^+$ T-cell count was increased (41.36%), which was statistically significant ($P<0.05$). On the other hand, it also

decreased the neutrophil percentage by 11.33% in a statistically significant ($P<0.05$) manner. Similarly, hemoglobin percentage was increased by 11.31%, which is also statistically significant ($P<0.05$). All other remaining hematological parameters do not get influenced in a statistically significant manner, even though they were found to be increased.

Effect of Ranahamsa Rasayanaya on biochemical parameters

Alanine aminotransferase (ALT) or SGPT level was found to be reduced by the test drug. which statistically nonsignificant.

Adverse drug reactions reported among the patients, who were treated with the test drug

Total number of six patients (22.2%) discontinued the treatment. Two patients out of them revealed incidence of adverse drug reactions. Both of them complained of mild burning sensation over the body, while one of them reported transient mouth ulceration (mucosal erosion?) after taking the test drug. Apart from that, another two patients (7.4%) complained of mild drowsiness after taking the drug with milk. It must bring to notice that, they did not leave the therapy. No other such adverse effects, including life-threatening condition, were seen during the therapy.

Comparison of the results of Group A with Group B

Statistical evaluation of the test drug's effect on major and minor signs of WHO case definition for AIDS surveillance with the control group using unpaired Student's t test:

By comparison between both the groups, it was found that the test drug produces only one statistically significant ($P<0.05$) result in relieving diarrhea (by 67.27%). Other symptoms excluding lymphadenopathy were found to get reduced with the test drug in comparison to the control group, but without giving statistically significant results.

Statistical comparison of the test drug's effect on nonspecific constitutional symptoms with the control group using unpaired Student's t test:

Nonspecific constitutional symptoms were influenced by the test drug in the treatment group in comparison to the control group. But it was statistically nonsignificant manner.

Statistical comparison of the test drug's effect on *Ojas* disorders with the control group using unpaired Student's t test:

Ojas disorders such as *dosha chyavana* and feeling of heaviness were only relieved by the test drug in comparison to the control group, but in a nonsignificant manner. All other symptoms except unconsciousness (no patient was suffering from unconsciousness during the clinical trial) were unaffected.

Statistical comparison of the test drug's effect on the 7-item Hamilton scale for depression (HAMD-7) for evaluation of mental health:

The test drug reduced all the symptoms except feelings of guilt and physical symptoms of anxiety, but in a statistically nonsignificant manner in contrast to the control group results. Comparison of the overall effect of the therapy is shown in the following Table 1:

Table 1: Overall effect of therapy

Groups	Unchanged		Mild Improvement		Moderate Improvement		Marked Improvement	
	No.	%	No.	%	No.	%	No.	%
Group A	06	22.2%	07	25.9%	02	07.4%	-	-
Group B	-	-	04	14.8%	02	07.4%	-	-
Total	06	22.2%	11	40.7%	04	14.8%	-	-

In the treatment group, there were six patients, who showed no change in their symptoms. Another seven patients showed mild improvement, while two patients showed moderate improvement.

In the control group, four patients showed mild improvement, while remaining two patients showed moderate improvement

Discussion

Human Immunodeficiency virus (HIV) infection causes acquired immuno deficiency syndrome (AIDS).[27,28] It is a newly found disease consisting various clinical presentations, which are primarily stemmed from profound immunodeficiency caused by the selective depletion of $CD4^+$ T-cells.[29] Ayurvedic texts lack the reference to the disease owing to its recent emergence. Fortunately, one can find several disease entities described in ayurvedic literature similar to the HIV/AIDS disease, but still they are different. The various clinical presentations of the advanced HIV disease or AIDS are the phenomenon of *Vyadhi Samkaratwa*.[30] At the end, it is the profound immuno deficiency, which causes all the disorders, thus the state of immuno deficiency could be well correlated with the loss of both the aspects of *Vyadhi Kshamatwa (Vyadhi utpada pratibandhakatwa avum vyadhi bala virodhitwa)*[31] and its communicability and prognosis (the prognosis of HIV infection has recently changed from a fatal condition to a manageable chronic illness)[32] with *yapya aupasargika roga*.[33]

To counteract the associated destructive control mechanisms[34] and AIDS-related wasting syndrome[35] in the progression of HIV infection, ayurvedic therapeutic modalities such as *Santarpana*,[36] *Brimhana*,[37] *Rasayana*[38-40] and *Vrishya*[41] therapies are indicated. Not only that, it was also postulated to exploit especially *Yuktikrita bala*,[42] thereby preventing or delaying *Aparirakshanaja vyadhi*, e.g., *jara* or metabolic derangement (seven types of aging damage[43]) associated with aging, etc. To modulate the psycho-neuro-endocrine-immune (PNI) axis,[44] *medhya rasayana, achara rasayana*[45] and *Sattvavajaya*[46] therapy are indicated.[47] By the treatment with *Ranahamsa Rasayanaya* (RR), the same purposes have been hoped for along with anti-HIV properties of its ingredients, such as ajoene, caffeic-acid, diallyl-disulfide, quercetin,[48] selenium (Se), zinc (Zn),[49] coriandrin (Singh *et al.* 2005),[50] apigenin, glycyrrhisoflavone, glycyrrhizin, licochalcone-A, lignin,[51] caffeic acid, chlorogenic acid, ellagic acid, epicatechin, gallic acid, myricetin, procyanidins,[52] etc. Besides that, the test drug contained renowned *medhya rasayana* drugs, i.e., *Guduchi* (*Tinospora cordifolia*), *Yashtimadhu* (*Glycyrrhiza glabra*),[53] *Brahmi* (*Bacopa monnieri*),[54] Go ghrita (butter oil, anhydrous),[55] etc., which help in modulating the

PNI axis. In general, it has been expected that, advantageous PNI modulation, anti-HIV properties, plus weakening of destructive control mechanisms would have produced a favorable homeostatic balance and restoration of wellness in the patient.

Age: Reported large numbers of HIV positive participants were young. An increased incidence of HIV in young age groups reflects the sexual activeness during this age, and maximum number of transmission through sexual route.

Gender: Majority of the patients registered for the present study were males with a frequency of 70.4%, and females belonged to 29.6%. High risk sexual practices reported among MSM (i.e., unprotected receptive anal sex – *kothis*, multiple partners, violent sex,[56] etc.) are also high in frequency, thus making them more vulnerable to contract the disease. However, in the developing countries, major transmission route is unprotected heterosexual contact. Even though, the disease burden among MSM should not be overlooked.

Educational status: Majority (85.2%) having either or primary education is a welcoming fact, because by educating the masses, this dreaded disease only can be prevented. Another alarming fact is that, this finding does not reveal the truth. In India and in Gujarat state, the literacy rate is not higher like that among the population.[57]

Habitations of the patients: Every participant (100%) was reported from an urban setting. This finding also does not show the reality, as higher percentage of the population belong to rural areas.

Risk level of the patients: Most of the patients (70.4%) were found to have an increased level risk in their life style. It is possible because many of them engage in same sex relationships with multiple partners. Both come under high risk activities.[58] Another finding showed that, despite the high risk sexual activities, the participants did not use intravenous drug use (IDU).[59] This may be due to the legal restrictions of alcohol and other drugs in Gujarat state.

Probable transmission route of HIV infection: More than half of the participants (55.6%) believed that, they got infected with HIV *via* unprotected homosexual contact. This figure is attributed largely to the sample contained MSM. Over one third of the patients (37.0%) believed that, they contracted the disease through unprotected heterosexual contact. There was one minor, it may be attributed to the contaminated injection caused the disease. Apart from that, one patient reported that, she does not have a clue about contracting the disease. These findings confirm that, the major route of HIV transmission in developing countries is *via* sexual route, and at the same time, it contradicts the major role of unprotected heterosexual contact, reporting 55.6% cases of unprotected homosexual contacts. Reporting more than 96.3%, from unprotected sexual contact and unsafe injections, the present findings were in accordance with the established theories of HIV transmission.[60]

History of exposure to injections: All of the patients (100%) admitted to have got injections in one time or the other in their life. This may be a possible way in the case of a single patient who reported to have no idea about how she contracted the disease. Even though many had casual sexual encounters, we could not rule out the possibility of transmitting HIV infection by this route. The recycling of medical waste in developing countries like India thrives in. Recent outbreak of hepatitis B infection was caused by the usage of recycled medical waste by the physicians, thus causing iatrogenic epidemics.[61] History of casual sexual encounters found among the patients. Many (85.2%) reported that, they had had casual sex apart from their regular partner either with a stranger or a known person. The remaining patients denied having casual sex, including a minor. As it is a well documented fact that the major route of HIV transmission is through unprotected sexual contact regardless of its nature.[62,63]

History of foreign travel: No patient travelled abroad, who came under the present study.

History of sexually transmitted infection (STI): Only 14.8% patients admitted that, they had suffered from an STI earlier. Majority claimed they were free from an STI in the past. Anyhow, this finding not exactly back the transmission of HIV infection, but still it credited the theory of facilitating the HIV transmission due to the presence of inflammation in the genital organs or where the contact occur.[64]

Sexual orientation and sexual practices: Majority (51.9%) reported that, they were bisexually orientated. Exclusively homosexual patients found to be 11.1% and 33.3% heterosexually oriented patients were also found during the present study. Apart from them, there was a child obviously without sexual activity. Under broad term of MSM or men-having-sex-with-men, the above mentioned both the categories, i.e., bisexually and exclusively homosexually oriented can be included. Then there were 63.0% of patients, can be categorized under MSM. Majority of the patients (85.2%) admitted to have vaginal intercourse. Around 60% patients admitted to have anal sex. This finding is in accordance with the sexual orientation finding, where both heterosexually and bisexually oriented patients were found in the same proportions. Anal sex is considered to be a high risk factor in the transmission of HIV infection. Compared to anal sex and vaginal sex, oral sex is considered to be less riskier,[65] but still there is a considerable chance of contracting the disease, if the ejaculation occurs in the mouth or if vaginal secretion gets swallowed.

Positive family history for HIV: The findings of positive family history for HIV showed 22.2% of the patients had one or more HIV positive members in the family. This figure included the three widows, whose husbands died due to AIDS. It is most of the husband. But there was an isolation case of wife is HIV positive and the husband is negative. This indicates the "*bridging population*", who links the gap between the high risk population (who practice unwise sexual choices) and the low risk populations, i.e., housewives, etc. Risk associated with this intimate act makes it a burden. This is evident from the quote "*Who ever having sex is in risk*". This phenomenon is named as "Silda Spitzer syndrome", New York Governor Eliot Spitzer, who involved in a prostitution scandal, was reluctant to use condoms. So his wife never thought she is in risk. At the same time, many Indian gay men get married to escape from the social stigmatization[66] and thereby exposing their spouses to a greater risk.

HIV infection: It was found that HIV-1 was responsible for the

most of the infections reported among the participants with 92.6%, the same is the most common cause of HIV disease throughout the world.[67] Also there were two patients, in whom the strain of HIV was not specified in their laboratory result form. It is well established, HIV-1 has a rapid pathogenesis compared to HIV-2.[68]

Clinical stages and CD4⁺ T-cell Categories found among the patients: Around 75% of the patients belonged to the Clinical Stage 2 of WHO classification, while 18.5% were in Clinical Stage 1 and followed by Clinical stage 3 (7.4%). No patient was reported from Clinical Stage 4 for the present study. This had happened due to the exclusion of such patients from the study. There were 33.3% of the patients reported with CD4⁺ T-cell count between 200 and 499 cells per microliter and another 33.3% of the patients reported with CD4⁺ T-cell count below 200 cells per microliter. The latter group (CD4⁺ T-cell <200 cells per microliter) were well categorized under AIDS, according to the 1993 revised CDC classification system for HIV infection and expanded AIDS surveillance case definition for adolescents and adults.[69] And normal CD4⁺ T-cell count was reported among 18.5% of the patients, while 14.8% patients were reported without such laboratory investigation.

Chronicity of the infection: It was found many patients became aware of their seroreactivity for HIV during the last 12 months. That may be due to the aggressive media campaigns and screening methods implemented by the Indian government in the recent past. Even though, they were recently diagnosed as HIV positive, that is not a reliable measure to decide the chronicity, because the disease itself is chronic in nature.

Effect of the test drug on major and minor signs: The treatment produced statistically significant reduction only in diarrhea and cough. *Ranahamsa Rasayanaya* contains *Tala*, *Brahmi*, *Bhanga*, *Twak*, *Narikela*, *Karavi*, *Parpati*, these all have antidiarrheal, anti-dysenteric and antibacterial properties. Besides that, opium is reported to have astringent properties, thereby arresting diarrhea. This may be the cause for 100% relief of diarrhea. Not only that, some patients sought the treatment with modern drugs, while continuing the test drug. That may be another reason for this antidiarrheal effect.

Effect of the test drug on nonspecific constitutional symptoms: The following statistically significant results were observed; reduction of debility by 41.18%, relieving of headache (75.0%), relieving of muscular aching (66.67%), reduction of loss of appetite (44.44%) and increasing the ingestive capacity by 100.0%. *Talispatra*, *Jatipatri*, *Kumkuma*, *Bhanga* and *Pippali* known to stimulate appetite. Opium and *Bhanga* are reported to have analgesic properties. During the experimental studies, it was observed that, the test drug produced statistically significant anabolic effects in the body weight and statistically significant reduction in forced swimming induced hypothermia in rats. Therefore, it can be inferred based on these results, the test drug had an apparent adaptogenic activity. The same adaptogenic activity of the test drug may be beneficial in the treatment of HIV associated nonspecific constitutional symptoms.

Effect of the test drug on 7-item Hamilton scale for depression (HAMD-7) for evaluation of mental health: Following statistically significant effects were observed; reduction in loss of interest, pleasure, level of activities by 37.50%, loss of energy level by 33.33% and total HAMD-7 score by 18.09%. This may be due to the presence of many *medhya rasayana* drugs, i.e. *Tala*, *Brahmi*, *Narikela*,*Guduchi*, *Yashtimadhu*, *Nilotpala*, etc.

Effect of the test drug on hematological and biochemical parameters: It was observed that, absolute CD4⁺ T-cell count was increased by 41.36%, which is statistically significant. Besides that, it was also observed reduction of neutrophil count by 11.33% and increment of hemoglobin levels by 11.31%, both were statistically significant. All other parameters such as CD4⁺ T-cell percentage, absolute CD8⁺ T-cell count, CD8⁺ T-cell percentage, CD4/CD8 ratio, total lymphocyte count and lymphocyte percentage were increased, but failed to reach a statistically significant level. Even the ALT (Alanine aminotransferase) level also was reduced without being statistically significant. This shows the probable hepatoprotective activity of the test drug. This may be attributed to the presence of hepatoprotective dugs like *Guduchi*, *Yashtimadhu*, *Pippali*, *Chitraka*, etc.

Adverse drug reactions reported among the patient treated with the test drug: It is worthwhile to report, three side effects were reported during the clinical trial. First two symptoms (e.g., mild burning sensation and transient mouth ulceration) were reported among women and mild drowsiness was reported among two male patients. Both burning sensation and mouth ulceration were mild in nature. That may be due to the presence of *Bhallataka bija* in the test drug. Mild drowsiness may be caused due to mdaka properties of opium and hemp. It must be noted that, not any other adverse effect was observed during the study and no life-threatening condition was occurred during the trial period of the test drug. Even during the pharmacological study, not any kind of adverse effect was observed.

Comparison of the results of Group A with Group B

Statistical evaluation of the test drug's effect with the control group using unpaired Student's *t* test: It was observed that, the test drug has produced only one statistically significant ($P<0.05$) result in relieving diarrhea (by 67.27%) compared to the control group. All the remaining effects on symptoms were statistically nonsignificant compared to the control group.

Comparison of the overall effect of the therapy

In Group A, no patient showed marked improvement. Moderate improvement was recorded in 7.4% of the participants, followed by mild improvement in 25.9% of the patients and unchange in 22.2% of the patients.

In Group B, similarly no patient showed marked improvement, while 7.4% of the patients showed moderate improvement and 14.8% of the patients showed mild improvement.

The management of HIV/AIDS disease is complicated owing to its complex clinical manifestations along with deep-rooted pathogenesis. The defense mechanism of the body becomes vulnerable for this infection, which resulted in a profound immunodeficiency. The state of susceptibility to disease, due to profound immunodeficiency, could be well correlated with the loss of both the aspects of *Vyadhi kshamatwa (Vyadhi utpada pratibandhakatva* and *vyadhi bala virodhikatva)*. This leads to the occurrence of *Vyadhi samkaratva*, the ayurvedic technical term for the syndrome (a group of symptoms that

consistently occur together or a condition characterized by a set of associated symptoms).[70]

HIV type 1 (HIV-1) is the most common causative agent in HIV infection worldwide, the same was found in this study also. The most common transmission route of HIV infection is the unprotected sexual contact. The findings of the present study confirm that adverse drug reactions were observed among four participants, but they were mild and no life threatening condition was reported. Mild burning sensation was reported among two female participants and one out of them also complained of transient and mild mouth ulceration. That may be due to the presence of *Bhallataka bija* in the test drug. Mild drowsiness, which was found among two male participants, may be caused due to *madaka* properties of opium and hemp. This finding is important from the pharmacovigilance point of view.

Even though, the overall effect of the test drug does not show better results compared to modern medicine, it increased absolute $CD4^+$ T-cell count by 41.36% ($P<0.05$) in nine participants. Absolute $CD4^+$ T-cell count is the laboratory test generally accepted as the best indicator of the immediate state of immunologic competence of the patient with HIV infection.[71] Recovery of the absolute $CD4^+$ T-cell count by 41.36% shows the test drug's ability to improve the deteriorated immunocompetence of a HIV infected patient, who receives the test drug. The same effect testifies to its powerful immunomodulatory properties.

Conclusion

Based on these findings, it can be concluded that, the test drug – *Ranahamsa Rasayanaya* seemed to be a safer adjuvant in people with HIV infection with respect to absolute $CD4^+$ T-cell count over a 90 days treatment.

The results of this study are encouraging, but for further reliability, another trial should be conducted on a larger sample with the incorporation of more laboratory investigation such as plasma levels of HIV RNA.

References

1. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, Harrison's Principles of Internal Medicine. 16th ed. New York: McGraw-Hill; 1120.
2. Kotler DP, Tierney AR, Wang J, Pierson RN Jr. Magnitude of body-cell-mass depletion and the timing of death from wasting in AIDS. Am J Clin Nutr 1989;50:444-7.
3. Wikipedia. Homeostasis Wikipedia – the free encyclopedia, Available from: http://en.wikipedia.org/wiki/Homeostasis [Last accessed on 2008 Nov 9].
4. Agnivesha. Charaka Samhita. In: Acharya JT, editor. Chikitsa Sthana 1/1/79. Varanasi: Chaukhamba Surbharati Prakashan; 2008.
5. Sushruta. Sushruta Samhita. In: Acharya JT, editor. Sutra Sthana 21/8. Varanasi: Chaukhamba Surbharati Prakashan; 2008.
6. Iran R, AnenaIA, Dwraknttha C, Introduction to Kyachikitsa. 3rd ed. Varanasi: Chaukhambha Orientalia; 1996. p. 1.
7. Ibid (4). Chikitsa Sthana 1/1/74.
8. Ibid (5). Sutra Sthana 21/8.
9. Dih Ghañ, Dwraknttha C. dih ghaj, Ibid (6), 2p. 2.
10. Ibid (4). Chikitsa Sthana 1/1/70-74.
11. Department of Ayurveda. Ayurvedic Pharmacopoeia of Sri Lanka. The Associated Newspaper of Ceylon. Vol. 1. Part 1. Colombo: 1985.p. 205.
12. Singha AK, Senevirathne RD, Dissanayake DM, Fernando WI, Rathnayake MB, Wijayawardhane KH. Sri Lanka Deshiya Chikitsa Samgrahaya – Prathama bhaga. Colombo: Department of Ayurveda; 1984. p. 673.
13. Liu JP, Manheimer E, Yang M. Herbal medicines for treating HIV infection and AIDS. Cochrane Database Syst Rev 2005;CD003937.
14. Central Council for Research in Ayurveda and Siddha (CCRAS). Application for Award of Contingent Grant for the year 2006-2007 for the Students of M.D. (Ay./Siddha) and Ph.D. Scholars (Ay./Siddha) and other interdisplinery sciences. CCRAS, Annexture – 1A: Proposed Clinical Research Areas for Programme Projection 2003 – 2008.
15. United Nations (UN), "The Millennium Development Goals (MDG) Report 2007", United Nations Department of Economic and Social Affairs (UN – DESA) – June; 2007. p. 18-21.
16. Osmond DH. Classification and Staging of HIV Infection. HIV InSite Knowledge Base Chapter, Univ of California. Available from: http://hivinsite.ucsf.edu/InSite?page=kb-01-01#S4X. [Last accessed on 2007 Dec 12].
17. Roy MJ, Damato JJ, Burke DS. Absence of seroreversion of HIV-1 antibody in seroreactive individuals. JAMA 1993;269:2876-9.
18. WHO. Risk Factors. The World Health Report. 2002.
19. Kasper DL, Ibid (1); 1076-1139.
20. Mitchell RN, Kumar V, Abbas A, Fausto N. Pocket Companion to Robbins and Cotran Pathologic Basis of Disease. 7th ed. New York: Saunders; 2007. p. 140.
21. Disease Control Priorities Project. Risk Factors. Available from: http://www.dep2.org. [Last accessed on 2008 Sep 20].
22. Sanchez T, Finlayson T, Drake A, Behel S, Cribbin M. Human Immunodeficiency Virus (HIV) Risk, Prevention, and Testing Behaviors – United States, National HIV Behavioral Surveillance System: Men Who Have Sex with Men, November 2003 – April 2005. MMWR Surveill Summ 2006;55:1-16.
23. Kasper DL. Ibid (1). p.1077.
24. Hoffmann C, Rockstroh JK, Kamps BS. HIV Medicine 2007. 15th ed. Paris: Flying Publisher; 2007. p. 42.
25. Osmond DH. Ibid (16).
26. Kasper DL. Ibid (1), 1076.
27. Hoffmann. Ibid (24), 23.
28. Hoffmann. Ibid (24), 51.
29. Mohan H. Pathology Quick Review and MCQs Based on Harsh Mohan's Textbook of Pathology - 2nd ed. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2005. p. 46.
30. Ibid (4), Nidana Sthana 8/21-22 and Ma. Ni. 1/20.
31. Ibid (4), Sutra Sthana. 28/7 and Cakrapani on Sutra Sthana 28/7
32. Hoffmann C. Ibid (24), p. 23p.
33. Su Ni. Ibid (5), Nidana Sthana 5/33-34
34. Wikipedia. Homeostasis. Wikipedia – the free encyclopedia. Available from: http://en.wikipedia.org/wiki/Homeostasis. [Last accessed on 2008 Nov 9].
35. Kasper DL. Ibid (1), p.1120.
36. Ibid (4) Sutra Sthana 23/40.
37. Ibid (4) Sutra Sthana 22/23
38. Ibid (4) Chikitsa Sthana 1/1/7-8, 70, 79, 5, 1. Ibid (4) Sutra Sthana 11/36.
39. Ibid (4) Chikitsa Sthana 1/1/70.
40. Ibid (4) Chikitsa Sthana 1/1/791/1/5.
41. Ibid (4) Cha. Chi. 1/1/5.
42. Ibid (4) Chikitsa Sthana 1/1/5.
43. Wikipedia. Aubrey de Grey – The seven types of aging damage proposed by de Grey. Wikipedia, the free encyclopedia. Available from: http://www.wikipedia.com [Last accessed on 2008 Nov 09].
44. Babu SS, Jyothi P. Research Methodology for Ayurvedic Scholars. 2nd ed. Varanasi: Chaukhambha Orientalia; 2004. p. 29
45. Cha. Chi. Ibid (4) Cikitsa Sthana 1/4/30-35.
46. Ibid (4) Sutra Sthana 1/58.
47. Cha. Chi. Ibid (4) Cikitsa Sthana 1/3/30-31.
48. Duke JA. Chemical Constituents with AntiHIV Activity in Allium sativum var. sativum L. (Liliaceae) – Garlic. Dr. Duke's Phytochemical and Ethnobotanical Databases, Available from: http://www.ars-grin.gov/cgi-bin/duke/plant_act.pl?GET+54+AntiHIV+BU. [Last accessed on 2009 Mar 14].
49. Foster S, Johnson RL, Desk Reference to Nature's Medicine. Washington: National Geographic; 2006. p. 65.
50. Singh IP, Bharate SB, "Anti-HIV natural products". Curr Sci 2005;89:25.
51. Duke JA. Chemical Constituents with AntiHIV Activity in Glycyrrhiza glabra L. (Fabaceae) – Smooth Licorice. Dr. Duke's Phytochemical and Ethnobotanical Databases, Available from: http://www.ars-grin.gov/cgi-bin/duke/plant_act.pl?GET+450+AntiHIV+RT. [Last accessed on 2009 Mar 14].
52. Duke JA. Chemical Constituents with AntiHIV Activity in Vitis vinifera L.

(Vitaceae) – Wine Grape. Dr. Duke's Phytochemical and Ethnobotanical Databases, Available from: http://www.ars-grin.gov/cgi-bin/duke/plant_act.pl?GET+1068+AntiHIV+FR. [Last accessed on 2009 Mar 14].
53. Ibid (4) Cikitsa Sthana 1/3/30.
54. Bhavamishra. Bhavaprakasha, Purva Khanda Guducyadi varga 170. Varanasi: Chaukhambha Sanskrit Bhawan; 2009.
55. Ibid (54), Purva Khanda Ghrita varga.
56. Rhodes T, Simi M, Baro S, Iki B. Police violence and sexual risk among female and transvestite sex workers in Serbia: Qualitative study. BMJ 2008;337:a811.
57. Census of India. Literacy rate in Indian States. Available from: http://www.cyberjournalist.org.in/census/cenlit0.html [Last accessed on 2009 Apr 29].
58. Pavri KM. Challenge of AIDS. 3rd ed. New Delhi: National Book Trust; 1996. p. 23.
59. WHO. Risk Factors. The World Health Report. 2002.
60. Klatt EC. Pathology of AIDS – Version 18. College of Medicine. Florida: Florida State University; 2007. p. 16
61. Ray J. Hepatitis-B outbreak in Gujarat worsens. NDTV. Available from: http://www.ndtv.com/convergence/ndtv/story.aspx?id=NEWEN20090084263. [Last accessed on 2009 Mar 22].
62. Klatt EC. 60. p. 16.
63. Pavri KM. Ibid (58), p. 11.
64. Myer L, Kuhn L, Stein ZA, Wright TC Jr, Denny L. Intravaginal practices, bacterial vaginosis, and women's susceptibility to HIV infection: Epidemiological evidence and biological mechanisms. Lancet Infect Dis 2005;5:786-94.
65. The Body Risk Behaviors and HIV Incidence Among Repeat Testers at Publicly Funded HIV Testing Sites in San Francisco. U.S. Centers for Disease Control and Prevention. Available from: http://www.thebody.com/content/prev/art17702.html. [Last accessed on 2008 Sep 2].
66. Thomas S. 70% gay men give in to social pressure and marry. The Times of India. Available from: http://timesofindia.indiatimes.com/Cities/Mumbai/70-gay-men-give-in-to-social-pressure-and-marry/articleshow/4236783.cms [Last accessed on 2009 Mar 22].
67. Kasper DL. Ibid (1), p. 1077.
68. Kanki PJ. Human Immunodeficiency Virus Type 2 (HIV-2). AIDS Rev 1999;1:101-8.
69. Kasper DL. Ibid (1), p. 1076.
70. Jewell JE, Abate F, McKean E. New Oxford American Dictionary. 2nd ed. Oxford: Oxford University Press; 2005
71. Kasper DL. Ibid (1), p. 1103.

हिंदी सारांश

एच.आइ.वी. पीड़ित रूग्णों में श्रीलंकन पारम्परिक औषधि रणहंस रसायन का अध्ययन

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प्रस्तुत अध्ययन का उद्देश्य एच.आइ.वी. पीड़ित रूग्णों में रणहंस रसायन के प्रभाव का मूल्यांकन करना था। कुल २७ रूग्णों को पंजीकृत करके दो समूहों में बाँटा गया। समूह अ में रणहंस रसायन - ५ ग्रा. दिन में दो बार गोदुग्ध एवं शर्करा के साथ दिया गया। समूह ब में नियमित आधुनिक चिकित्सा दी गयी। चिकित्सा पूर्व और पश्चात सीडिफोरप्लस, टी-सेल काऊंट, टोटल लिम्फोसाइट काऊंट परिक्षण किया गया। रणहंस रसायन एच.आइ.वी.पीड़ित रूग्णों में एक उपयुक्त औषधि हो सकती है।