Clinical Researches
Clinical Evaluation of Shilajatu Rasayana in patients with HIV Infection

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Abstract

AIDS is one of the serious global health concerns caused by Human Immuno Deficiency (HIV) virus and is predominantly a sexually transmitted disease. Currently there is no vaccine or cure for AIDS still Anti Retroviral Therapy (ART) is successful. It reduces both the mortality and the morbidity of HIV infection, but is expensive and inaccessible in many countries. However intense the therapy may be, HIV virus is rarely eliminated, and drug resistance is a major setback during long-term therapy. The development of new drugs and strategies and exploring alternative systems of medicine for antiviral herbs or drugs is the need of the age to improve treatment outcomes. Ayurveda describes many diseases which incorporate HIV like illness e.g. Rajayakshma, Oja Kshaya, Sannipata jwara etc. HIV infection affects multisystems, chiefly the Immune System which can be correlated to Oja Kshaya. Rasayana Chikitsa is the frontline therapy employed to treat Ojus disorders. Therefore Shilajatu (Mineral pitch), Centella asiatica (Mandukaparni), Tinospora cordifolia (Guduchi) and Emblica officinalis (Amalaki), well known for their Immuno-modulator and antioxidant properties were selected to evaluate their role on immune system. The study was carried on 20 patients from OPD and IPD of Kayachikitsa, S.S.Hospital, IMS, BHU and was randomly allocated into Treated group (Shilajatu+ART) and Control group (ART). Treated Group responded better to ART both clinically and biochemically. The results show that Shilajatu decreases the recurrent resistance of HIV virus to ART and improves the outcome of the therapy.

Key words: HIV Virus, AIDS, ART, Rasayana, Shilajatu and CD4 count.

Introduction

AIDS is one of the major global health concerns, highly infectious, and stands first as a sexually transmitted and incurable disease. AIDS is now a pandemic and globally, an estimate of 33 million people are affected with AIDS and AIDS has killed an estimate of 2.1 million people in 2007. Over three-quarters of these deaths occurred in sub-Saharan Africa, retarding economic growth and destroying human capital.

AIDS is caused by Human Immuno Deficiency virus (HIV). HIV is a retrovirus that primarily targets CD4+ helper T (a subset of T cells), cells that are responsible for the Immunity of an individual. Once HIV has killed so many CD4+ T cells and there are fewer than 200 of these cells per microliter (µL) of blood, cellular immunity is lost and the person has said to be suffering from AIDS. This infection progressively reduces the effectiveness of the immune system and leaves individuals easily susceptible to opportunistic infections and tumors. HIV is transmitted through direct contact of a mucous membrane or the bloodstream with a bodily fluid containing HIV, such as blood, semen, vaginal fluid, seminal fluid, and breast milk. This transmission can involve anal, vaginal or oral sex, blood transfusion, contaminated hypodermic needles, exchange between mother and baby during pregnancy, childbirth, breastfeeding or other exposure to one of the above bodily fluids.

As per (UNAIDS definition): ABC of AIDS prevention are:
A- bstinence or delaying first sex.
B- eing safer by being faithful to one partner or by reducing the number of sexual partners.
C- orrect and consistent use of condoms for sexually active young people, couples in which one partner is HIV-positive.

Currently there is no vaccine or cure for AIDS. Anti Retroviral Therapy (ART) is successful. It reduces both
the mortality and the morbidity of HIV infection, but is expensive and inaccessible in many countries.

Clinical picture of AIDS, described in Ayurveda is found scattered in all authentic texts. Immunity has been explained under the concept of Ojus. Clinical features of Ojus, its formation, features of derangement-Visramsa, Vyapat and Kshaya are explained in detail by the authors like Charaka, Sushruta and Vagbhata in their texts. Stages of AIDS resemble Hatoajas a complicated type of fever, Ojanirodhaka Jvara, Shosha, Madhumeha, Asadhya Pandu, Rajayakshma and Udanavraitsa Prana Vata in Ayurveda. Here AIDS and its opportunistic infections have been correlated with Ojo Kshaya. The virus invades the Rasadi sapta dhatus and causes decrement in their quality and quantity. In Ayurveda, Ojus is the essential substance of all dhatus and determines the capacity of the individual to combat the disease (Vyadhibala virodhitvam) and the power to the resist the virulence of disease (Vyadih utpadaka pratibandhakatvam) causing factors in future.

For the process of rejuvenation, Ayurveda has described a unique therapy-Rasayana therapy. Drugs described under Rasayana act on Agni, Dhatu and Srotas level and help in formation of prashasta dhatus maintaining a perfect equilibrium of all the doshas and dhatus. Shilajatu is one of the best of the rasayanas described by Charaka, Sushruta in all diseases where Bala i.e Ojus is involved. Hence Shilajatu along with Mandukaparni, Guduchi and Amalaki, well known rasayana herbs were selected to evaluate their role in boosting the immunity.

Aims and Objectives

1. To study the concept of Ojus in HIV Infection/AIDS in Ayurveda.
2. To study the effect of Shilajatu (Mineral pitch) in HIV positive cases associated with opportunistic infection receiving ART.
3. To study the probable mode of action Shilajatu treated with Centella asiatica, Tinospora cordifolia and Emblica officinalis in the patients of HIV.
4. To study the short term safety profile of Shilajatu Rasayana in the patients of HIV.

Material & Methods

A total of 20 diagnosed cases of HIV infection receiving ART were selected from the OPD and IPD of Kayachikitsa, S.S.Hospital, IMS, BHU, after thorough examination and obtaining informed consent.

Inclusion criteria
- Newly diagnosed cases.
- Patient not having many complications or many secondary infections.
- Patient of 20-50 yr. age group.
- CD4 count not less than 150/ micro liter.
- Patients willing to participate and giving informed consent.

Exclusion criteria
- Patients below 20 yr. and above 40 yr. age group.
- Patients having multiple opportunistic infections and with complications like Diabetes, HTN, Asthma etc.
- Pregnant and lactating women.

Diagnostic criteria
1. History taking like profession, having sex with many partners, blood transfusion etc.
2. Presence of clinical sign and symptoms suggestive of HIV.
3. Biochemical investigations like ELISA for HIV I/II and CD4 count.

Study Design
This was a randomized, controlled clinical trial conducted in Dept.of Kayachikitsa after obtaining permission from the Institutional Ethical Review Committee of IMS, BHU.

The 20 selected and diagnosed cases of HIV infection were randomly allocated into two groups. The selected patients have undergone undergone complete general examination to rule out any gross abnormalities and were evaluated clinically and biochemically to confirm the diagnosis.

Grouping
Control Group (Gr-B) (N=8): Patients were given HAART Therapy from the AIDS clinic of Modern Medicine, S.S.Hospital, IMS, BHU.

Treated Group (Gr-A) (N=12): Patients were given ART along with Shilajatu Rasayana for 3 months.

Form of the trial drug: Capsules of 500mg each.

Route of Administration: Oral

Duration: 3 months.

Selection of drug:
Shilajatu Rasayana was selected as a trial drug in the treatment of HIV positive patient. Shilajatu had been explained a very popular drug for Oja Kshaya in case of Madhumeha by Charaka in Chikitsasthana, chapter 1/364-367, and Sushruta in Chikitsa sthana 13/16.

Dose: Shilajatu Rasayana was used for 3 months in two methods.

1. Kalpa Prayoga: Shilajatu capsules was used for 15 days. Starting with 1gm and increasing 2 gm on every day for 5 days unto 9g. (1 gm, 3 gm, 5 gm, 7 gm, 9 gm); 9 grams was continued for further 5 days.
and finally decreased in the similar fashion, 2 gms. every day for 5 days up to 1 gm.

2. Continued Prayoga: After 15 days of Kalpa therapy, a single dose of 6 gram per day was given up to 3 months of trial period.

Preparation of Shilajatu Rasayana
The trial drug was prepared in the the Dept.of Rasa Shastra, IMS, BHU. Shilajatu was first purified with Comutra for 7 times and then powdered. The powder was triturated with Swarasa of Amlaki, Guduchi and Mandukaparni 7 times each, and packed into 500mg capsules and stored.

Follow-up and Assessment: The initial two follow-up were done at an interval of 15 days in a month. Then other two follow-ups were done in 1 month. Efficacy of trial drug was assessed by (I) Relief in symptoms on a point rating score. (II) Changes in Biochemical investigation. Response was graded as follow:

1. Improved: The patient were getting better change in clinical sign and symptom, changes in biochemical reports (LFT, Renal profile) and gradual increase in value of CD4.
2. Unchanged: There is no improvement in the clinical feature and CD4 count.

Symptoms grading
1. Depression:
   Absent - 0 - Normal behaviour
   Mild - 1 - Recurrently disturbed
   Moderate - 2 - Difficult to do job work
   Severe - 3 - Unable to work any job

2. Weight loss
   Absent - 0 - No change in wt or increase in wt.
   Mild - 1 - Wt. loss <3 kg in 1month
   Moderate - 2 - Wt. loss >8 kg in 1 month
   Severe - 3 - Wt. loss >8 kg in 1 month

3. Diarrhoea
   Absent - 0 - Stool 1-2 time/day with normal Consistency
   Mild - 1 - Stool 3-5 time/day
   Moderate - 2 - Stool 6-8 time/day
   Severe - 3 - Stool >8 time/day or passes of stools or on in take of any diet

4. Fever
   Mild - 98.6°F - < 100°F
   Moderate - >100°F - <102°F
   Severe - >102°F

5. Oral Thrush
   Absent - 0 - No foul smelling
   Mild - 1 - Occasional foul smelling
   Moderate - 2 - Continuous foul smelling
   Severe - 3 - Foul smelling with stomatitis

6. Nausea/Vomiting
   Absent - 0 - No nausea & vomiting
   Mild - 1 - Occasional feeling
   Moderate - 2 - Feeling after intake of meal
   Severe - 3 - Recurrently vomiting habit

7. Loss of Appetite
   Absent - 0 - Normal appetite
   Mild - 1 - Unable to take evening meal
   Moderate - 2 - Unable to take Solid meal
   Severe - 3 - Vomiting just after intake of meal

8. Anaemia (Hb%)
   Absent - 0 - >14mg/dl in male
   Mild - 1 - <14mg/dl - >12mg/dl in male
   Moderate - 2 - <12mg/dl - >10mg/dl in male
   Severe - 3 - <10mg/dl in male

#### Observation & Results

| Table 1: Effect of Shilajatu Rasayana on Various Symptoms: |
|----------------|----------------|
| S. No | Symptoms | Control | Treated | t value | p value |
|       |          | Mean ± S.D | Mean ± S.D |       |        |
|       |          | BT | AT | BT | AT |       |
| 1     | Loss of Appetite | 2.50±0.54 | 1.83±0.75 | 2.00±0.56 | 0.00±0.00 | 11.76 | HS |
| 2     | Nausea/Vomiting  | 2.16±0.00 | 0.16±0.40 | 1.62±0.51 | 0.00±0.00 | 9.70 | HS |
| 3     | Anemia          | 0.66±1.03 | 0.00±0.00 | 0.80±0.90 | 0.06±0.00 | 2.44 | S |
| 4     | Weight Loss     | 2.16±0.25 | 0.33±0.51 | 2.30±0.67 | 0.00±0.00 | 11.6 | HS |
| 5     | Diarrhoea       | 2.30±0.51 | 0.50±0.54 | 2.30±0.67 | 0.50±0.22 | 6.33 | HS |
| 6     | Depression      | 2.50±0.54 | 0.83±0.15 | 2.00±0.94 | 1.00±0.81 | 7.74 | HS |
| 7     | Fever           | 2.30±0.57 | 0.33±0.45 | 2.10±0.73 | 0.40±0.69 | 8.57 | HS |
| 8     | Oral Thrush     | 2.10±0.40 | 1.16±0.75 | 2.10±0.56 | 0.5±0.70 | 6.79 | HS |
| 9     | Pul.Tuberculosis| 0.60±0.80 | 0.00±0.00 | 1.00±0.94 | 0.00±0.00 | 3.67 | HS |
Table 2: Effect of Shilajatu Rasayana on biochemical parameters:

| S. No. | Biochemical Parameter | Control | Treated |
|--------|-----------------------|---------|---------|
|        | Mean ± S.D            | Mean ± S.D | t value | p value |
|        | BT | AT | BT | AT |          |          |
| 1      | CD₄ Count             | 170±40.9| 247±28.3| 164±33.1| 253±31.0| -31.34 | <0.001HS |
| 2      | SGOT ( )              | 40.8±5.26| 45±11.7| 31.0±4.65| 24.3±5.1| 12.10 | <0.001HS |
| 3      | SGPT ( )              | 37.66±2.2| 47.8±11.6| 36.3±4.1| 292±5.61| 8.10 | <0.001HS |
| 4      | Alk.Ph ( )            | 230.3±5.1| 335±76.1| 195±16.9| 131.4±6.9| 11.14 | <0.001HS |
| 5      | Urea ( )              | 29.3±4.0| 50.33±4.4| 29.3±5.3| 22.4±2.0| 5.85 | <0.001HS |

9. Tuberculosis

- Absent - 0 - No feature of tuberculosis
- Mild - 1 - One system involvement
- Moderate - 2 - More than 2 system involvement
- Severe - 3 - Multiple system involve or miliary or MDR tuberculosis.

Discussion

Total 20 patients HIV cases with various symptoms were enrolled in the trial. On randomization, 12 were kept on ART+Shilajatu Rasayana (treated group) while 8 patients received only HAART therapy. Two patients in each group were dropped out as they discontinued the trial drug without the permission of the investigator. Confirmation of HIV was done only by ELISA for HIV 1 and II. The history taking showed that out of 20 registered cases, 18 were males with Vata-Pitta prakriti, aged between 31-40 years, belonging to labour class (drivers and coolies) all married and majority with multiple sex partner history.

Shilajatu (Mineral pitch) is a herbo mineral compound with many beneficial therapeutic properties. It has been extensively used by all the Ayurvedic scholars in all chronic debilitating disorders since decades. It has Kushaya Tikta rasas, Sheeta virya, TridoshAhara, Vrishya, Balya, Mutrala, Lekhana, Yogavahi and Rasayana properties. It has many rich, bioactive molecules (nutrients, iron, manganese, phenols etc) acts a powerful adaptogen in the wear and tear phenomenon of aging process.

Amalaki and Guduchi, share common properties. Amalaki is best among Vayasthpaka herbs. Amalaki is fortified with Vit-C which is a natural, abundantly available powerful antioxidant, anti-inflammatory and free radical scavenger of the metabolism.

Guduchi among all Rasayanas. They possess TridoshAhara, Sheeta Virya, Dahuaprasamana, Chakshushya, Kesha, Vayasthpaka, Hridhya, Rasayana, Vrishya, Pramehaghn, Yakriduttejak properties. Guduchi (Giloy) a bitter active principle has anti-inflammatory and hepato-protective properties. It acts on liver, the chief site of metabolism of food and drugs, normalizing the elevated transaminases and repletes the hepatocyte glutathione sod dismutases responsible for scavenging of free radicals.

Mandukaparni possesses Tikta, Kashaya rasas, Sheeta Virya and Madhura vipaka and best among Madhya rasayanas. Fresh leaf extract has shown nootropic, tranquilizing, memory enhancing, and adaptogenic properties on experimental models. All the above drugs act as immune-boosters and adaptogenic, which act both on the body and the mind to improve physical strength of the individual to fight against opportunistic infections and allergies and correct the mood disturbances in AIDS.

Drug was prepared in Department of Rasa Shastra, IMS, B.H.U. Shilajatu was triturated seven times with the swarasa (fresh juice extracts) of all the three herbs separately for 7 days each dried, powdered and then filled in 500mg capsules. It was administered as mentioned in the material and methods for 3 months. Response was assessed on the basis of improvement in signs and symptoms and CD₄ count. Safety profile of the drug was assessed by its impact on Liver enzymes and Urea, Creatinine which were evaluated before and after trial.

Symptoms and signs were graded as 0-3 depending on the severity. After completion of trial period, observations are shown in Table1.

Treated Group (HAART+Shilajatu Rasayana) showed 100% improvement in loss of appetite, nausea and vomiting and depression, 80% in diarrhoea and weight loss, 60% in fever, anaemia and cough, 50% in the oral thrush and sore throat. The control showed only 70% improvement in anemia, fever, diarrhoea and weight loss, 100% improvement in loss of appetite, nausea and vomiting and depression, 80% in diarrhoea and weight loss, 60% in fever, anaemia and cough, 50% in the oral thrush and sore throat. The control showed only 70% improvement in signs and CD₄ count. Safety profile of the drug was assessed by its impact on Liver enzymes and Urea, Creatinine which were evaluated before and after trial.

Objective improvement was assessed by the increase in CD₄ count. Both groups responded more or less similarly but the control group showed rising values of SGOT, SGPT, Alkaline Phosphatase, Urea and Creatinine. The HAART is associated with hepatic and kidney decompensation which was successfully overcome by giving Shilajatu rasayana. Shilajatu, Amalaki and Guduchi by virtue of its properties enhances the immunity by increasing CD₄ T helper cell counts, prevents the resistance of HIV virus to ART drugs. It also enhances the excretion of Virus load from the body but needs to be substantiated by the data. AIDS has social stigma...
and individuals with AIDS are socially boycotted and subjected to frequent insult, which makes their lives lead burdensome and frustrated. Mandukaparni is a Medhya herb with tranquilizing properties successfully improved the overall outcome of the trial drug.

Shilajatu has many rich, bioactive molecules (nutrients, iron manganese, phenols etc) acts a powerful adaptogen in the wear and tear phenomenon of aging process. Shilajatu Rasayana on triturating with Amalaki, is fortified with Vit-C which is a powerful antioxidant, Guduchi (Giloy) a bitter active principle has anti-inflammatory and hepato-protective properties. It acts on liver, the chief site of metabolism of food and drugs, improving its functions. ART is chiefly associated with alteration in Liver Function Tests, these were reversed and normalized by Guduchi. Mandukaparni fresh leaf extract has memory enhancing and tranquilising properties which treat the depression often associated with HIV patients.

Conclusion

The compound formulation was found to be safe, (on prolonged use for 3 months in the dose of 6 gm) and it has decreased the intensity of the clinical symptoms and signs and also protected the liver from the hepatotoxicity of ART as evident by normal LFT or Kidney function tests.

References

1. http://data.unaids.org/pub/GlobalReport/2008/jc1510_2008_global_report_pp29_62_en.pdf
2. Braunwald et al., Harrison's, Principles of internal medicine, Vol.- I, Mc Graw Hill, 17th Edition, 2008, Part -7, Section 182, pp. 1137-1192.
3. http://www.emedicinehealth.com/hiv aids/page8_em.htm!Prevention
4. Sushruta Samhita, by Ambika Datta Shastri Chowkhamba Sanskrit Series, 14th Edition, 2004: (a) Sutra sthana 15/29-30 pp. 60-61 (b) Chikitsa sthana, 13/4-16 pp. 65.
5. Charaka Samhita, Kashinath Shastri, Y. Upadhyay etal Vol-II, Chowkhamba Sanskrit Series. Reprint 1998: (a) Sutra sthana 17/117 -118, pp. 366. (b) Chikitsa sthana Chapter I/Sec-3 sloka 62-65, pp. 44-49.
6. Charaka Samhita with Chakrapani commentary by Yadavji Trikamji Acharya on C. Su 28/7, pp. 178, edition 2004.
7. Bhava Prakash Nighantu, Indian Materia Medica, Dr. K.C. Chunekar; Edition: Reprint 2002, Chowkamba Sanskrit Series; ( a ) Amalaki, Haritakyadi Varga, page no. 10 - 12. (b) Mandukaparni, Guduchyadi Varga, pp. 269-271. (c) Guduchi, Guduchyadi Varga, page no. 462-463.
8. Spectroscopic characterization of fulvic acids extracted from the rock exudate Shilajit: Rajesh Khanna, etal Organic Geochemistry Volume 39, Issue 12, December 2008, pages 1719-1724.
9. M.Sai Ram, D. Neetu et.al. Cytotoxic and immunomodulating properties of Amla (Emblica officinalis) on lymphocytes: an in-vitro study. Journal of Ethnopharmacology, 2002; 81(1) June: pp. 5-10.
10. Evaluation of relationship between the Centella asiatica (Linn) fresh leaf extract induced spatial learning and memory enhancement and increased body weight gain in neonatal and adult rats, The Internet Journal of Alternative Medicine. 2008 Volume 5 Number 2 ISSN: 1540-2584.
11. P. Stanely and Venugopal P. Menon. Antioxidant activity of Tinospora cordifolia roots in experimental diabetes, Journal of Ethnopharmacology, June 1999; 65 (3): pp. 277-281.