

Cognitive Remediation to an Adolescent to Improve Mild Cognitive Deficits co Morbid to AIDS and to Enhance Medical Compliance for E-Wing Sarcoma- Intervention Based Case Study

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Received: December 11, 2017; **Published:** January 11, 2018

Abstract

Cognitive impairments from mild to moderate level secondary to AIDS has been reported in most of the previous studies. Review of the literature also reported about the decreased immunity levels due to the Human Immuno deficiency virus. This study was taken to treat therapeutically, to an adolescent who got diagnosed with AIDS at an earlier age and presently suffering with E- Wing sarcoma. Due to non compliance of the ART drugs how she might turned to be more vulnerable to the cancer, when compared to people of same age group. The aim was to target the neuro cognitive deficits which in turn would enhance medical compliance and psychosocial functioning. The single case pre and post design was used by conducting baseline assessment to intervene by using cognitive retraining techniques followed by post assessment. Results were positively significant, qualitatively medical compliance was improved and quantitatively cognitive abilities were improved.

Keywords: AIDS; Mild cognitive impairment; Poor medical adherence; E-Wing Sarcoma; Cognitive remediation

Volume 2 Issue 1 January 2018

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Introduction

National AIDS Control Organization (NACO), Ministry of Health and Family Welfare, Government of India periodically undertakes HIV estimations to provide the updated information on the status of HIV epidemic in India.

According to the NACO in 2015 estimate The total number of people living with HIV (PLHIV) in India is estimated at 21.17 lakhs (17.11 lakhs–26.49 lakhs) in 2015 compared with 22.26 lakhs (18.00 lakhs-27.85 lakhs) in 2007. Children (< 15 years) account for 6.54%, while two fifth (40.5%) of total HIV infections are among females. Undivided Andhra Pradesh and Telangana have the highest estimated number of PLHIV (3.95 lakhs) followed by Maharashtra (3.01 lakhs), Karnataka (1.99 lakhs), Gujarat (1.66 lakhs), Bihar (1.51 lakhs) and Uttar Pradesh (1.50 lakhs). These seven States together account for two thirds (64.4%) of total estimated PLHIV (Figure 2). Rajasthan (1.03 lakhs), Tamil Nadu (1.43 lakhs) and West Bengal (1.29 lakhs) are other States.

Citation: Guru Prasanna Lakshmi. "Cognitive Remediation to an Adolescent to Improve Mild Cognitive Deficits co Morbid to AIDS and to Enhance Medical Compliance for E-Wing Sarcoma- Intervention Based Case Study". *Current Opinions in Neurological Science* 2.1 (2018): 344-355.

Combinations of antiretroviral drugs administered as highly active antiretroviral therapy (HAART) have decreased the HIV disease-related mortality and the severity of the illness [1]. Due to the advanced treatments HIV is also managed as a chronic disease, and can prevent the progression towards AIDS and AIDS Dementia. But still the neuro cognitive disturbances/impairments due to the HIV virus is becoming a complex phenomenon to deal clinically considering as priority.

Changes in memory, concentration, attention, and motor skills are common in HIV-infected patients and present a diagnostic challenge to the clinician [2]. In 1986, HAD (HIV associated dementia) was reported in up to two-thirds of AIDS patients [3]. But it is less frequent now in patients receiving HAART.

Clinical Characteristics of HIV- associated Neuro cognitive impairment to HIV - associated Dementia

HIV enters the central nervous system (CNS) during acute infection; however, neurons remain largely uninfected and the primary mechanism of brain injury relates to extensive inflammation leading to neuronal dysfunction and synaptodendritic injury [4].

Understanding the mechanisms that contribute to HAD would help with better identification of the symptoms and clinical management. Although an active area of investigation, the prevailing theories involve infection of the virus in brain macrophages and activated microglia in the CNS [5,6]. Neurons, astrocytes, and oligodendrocytes do not appear to be directly infected by the virus. A cascade of chemokines and cytokines mediated by activated microglia cells leads to cell death through decreased arborization of neurons. Therefore, the immune system involvement may explain the subtlety of the clinical symptoms and global progression of the dementia over a period of time. At the early stages, the chief complaints in HAD are a combination of short-term memory impairment, low mood, and motor slowing. But involve some disruption of the normal daily routines of managing financial obligations, following directions, reading, remembering names and dates, and remembering appointments. Although memory deficits occur, the pattern typically involves inefficient learning and problems with executive functioning and retrieval rather than pure difficulty in formulating a memory itself (encoding deficits) [7].

These symptoms are often indistinguishable from other types of dementia, misinterpreted as lethargy or missed because the signs are below clinical detection. As symptoms become more profound, they involve multiple regions of the brain that control long-term memory, name and facial recognition, language expression and comprehension, and organization and management [8].

Neuro cognitive disorders in people might also be the result of weekend immune system due to the virus which enabling the infections and cancers to attack. In a meta-analysis of HIV-related impairments, asymptomatic HIV-infected individuals were found to have the largest deficits in language and verbal functions, while individuals with symptomatic HIV and AIDS were found to have the greatest deficits in motor and executive functioning. As HIV disease progresses, motor functioning, executive skills, and speed of information processing demonstrate the greatest decline [9].

The onset of HIV-related neurological symptoms occurs when infected monocytes and CD4 cells transport the virus across the blood–brain barrier within hours or days of initial infection. Although HIV rarely infects neurons, mediators shed by other infected cells, such as pro inflammatory cytokines, chemokines, excitotoxins, and proteases, as well as HIV-1 proteins Tat and gp120, induce neuronal apoptosis and lead to documented cerebral atrophy [10].

Poor medical adherence associated to cognitive impairments in HIV

Several more recent studies have focused on specific impairments that may contribute to poor adherence. Two studies tested cognitive function with a memory task that employed a distracter and a prescribed task to measure prospective memory, the type of memory required to execute a future intention. The tests measured both content recall at the prescribed task and the time at which it was accomplished relative to a target execution time [11].

A number of studies have found associations between cognitive factors such as memory impairment and executive dysfunction and medication adherence [12]. Although a comprehensive review of studies characterizing the relationship between cognitive function and adherence [12] has recently been published, several relevant findings will be briefly discussed here. A study of adherence found that both neurocognitive impairment and the complexity of a medication regimen were predictive of lower adherence rates; cognitively impaired participants prescribed more complex regimens demonstrated the lowest rates of adherence. The cognitive impairments most closely associated with poor adherence were deficits in executive function, memory, and attention [13].

When other biological and psychosocial factors were accounted for, non-adherent individuals were found to have significantly poorer prospective memory by contrast to adherent individuals. Moreover, the index of difference was time scale-although the non-adherent individuals remembered to perform the prescribed task, they did so at the wrong time. The authors cite findings from an HIV-associated prospective memory impairment trial, and suggest that non-adherent individuals have cognitive deficits that hinder their ability to adequately monitor time, thereby missing cues to take scheduled medication doses [14,15]

Risk of Cancers among HIV infected individuals

The factors leading to an increased cancer risk among HIV-infected individuals remain poorly understood. Whereas evidence is emerging that a direct pro-oncogenic effects of HIV, activated inflammatory and coagulation pathways, and cART (combination of ARV therapy) toxicity may also contribute [16-19]. Some studies have reported an association between ongoing viral replication and cancer risk [20].

The potential mechanisms are multiple and complex, involving synergism with other pro-oncogenic viruses [21], disruption of cell cycle regulation [22], blockage of tumour suppressor gene function [23], promotion of chromosome instability through the inhibition of telomerase activity [24], impairment of DNA repair function [25], induction of tumour angiogenesis [21,26] and enhancement of the effects of exogenous carcinogens [27,28]. Strategies for Management of Antiretroviral Therapy (SMART) Study [29], structured cART interruptions were reciprocally associated with higher levels of coagulation and inflammatory biomarkers [30] and increased risk of cancer [31].

HIV risk reduced Psychological interventions

Behavioral interventions

Successful behavioral risk-reduction interventions must tailor learning to those likely to be at least minimally cognitively impaired, either by incorporating strategies to remediate impairment or by incorporating motivation and reinforcing behavioral skills through a focus on applications and improved outcomes [11].

Cognitive Remediation: Several therapeutic approaches have been identified as effective at remediating the effects of cognitive impairment on risk behaviors and adherence through compensatory techniques and cognitive enhancement. The extent of cognitive recovery was found to increase through cognitive remediation focusing on memory training and the development of problem-solving strategies. Memory training focuses on improving attention and strategies such as visual imagery and peg-words, while problem-solving sessions focus on strategies such as goal identification, brainstorming, and approach flexibility based on success rate [32].

Method

Participant's information

Child named "S", female, aged about 13 years, Hindu, studying 5th grade, hails from rural domicile, lower socio economic strata. Child was symptomatic from the childhood, with delayed developmental milestones. During the postnatal period she was diagnosed with Z+ve. Always she used to suffer with some or other health issues, and always used to be under antibiotics. At the age of 1 year, mother got expired with the diagnosis of AIDS. Father and grandmother took care of the child. With the suggestion of a local doctor child was

under medication from then, she continued with irregular compliance. She was admitted into the school at the age of 6 years, but was not able to cope up according to the other peer group, so 1st and IInd classes she had to repeat each for twice. But from IIIrd class onwards she used to get promote (by the request of father), and after reaching to Vth grade she couldn't make it, and discontinued her studies and started staying in home. Her father expired with Z+ve 8 months prior to the present date.

Hence she is been left with grandmother where she used to be happy in the village. (Medication was stopped due to lack of awareness about the availability in village) Her uncle wants her to study well so he got her in to his home to the town place. But the issues with his spouse made him to join in hostel showing the reason of having small children in home. Since then she stayed in a hostel and continued her studies, with frequent complaints of diarrhea, vomiting, fever but no one took her home back. Child became bedridden due to not able to walk, weakness, decreased sleep, crying with pain in the leg, so the hostel authority felt risk and detained from the hostel and informed her uncle to take home. As her condition was not well consulted local hospital, and was referred to NIIMS. After diagnostic reports they came to know that the child is suffering with E- wings Sarcoma. She was not supporting to the treatment, not taking medicines (ART), with difficulty 2 cycles of chemotherapy was completed, with the consultation of Oncologist, referred to the psychological intervention.

Diagnostic reports: Photograph of a gross specimen demonstrates that the sulci are prominent for the patient's age, consistent with a marked reduction in brain volume.

PET/CT image of a 13-year-old female patient diagnosed with Ewing's sarcoma. One observes a permeative, destructive lesion compromising the epiphysis, metaphysis and proximal diaphysis of the right tibia, with extraosseous extension, revealing sharp glycolytic activity.

Negative History of head injury, Neonatal jaundice, seizures. On Clinical Observation, child appeared well kempt and tidy, dressed appropriately, Rapport could not be established and eye to eye contact was not maintained, Psycho motor activity was decreased, Speech was coherent and goal directed. Attention was aroused but couldn't sustain for a considerable period of time. Hence the MSE, was scheduled for the next day.

On MSE, child appeared well kempt and tidy, dressed appropriately, Rapport could be established and eye to eye contact was maintained, Psycho motor activity was within normal limits, Speech was coherent and goal directed. Attention was aroused and could not sustained for a considerable period of time. Cognitive functions were observed to be at below average level.

Provisional diagnosis was considered

- Mild cognitive impairment co morbid to AIDS.
- E-wing sarcoma

Child was referred for the intervention to target the problem behaviors and make her adherence to the treatment. Attempted using techniques from Cognitive Remediation, Behavioral modification.

Measures

1. Distress Thermometer and screening tool: Distress screening is a comprehensive process that achieves the quality care standard of whole-patient care, which is the integration of both psychosocial and biomedical cancer care. The NCCN recommends using the validated Distress Thermometer (NCCN-DT), a visual analogue scale that allows patients to rate their perceived level of distress in the last 7 days on a scale of 0 ("no distress") to 10 ("extreme distress"). Patients clarify the source of distress using a 39-item problem list with 5 categories: practical, family, emotional, spiritual/religious, and physical. A score of 4 or greater has been established as the cutoff point for providers to further assess identified patients and their need for treatment.

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Distress thermometer – NCCN (National Comprehensive Cancer Network) clinical guidelines - 2016 Table - 01

Levels	Scores
Mild	1 - 4
Moderate	5 - 7
Severe	8 - 10

2. Folstein Mini–Mental State Examination: It is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. It is commonly used in medicine and allied health to screen for dementia. It is also used to estimate the severity and progression of cognitive impairment and to follow the course of cognitive changes in an individual over time; thus making it an effective way to document an individual’s response to treatment. Administration of the test takes between 5 and 10 minutes and examines functions including registration, attention and calculation, recall, language, ability to follow simple commands and orientation. The most widely accepted and frequently used cutoff score for the MMSE is 23, with scores of 23 or lower indicating the presence of cognitive impairment. Because the MMSE was developed as a screening tool for cognitive impairment, a low score (≤ 23) indicates both the likelihood of cognitive impairment and the need for further evaluation. The authors recommend that the following cutoff levels be used for classification purposes: normal cognitive function = 27-30, mild cognitive impairment = 21 - 26, moderate cognitive impairment = 11-20, and severe cognitive impairment = 0-10.

Validity and Reliability

1. The Distress Thermometer was developed to measure distress as defined by the NCCN (2000). In subsequent sections, the NCCN definition of distress will be used. In contrast, the terms “emotional illness”, “psychiatric diagnosis” or “mental illness” are used to refer to conditions that meet DSM-IV (American Psychiatric Association; APA, 1994) diagnostic criteria. 2. The MMSE is one of the most extensively used and studied clinical assessment instruments in the world. Its popularity is due, in large part, to its excellent reliability and validity. In their comprehensive review of the MMSE, Tombaugh and McIntyre (1992) found reported test-retest reliability results for the MMSE ranging from about .80 to .95. In addition, most studies (using the cutoff score of 23) have found the MMSE to have a sensitivity of at least 87% and a positive predictive value of at least 79%., As reviewed by Tombaugh and McIntyre, most studies also reported moderate-to-high levels of specificity and relatively high negative predictive values.

Design

A single case experimental design with pre-and post- assessment was used, to evaluate the effectiveness of the intervention outcome qualitatively and quantitatively in the patient.

Procedure

The pre-assessment was carried out, following the presenting symptoms, history and clinical observation. Based on the assessment profile and the necessity of intervention to enhance medical compliance (Chemotherapy and ART) in order to prevent the progression of tumor and also the cognitive impairment. The program consisted of daily sessions during beginning i.e for 2 weeks and continued for thrice in a week on followed sessions for a period of 2 months, each session lasting on an average for 45 minutes. Total number of sessions were conducted in the hospital setting on an in-patient basis. During this period, the patient and the care givers were also psycho educated and counseled. The completion of the program was followed by a post-assessment (i.e post- intervention).

Results

Pre assessment

1. On F- MMSE child's score was found to be 21 significant with mild cognitive impairment.
2. On administering Distress thermometer scored (9) extreme distress and screening tool, scores (19) were significant with problems mentioned in the areas of emotional, physical, financial aspects.

According to the caregiver explanation and the clinical observation it can be mentioned that the child was easily distractible, stubborn in taking medicines and food.

Post assessment

On F-MMSE child's score was found to be 26 showed improvement in cognitive abilities. On administering Distress thermometer scored (3) mild distress and screening tool, scores (8) were showed improvement in coping with stressful situations but still mild concern about physical and financial aspects due to her condition.

Summary of Distress thermometer

Session	Scores of Each Session
1 st and 2 nd	9 - severe
3 rd and 4 th	7.5-moderate to severe
5 th and 6 th	7- moderate
7 th and 8 th	6 - moderate
9 th and 10 th	6.5- moderate
11 th and 12 th	5 - moderate
13 th and 14 th	5 - moderate
15 th and 16 th	4 - mild
17 th and 18 th	3- mild

Therapeutic techniques

Psycho –education: Care giver was made to understand the cause for the symptoms Prevalence rate about the condition, child's ability to recover, the suffering and problems can be reduced with treatment, importance of therapy and medicines compliance.

Cognitive Remediation: CRT is also called (CET) Cognitive Enhancement therapy, is designed to improve neuro cognitive abilities such as attention, working memory, Cognitive flexibility, planning, executive functioning, which leads to improve the psychosocial functioning.

Attention enhancement

- Beads and thread
- Sorting of beads
- Disc board
- Segregating tokens

Memory retraining

- Mnemonic strategy training –

- a. Visual imagery
 - b. Verbal organization strategies –Verbal stories, making paired associations
 - c. Semantic elaboration (linking target words or ideas in a story)
- Expanded rehearsal time- spaced retrieval methods – in this individual practices successfully recalling information over longer interval of time.

Behavior Modification: It draws primarily on operant conditioning as the basis for developing interventions in order to modify her behavioral problems.

Content of the therapeutic sessions

Week - 1 and 2

During the beginning of the week time was taken to build a rapport by encouraging her to involve in Art and Painting without the time limit. Psycho-education was given to care giver along with the child, discussed about the diagnosis and treatment. Care giver was discussed about Psychological assessments results, also attributed the symptoms towards the illness. They were informed about the necessity of the treatment i.e chemotherapy its pros and cons. Also discussed about the importance of medical compliance. Treatment with Anti Retroviral drugs, how this drugs could prevent further progression of the disease. After the session took the feed back of their understanding.

Behavioral modification

After recording the baseline measures and analyzing the antecedents and consequences of behavior, the behavior management has planned. All therapeutic procedures involve either changing antecedents or changing consequences.

Session - 3

Child was expressing her emotions through the drawings, in one of the drawing she clearly mentioned that she need nurturance and love.

Session - 4

Cognitive remediation

Attention enhancement - Child was asked to segregate the Beads of one color from 50 beads, she did with some errors. After this placed a disc board and was asked to place the discs on right side rod of the stand with right hand repeat same with the left hand. Now instructed to do in opposite. The time limit to complete the task was gradually decreasing from 20 minutes to 14 minutes.

Session - 5

Memory retraining

Visual imagery - Exposed a set of 5 objects and asked to recall after 1 minute not restricted to sequence. Child actively participated but could name only 4 object names in a random way.

Behavior therapy

Play therapy was started to reduce Externalizing behaviors and increase child's social skills and cooperation, to understand her feelings. Hand puppets (family) was showed by the therapist narrated about her family. She took the puppets and was interested in mother puppet. But didn't say anything. Child was encouraged to take ART medicines regularly, had a commitment between therapist and the child - that if she is going to take it, then she will be allowed to go outside to sit for some time.

Session - 6

Cognitive remediation

Child was asked to segregate the Beads of 1 color from 75 beads, she did actively but with some errors. Disc board was placed to repeat as previous session but in a constricted time limit of 12 minutes.

Session - 7

Memory retraining

Visual imagery - Exposed a set of 6 objects and asked to recall after 1^{1/2}- 2 minute. Child actively participated, she could recall 5 object names in 1minute 40 seconds.

Behavior therapy

In Play therapy, puppets were given to explore and she started saying about her family, father and grandmother, touching the mother puppet said that she didn't see her mother and she kept aside. Care giver asked to make a call to her grandmother immediately, and child had a talk. Informant said that his mother wants to come but she is 70 years old person thus she cannot come. Acknowledged his concerns but at the same time informed him to take care of her, and explained the issues related to stigma. Reassurance was given.

Session - 8

Cognitive remediation

Child was eager to participate, waiting for the activities to start with -Beads were given to segregate – 1 color from 100 beads, she was excited to do, instructed her to do without errors. She completed it in 15 minutes with 2 errors. Tokens were given of different colors with numbers mentioned on them, asked her to place them sequentially.

Session - 9

Behavior therapy

Child was asked to tell some story using puppets and she hesitated to do it in beginning, but on reinforcement she could start slowly and she continued for 3- 5 minutes, introducing toys as her father, grandmother and herself in the story, how she used to get ready to school and grandmother feeds her, father used to drop her in the school and gives 5 rupees daily for chocolates. "Now uncle is giving me (she smiled)". Acknowledged her emotions, and asked her to talk to her grandmother.

Session - 10

Cognitive remediation

Child was asked to do segregate the Beads 2 colors from 50 beads. She completed it in 20 minutes with 2 errors. This shows that the child developed tolerance and is not skipping the task, and equally listening to the instructions.

Session - 11

Memory retraining: Using verbal

Organization strategies, Story making was asked to do with using a set of cards, she was very attentive and following cues to complete the task at the same time. She completed 2 stories saying by arranging sequentially.

A sets of cards were given to associate with its pair, given the box with 30 cards i.e 15 sets and gave 15 minutes of time period to complete the task. During the activity she was involved attentive and was following the instructions and after appreciation she felt very happy and was confident.

Session - 12

Child was given support during chemotherapy cycle and also explained her the importance of cooperating to the treatment will decrease the pain. She was also explained about the consequences of not taking medicines.

Session - 13

Cognitive remediation

Child was asked to segregate the Beads 2 colors from 50 beads. She did it in 15 minutes without any errors. Book was given for the shading task in which asked to shade in a given shape with appearance of equal shading. As it was new for her completed with active participation.

Behavior therapy

Child was given a puppets without the father and mother puppets. Other members of the family and she was asked to narrate the story, child showed affection on the small girls, and even on uncle puppet so during she said that “ he is very good person, staying with me as grandmother can’t come”

Session - 14

Memory retraining

Visual imagery - Exposed a set of 8 objects and asked to recall after 2 minute. Child actively participated, she could recall 7 object names in 1minute 57 seconds.

Cognitive remediation

A set of 75 beads in 3 different colors was given to make a chain using a thread following a color pattern. Child completed it in a period of 25 minutes. She took time by correcting her errors.

Session - 15

Child was well cooperated during chemotherapy cycle and also asked to have the previous session task, in which she wants to complete making chain with 3 different color beads it in 20 minutes.

Cognitive remediation

A set of 75 beads in 3 different colors was repeated as previous given to make a chain using a thread following a color pattern. Child completed it in a period of 25 minutes. She took time by correcting her errors.

Session - 16 & 17

Memory retraining

visual imagery - Exposed a set of 10 objects and asked to recall after 2 minute. Child actively participated, she could recall 8 object names in 2 minutes. A sets of cards were given to associate with its pair, given the box with 30 cards i.e 15 sets and gave 12 minutes of time period to complete the task.

Session - 18

Concluding the therapy: Therapy was discontinued as the child was getting discharge from the hospital and would be reporting for the next chemotherapy cycle, after 20 days. Care giver was encouraged to take care of her, asked him to meet social worker to get information related to the availability of ART medicines in their area. He was explained to make her continue the techniques learnt using available home goods. Instructed child to engage in play time and spend time with her grandmother. Post assessment was done

Conclusion

AIDS - It's a condition cannot be treated permanently, but drugs like HAART can be used to prevent progression of the disease in turn can extend the life span. Along with the other co-morbid infections, Cancer is a growing burden in HIV infected individuals. HIV associated neuro-cognitive impairments has a greater impact in psychosocial functioning. Over all, early detection of cognitive impairments and intervention plan has to be made. The complex condition of double diagnosis, with the poor concept of management skills cannot be treated in unimodal way, instead multimodal or multidisciplinary approach would be beneficial for well being of the client. Prior studies suggest that interventions incorporating cognitive remediation strategies, diverse presentation of information, and a focus on practical applications (e.g. motivation and role play) are the most successful at reducing risk among cognitively impaired populations [11].

As suggested by one of the study [33], the efficacy of integrated interventions designed to manage both medication adherence and HIV risk behavior should be investigated, and future studies should focus on the feasibility of incorporating cognitive-behavioral and cognitive remediation strategies into existing treatment programs. Addressing the cognitive impairment could enhance HIV prevention and coping with other chronic diseases.

Recommendations

In developing countries like India, everything has to begin with huge efforts to come into practice. Cognitive remediation or the retraining approach has to be a part of collaborative process. Treating cognitive deficits as a part of chronic illness management has to be prioritized. Understanding the factors that contribute to non compliance to the treatment would help with better identification of symptoms and clinical management.

Acknowledgement

I am great full to the department of Oncology for providing access to study participants.

Conflict of interest

The author have no conflict of interest to declare for this study.

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