Effect of Chemotherapy Treatment on Cognitive Function

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Abstract— Cognitive dysfunction is a gradually more recognized complication of cancer and its treatment. Most research in this arena has found that chemotherapy stimulated cognitive dysfunction was mostly experienced by the cancer patients. The primary objective of this study is to find out the effect of chemotherapy treatment on cognitive function of cancer patients. NIMHANS neuropsychological test were used to find out the cognitive functions such as attention and memory. Cognitive dysfunction was assessed at three time point's first course baseline, short term chemotherapy (6cycles) and long- term chemotherapy (one year) by using neuropsychological battery. Results shows there is changes in cognitive dysfunction during short term chemotherapy and long term post chemotherapy.

Keywords— Cancer; Chemotherapy; Cognitive function

1. Introduction

Chemotherapy related cognitive impairment known as chemo brain, involves a decrease in the cognitive chemotherapy (Biglia, Bounous, Malabaila, Palmisano, Torta and Sismondi and Torta,2012). A diverse range of cognitive domains has various forms of memory, attention and concentration, speed motor function, language, executive function and visuospatial skill (Iconomous et al., 2004: Jansen, Dodd,Miastowsla, Dowling and Cramer, 2008; Prokshna et al 2011). Although not all patients treated with chemotherapy will experience cognitive dysfunction. Such cases have generally reported a reduced capability to engage in daily tasks, with consequential reduction in quality of life. (Boykoff, Moiehi and Subramanian 2009; Hede 2008: Myers 2009).

Chemotherapy, after surgery, is becoming wide range and age is no longer a limiting factor. Moreover, treatments of advanced disease, like chemotherapy, toxicity of antituimoral agents is also major issue (Andreis, F., Ferri, M., Mazzocchi, M., Meriggi, M., Rizzi, A et al, 2012). Among these side effects difficulty with memory, attention and concentration defined as "chemo brain" (Avidan, M. S. & Evers, A. S, 2011), in reference to chemotherapy induced cognitive impairment. This cognitive impairment has been shown to be moderate and most often transient, but they can sometimes persist for several years after the end of therapy (Biglia, Bounous, Malabaila, Palmisano, Sismondi & Torta,2012). Nevertheless, cytotoxic drugs are not only factors involved in the occurrence of cognitive dysfunction. However, hormone therapies would be associated with increase risks of cognitive changes. Furthermore, psychological distress associated to the statement of diagnosis, fatigue and genetic factors could be involved. The changes in cognitive dysfunction during chemotherapy which affects the patient's ability to perform daily activities require maintaining functional independence or not. Cognitive functioning like slow down in processing speed(Bowel Cancer Australia 2010) a reduced efficiency of inhibitory control and decrease in performance related to working memory (responsible for temporary maintained and manipulation of information when carrying out complex cognitive tasks)(Hede, K. 2008) and episodic memory (capacity to remember personality experienced events and situation)(Hermelink, K., Untch, M., Lux, M. P.,Kreienberg, R., Beck, T., Bauerfeind, I. &Munzel, K. 2007).

1.1 Impact of Cancer Treatments on Cognition

Chemotherapy is expected to induce a long term risk of a few cognitive domains. In that respect, chemo brain refers to impairments of working memory, executive functions, attention and information processing speed (Mike F el al, 2010; Hutchinson, A. D, 2012 & Johnson I N, 2011). In practice, patients experience difficulties regarding memory information while processing. The capacity to adapt their behaviour to new situation is impairment that could be assessed by cognitive test batteries.

1.2 Need of the Study

Cancer is considering as one of the dreadful and painful diseases. Though there are various spectrums of inception studies, mainly in the field of psychology. The main of the study about cognitive dysfunction is to identify the major problems and causes faced by the cancer patients both mentally and physically, which cannot be unbalanced by the patients, though chemotherapy help the patients to minimize the growth of the disease. It creates mental distress among the patients, out of various psychological problems. The research is to understand short and long-term effects of chemotherapy on the cognitive functions and cognitive assessment of the cancer patients it is an important issue to detect patients at risk. Diseases related factors that may contribute to cognitive dysfunction. It is necessary to increase effort to be channelled not only

toward the identification of cognitive decline in association with cancer treatment. There is a need for prospective research to better understand the major impact of chemotherapy on cognitive function among cancer patients so that effective, preventive and treatment strategies can be developed.

2. Materials & Method

This study is to know the changes in cognition dysfunction during chemotherapy between short-term chemotherapy and post-term chemotherapy. Hence descriptive method of research used in present study.

2.1 Sample Size

Individuals who are affected by the cancer disease were selected based on their diagnosis of (2 and 3) independent samples has been taken for cognitive assessment. Based on their clinical process, which includes hospitalization had standard chemotherapy in Chennai. All individual provided consent form and collected relevant demographic information.

2.2 Inclusion Criteria

Individuals who lie between 30 to 50 years were taken as sample. Both male and female who has been diagnosed has cancer patient (2^{nd} and 3^{rd} stages of cancer)

2.3 Exclusion Criteria

Individuals age below 30, and stages of cancer 1st and 4^{th}, and divorcees, widower, are come under exclusion criteria. According to geographical extend selection of sampling refer researcher where limited only in Chennai.

2.4 Tools Used

NIMHANS Neuropsychological battery-2004 was used. Neuropsychological assessment is a clinical examination of both the working brain and dysfunction brain. The objective of neuropsychological assessment is to chart the deficits and adequacies in the behaviour of patients. The behavioural deficits are explained by underlying cognitive, emotional and volitional deficits as well as changes in the personality of the patient. Attention is an essential element of cognition. There are three different types of attention; these are focused attention, sustained attention and divided attention. (Posner, 1978). The first attention, focused attention refers to the capacity to perform a task in the presence of distracting stimuli. The capacity to listen to conversation at a train station, to identify the friend in the crowd, is some examples of focused attention. The second, sustained attention refers to the capacity to attend to a task in hand for a required period of time. It is closely associates with task difficulty or task complexity. The capacity to study or capacities to listen to a lecture for an extended period of time are the examples of sustained attention. The third parameter of attention is the capacity to attend to two or more task simultaneously. Focused attention colour trial test (D'Elia, satz, Uchiyama & White, 1996) was developed WHO. The test is an analogue of the trial making test and considered to be free from the influence of language. It has two parts. Part 1 requires sustained attention, perceptual tracking and simple sequencing, while part 2 requires mental flexibility. The test is considered as a measure of focussed attention because the subject has to ignore irrelevant numbers while scanning for the numbers which is next in sequence. In each part a practice form precedes the test. The test could not give to illiterate subjects, as they could not recognize numbers.

2.5 Procedure

Colour trial 1: consists of practice sheet and a test sheet. The numbers are printed in black red colour for odd numbers and yellow for even numbers in circle. Beneath the box is a row of numbers arranged in serial order. Arrows connect these numbers in an ascending order, which example the principle that the numbers inside the box should be pointed to in an ascending serial order the main part of colour trial1, numbers 1-25 are randomly spread, with odd numbers in circles and even numbers in yellow ones. The subject is asked to pint to successive number ascending order from 1 to 25.

Colour trial 2: there is practice sheet and a test sheet. The practice sheet, all numbers 2-8 or presented twice, once on the pink circle and once on the yellow circle. The number presented only once, in pink circle. These numbers are randomly arranged in a box. Beneath box are two rows of numbers in serial order. The first row consists of number printed on circles and the second row of numbers printed on yellow circles. Arrows point to alternate and yellow circles progressing in an ascending order, which exemplifies the principle the numbers inside the box should be pointed to in an ascending serial order, with colours alternate between successive numbers. In the main test of colour trials 2, numbers from 2 through 25 are printed twice, once on pink circles and once on yellow circles. These are randomly arranged on the test sheet. The subject is asked to point to numbers in alternating colours with the successive numbers being in an ascending order. The main parts of the test for colur trial 1&2 are given only after the subject has understood the principle involved and has performed the practice sheet satisfactorily.

2.6 Learning and Memory

Learning and memory are the capacity by that a person is able to gain experiences and retain learning is means of acquisition of new information about the environment and

memory the process of retaining it. Learning and memory are interdependent processes. Memory processes are divided into short-term and long-term memory. Long-term memory is a system of theoretical unlimited capacity enduring over the life the life time often an individual. (Baddeley, 1990). One of the important aspects of memory is declarative are explicit memory, that is memory can be brought to conscious awareness. Memory for events, figures, words, scenes and fax are in the domain of explicit memory. Encoding and retrieval of personally experienced events is termed as episodic memory (Tulving, 1999). A gradual acquisition process from episodic to semantic memory is likely as semantic memory would at some stage have been encoded as episodic memory (Faetcher, Frith, Grasby, Frackowiak& Dolan, 1995). Learning memory for visual and verbal material are two important domains of explicit memory.

*Rey's Auditory verbal learning test:*Rey's Auditory verbal learning test(AVLT) (Schmidt, 1996) adapted for different cultures by WHO (Maj et al. 1994) was adapted to suit condition in India. Rey originally developed the test in 1964. It consists of words designating familiar object like vechicles, tools, anmals and body parts. There are two list A and B, with 15 different words in each list. The words were translated into the four Indian languages of Kannada, Tamil, Telugu, words in the Indian languages are given in English Script.

Words in list are presented at the rate of one word per second during 5 successive trials. The words are presented in the same order in every trial. Each trial consists of the presentation of all 15 words, immediately follow by recall of the same. In each trial after the presentation the subjects is asked to recall the words but no clues are given. The examiner note down the responsive verbatim in the order in which the subject gives them. On a average, recall in each trial takes about two minutes. After the completion of all the 5 trials of list A, words in list B are presented once and an immediately recall is taken for the same. The presentation of list B serves as an interference and prevents the subject from the recalling the words from list A subsequently from immediate memory. This is followed by the immediate recall of words from list A. After delay of 20 minutes, words from list A are recall to form the delay recall score. List A is not read out again for immediate and delay recall. Following delayed recall, recognition of the words in list A is tested. The words in list A are randomly mixed with 15 news words. The new words are either phonemically are semantically similar to words in list A the words are called out one at a time and the subject indicates whether each word belongs to list A or not. Hits and errors are recorded.

3. Result and Discussions

Twenty five patients were enrolled in this study. Table 1 it shows that the distribution of sample on the basis of respondent gender out of 25, 16 (64%) were males and 9(36%) are females. So majority of the respondent are males. In the level of education out of 25, 14(56%) were educated in school level and 11(44%) are educated up to college level.

Table 1: Demographic Details

Personal Details			
Demographic Variables	**Sub variables**	**N**	**Percentage**
Gender	Male	16	64.00
	Female	9	36.00
Age	30-40	13	56.00
	41-50	12	48.00
Education	School level	14	56.00
	College level	11	44.00

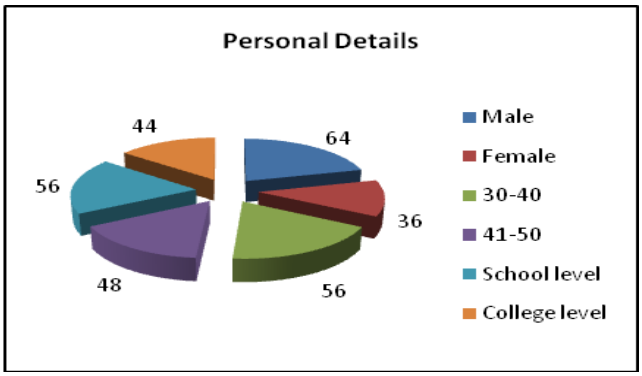

Fig.1: Diagrammatic Representation of the Demographic Details

Table 2: Distribution of the respondents on the basis of personal details

Clinical Characteristic			
Demographic Variables	**Sub variables**	**N**	**%**
TNM	I - Stage	10	40.00
	II- Stage	10	40.00
	III – Stage	5	20.00
Surgery	Extend of surgery	7	28.00
	Biopsy	7	28.00
	Chemotherapy	11	44.00

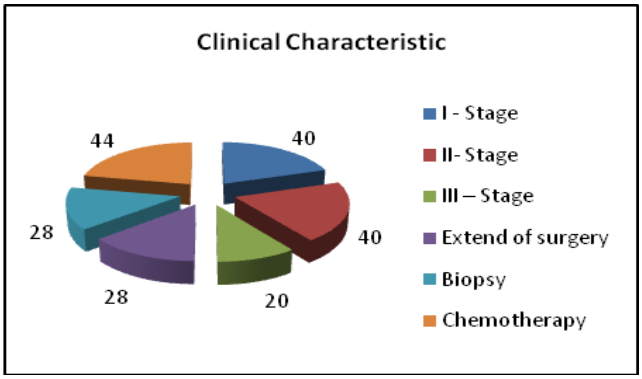

Fig.2: Diagrammatic Representation of the Clinical Characteristics

Table 2 it shows the clinical characteristic, the distribution of samples on the basis of TNM classification 10(40%) were diagnosed as 1st stage, 10 (40%) were diagnosed as 2nd stage and 5(20%) are grouped as 3rd stage of cancer. In the level of surgery 7(28%) pertain under extend of surgery, 7(28%) were grouped under biopsy and 11(44%) underwent chemotherapy.

Table 3: Overall groups

	Groups	N	Mean	SD	t-value	P- value
SH CCT	AVL	25	37.72	7.29	3.87	0.001 (S)
	Colour trail A	25	30.60	5.59		
SH AVLT	AVL	25	7.72	.94	31.36	0.001 (S)
	Colour trail a	25	56.40	7.70		
LT CCT	AVL	25	28.60	7.09	9.20	0.001 (S)
	Colour traila	25	48.08	7.86		
LT AVLT	AVL	25	6.56	1.23	12.81	0.001 (S)
	Colour traila	25	167.12	62.65		

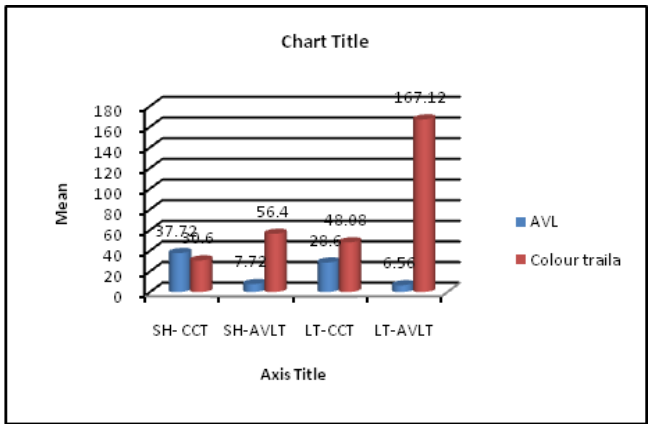

Fig.3: Diagrammatic Representation of the Overall groups

Table 4: Mean, SD and t-value of Colour Trial Test (A AND B)

Attention Test	N	Mean	SD	t- value	P-value
B-A	25	21.76	4.67	12.10	0.001 (S)
B-B	25	36.00	5.00		
SH-A	25	30.60	5.59	19.07	0.001 (S)
SH-B	25	56.40	7.70		
LT-A	25	48.08	7.86	9.06	0.001 (S)
LT-B	25	167.12	62.65		

Table 4 shows the mean, SD, and t-value computed for attention test (colour trail A and colour trial B) for three groups Baseline, Short-term post chemotherapy and Long-term post chemotherapy. The table given above exhibits the t-test between short-term post chemotherapy value is (19.07) and long-term post chemotherapy value is (9.06).The results indicate there are significant changes in short-term and long-term post chemotherapy at level of 0.001.

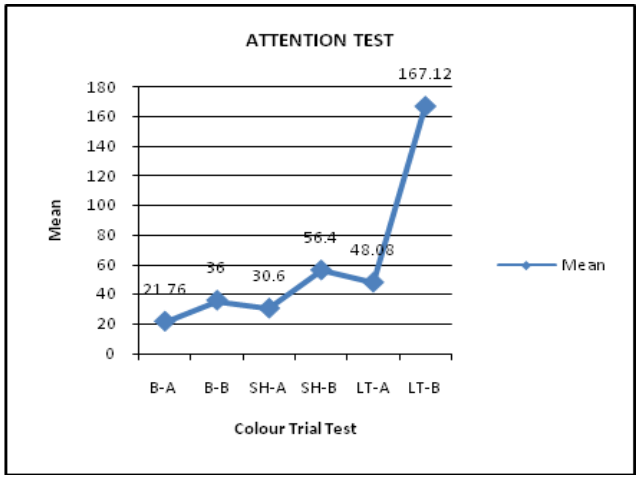

Fig.4: Attention Test Result

Table 5: Mean, SD and t-value of AVLT

AVL Test	N	Mean	SD	t- value	P-value
B-DR	25	9.80	1.44	5.70	0.001 (S)
SH-DR	25	7.72	.94		
B-DR	25	9.80	1.44	8.43	0.001 (S)
LT-DR	25	6.56	1.23		
SH-DR	25	7.72	.94	5.07	0.001 (S)
LT-DR	25	6.56	1.23		
SH-IR	25	7.96	1.06	7.18	0.001 (S)
LT-IR	25	6.68	1.14		

Note: AVLT: Auditory Verbal Learning Test, IR-Immediate Recall, DR- Delay recall

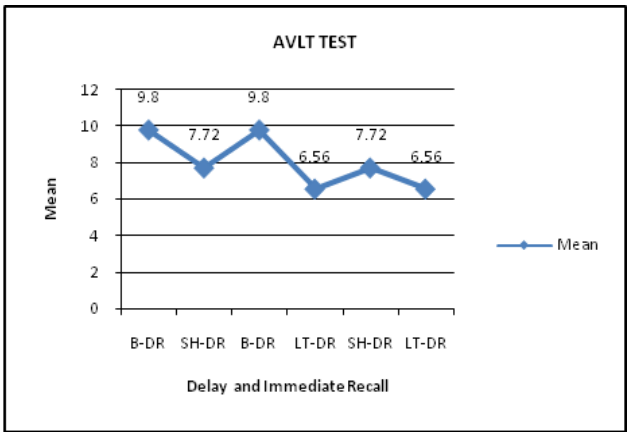

Fig.5: AVLT Test Result

Table 5 shows the mean, SD and t-value measures the Auditory verbal learning test between Immediate recall and Delay recall for Base line and long-term post chemotherapy. The above table illustrate the t-test value is

(7.18) for immediate recall between Baseline and long-term post chemotherapy and the t-test value is (5.07) for Delay recall between Base line and long-term post chemotherapy. The results reveal there is a significant change in immediate recall and Delay recall.

4. Conclusion

In this study, researcher investigates personal and clinical treatment factors like chemotherapy which is associated with cognitive function. It is identified that two domains of cognitive dysfunction (Attention and Learning and memory) there is changes during short-term and long-term post chemotherapy. Patient reports has been utilized to assess patients cognitive dysfunction due chemotherapy. It is recommended for the future studies that requires a strict study line for study assessment (cognitive study) **so**, this will reduce the communication barriers and rate of missed visits. This study was also not design to comprehensive assessment, for neuro cognitive dysfunction but focussed on two domains it is possible that, many other domains of cognitive function could be impact by chemotherapy, that were not evaluated in this study. Many patients were also taking anti-depressant medications in the period of study; however these were not new prescription and were also been taken at the baseline assessment. Nevertheless these limitations, that the study provides preliminary data demonstrating cognitive dysfunction, during chemotherapy among cancer patients, there is impairment on two cognitive domains, which influence their quality of life and ability to perform routine activities e.g taking medications, returning to work.

Cognitive behaviour therapy is implemented among the cancer patients, it will self motivate them to decrease their psychological distress and further motivate them prolong their life span and also helps them to overcome death anxiety which will create good impact and improve their quality of their life and provides their ability to lead their day to day life.

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