



**ASSOCIATION OF COGNITIVE DYSFUNCTION AND
ANAEMIA EMPLOYING TMT-BAND DSST TESTS**

MOHIT TRIVEDI^{1*} AND R. K. DIXIT²

¹*Junior Resident Pharmacology E.L.M.C. Lucknow.*

²*Professor Pharmacology and Therapeutics K.G.M.U. Lucknow.*

ABSTRACT

Anemia is one of the commonest conditions worldwide and it is known to produce cognitive deficits in children adolescents and adults. Now compelling evidence is emerging about the detrimental effect of anaemia on the cognitive functions of the brain. 30 patients with anaemia were matched against 30 controls . The tools used were TMT-B and DSST. Data were presented as mean and analyzed using students t test , and chi square test. RESULTS: Anaemics performed poorly in TMT-B and DSST and made more number of errors in both the tests which was very highly significant. CONCLUSION: Anaemic patients had significant circumscribed areas of cognitive dysfunctions compared to the control group but a clear relation between the severity of anaemia and the severity of cognitive dysfunction could not be established .

KEY WORDS: anaemia ,cognitive dysfunctions , hemoglobin, TMT –B, DSST.



MOHIT TRIVEDI

Junior Resident Pharmacology E.L.M.C. Lucknow.India

INTRODUCTION

Anaemia is related to cognitive performance, especially attention, in preschool and school children. Pollet et al (1989) found significant differences in IQ between children iron deficiency anemia and iron replete children. They also found that vocabulary scores differed significantly among iron deficit anaemics and iron deficit replete groups. In a study of iron deficient adolescent girls, Burner et al (1996) found improvement in vocabulary performance after eight weeks of iron supplementation although there was no change in attention measures. All the chronic medical conditions with restored hemoglobin levels did not have much neurocognitive deficits. Soemantri et al (1989) suggested that supplementation with 10mg ferrous sulfate per kilogram body weight per day for 3 months in anaemic subjects resulted in apparent improvement in hematological status and learning achievement scores. Soewond S. et al (1989) from pre and post psychological test data showed that iron deficient anemia produces alterations in cognitive process related to visual attention and concept acquisition and these alterations are reversed with iron treatment. Pollett E. et al (1989) found that there is evidence of a positive association between iron status and IQ, language and school achievement test but there is no support for the internal validity of the hypothesis that this association is casual. A Driva et al (1985) states that 6-7 year old children who had suffered from iron deficiency during the 6th-18th months of life, showed less ability to concentrate, were more clumsy and more hyperactive when compared to a group of children who did not have iron deficiency during the first 2 years of life. In the recent years attention has been focussed on the behavior disturbances which accompany iron deficiency. A

considerable number of studies have shown that infants with iron deficiency have a lower developmental index, lack interest in their environment, have a shorter attention span and diminished cognitive ability. Sally Grantham – McGregor et al (2001) by correlation studies have found association between iron deficiency anemia, poor cognitions, motor development and behavioral problems. Longitudinal studies consistently indicate that children anemic in infancy continue to have poor cognition, poor school achievements and more behavioral problems in mid of their childhood. The problem in its vast magnitude if identified at an appropriate time warrants management to modify neurocognitive defects caused by it. This subject cognitive dysfunction in anaemias assessed by Trail making test-B (TMT-B) and Digit symbol substitution test (DSST) is of extreme importance and sparsely studied in psychiatry and needs to be studied using structured instruments. Therefore present study was done to know the impact of anemia on various cognitive functions. The objectives of the study were to determine the cognitive dysfunctions in anemia patients. and its comparison with that of controls .

MATERIALS AND METHODS

This was a single point non-invasive study of cases of anemia involving administration of a battery of neuropsychological tests to assess the cognitive function in the patient group and the control group which has been group matched for age, gender and education. All subjects gave informed consent for the study. Purposive random sampling technique was applied. The sample consisted of first 30 patients

diagnosed as anemia selected from the various in patient wards.

Inclusion Criteria (Anaemic Patients)

1. Informed consent
2. Age group 18-55 years
3. Diagnosis of Anemia confirmed by haematological tests

Exclusion Criteria: (Anaemic Patients)

1. History suggestive of other significant physical (such as HIV, Hepatitis etc.) or neuropsychiatric disorder which can cause cognitive impairment such as; seizures, cerebrovascular disorders, dementia, neurodegenerative disorders, systemic illness with known cerebral consequences, depression, anxiety, psychotic illnesses either presently or in the past.
2. Evidence of psychoactive substance dependence or significant abuse.
3. Those patients receiving the medication associated with cognitive side effects like tricyclic antidepressants, antipsychotics and lithium.
4. Family history of psychiatric illness in first degree relative.

The control group subjects consisted of subjects not having anemia (Hb > 11.0g/dl). A written informed consent had been taken for participation after explaining the purpose and design of study to each subject. The psychiatric status was assessed by using a structured clinical interview to know the psychiatric status. Hematological investigations like hemoglobin, TLC, DLC, ESR, peripheral blood film were done. The psychiatric status was assessed by

using a structured clinical interview. These patients were then assessed for cognitive functions using standardized neuropsychological tests. Tools Used were Socio Demographic and clinical proforma, Trail making test-B (TMT-B) and Digit symbol substitution test (DSST). Data were presented as mean \pm SEM and Students 't' test used to find the significant differences between the two groups. Chi-square test has been used to study the association between socio-demographic and clinical parameters.

RESULTS

There were 13 (43.33%) males and 17(56.67%) females in the case group. There were 15(50%) males and same females in the control group. There was no significant gender difference between the case and the controls. There was no statistically significant difference between the controls and cases in their place of residence. People from the urban base formed the largest group in the cases followed by people from the rural (36.67%) and semi urban (23.33%) groups. In the control group maximum number of people came from urban base (40%) followed by people from semi-urban (36.7%) and rural (23.3%) base.

Table 1. Shows the results from Trail Making Test (Number of Errors) of Anaemic and Control group subjects in different age groups. Table 2 shows Digit Symbol Substitution Test (Time taken in seconds) of Anaemic and Control group subjects in different age groups. Table 3. Shows Digit Symbol Substitution Test (Number of Error) of Anaemic and Control group subjects in different age group

Table – 1
Trial Making Test (Number of Errors) of Anaemic and Control group subjects in different age groups

Age Group (in years)	Anemic Patients			Control			Significance	
	N	Mean	S.D	N	Mean	S.D	t	p
Upto 30	14	2.85	0.77	13	1.31	0.75	5.28	<.001
30-40	7	3.14	1.46	8	1.37	0.51	3.21	<.01
41 and above	9	3.88	2.02	9	1.44	0.72	3.40	<.01

Table – 2
Digit Symbol Substitution Test (Time taken in seconds) of Anaemic and Control group subjects in different age groups

Age Group (in years)	Anemic Patients			Control			Significance	
	N	Mean	S.D	N	Mean	S.D	t	p
Upto 30	14	327.85	64.92	13	284.46	57.89	3.60	<.01
31-40	7	323.00	53.53	8	251.00	45.70	2.81	<.05
41 and above	9	330.88	63.18	9	256.11	40.69	2.98	<.01

Table – 3
Digit Symbol Substitution Test (Number of Error) of Anaemic and Control group subjects in different age groups

Age Group (in years)	Anemic Patients			Control			Significance	
	N	Mean	S.D	N	Mean	S.D	t	p
Upto 30	21	9.14	3.00	13	3.69	1.10	6.14	<.001
31-40	7	8.71	1.80	8	2.75	1.03	8.01	<.001
41 and above	9	9.11	2.97	9	3.77	1.20	4.98	<.001

DISCUSSION AND CONCLUSION

The study revealed that there is a significant cognitive impairment in anaemia patients compared with controls which persisted even after correction for confounding factors. Various neuropsychological tests to test different cognitive abilities were administered to the anaemic patients at the time of detection of anaemia. The mean age in the present study was 28.3 years for control group and 28.5 year for the cases. It is well established that impairments in cognitive functions are often seen with anaemia but a number of confounding factors are also known to

play an important role. (Hallberg et al, 1989). The confounding factors which occur in association with anaemia could be malnutrition, poverty, low maternal IQ, poor maternal education, low birth weight. In general, there are well circumscribed areas of cognitive deficits in anaemic patients. These deficits have been observed at all stages of life-infancy, childhood, adolescents and adults. Neuropsychological examination of specific cognitive functions indicates that some cognitive functions are affected more than the others by age. In

the current study, trail making test and DSST were adversely affected by age in both anaemic patients and non-anaemic controls. Majority of the subjects in this study were females in the cases and an equal number of males and females in the control group (50% each). Gender matching has not been done in previous studies in case of infants but most of the studies done in the adult population have involved females. The majority of the subjects in this study were married (Beard JL, 2005). This sample composition was similar to the sample composition done on adult females but one other study was done on non anaemic adolescent girls who were unmarried. (Bruner AB, 1996). studies. Even in recent studies (Walter T et al 1989, Somentri and Hussain 1989) on pregnant females and on iron deficiency anaemia adolescents, more comprehensive neuropsychological testing has been done and has revealed. The current study employed two domain specific tests – TMT and DSST to comprehensively assess cognitive functions. This is a notable strength of the study. TMT is a test of attention, visual scanning, sequential abilities. The TMT revealed very highly significant ($p=0.001 < 0.01$) differences between the anaemics and the control group, with the anaemics taking nearly twice the time consumed by the control group to complete the test. Anaemics also made more number of errors-thrice than that by the control group. These findings are in agreement with results from other studies. TMT is more sensitive to cognitive decline than SMMSE which was primarily designed to screen for dementia rather than to measure for cognitive dysfunctions. The use of TMT helped to detect the presence of

preclinical cognitive decline and circumvent the ceiling effects of SMMSE, which gives strength to the findings of this study. DSST is a timed test of attention, psychomotor performance and perceptual org. The performance of DSST was adversely affected by anaemia and difference in the performance between the cases and the control group was very highly significant. DSST has been employed in a number of studies and in each of these studies, anaemics took significantly longer time and made more number of errors while completing the test. Current study was a cross-sectional one. Since cognition is a measure of change in an individual over time, longitudinal studies are more reliable. The genesis of cognitive deficits in the anaemic patients is complex. However it appears that such deficits do exist and are associated with longer duration of anaemia and also increased severity of anaemia and also the occurrence of nutritional anaemia during the period of active brain development. Even modest reduction in cognitive function results in substantially increased risk of dementia over several years. Since the different studies provide conflicting reports on the reversibility of the cognitive deficits cost by anaemia, it is better to prevent the onset of cognitive deficit due to anaemia by preventing the anaemia itself rather than to treat them once they have appeared This study found cognitive dysfunctions in anemic patients, (having nutritional anemias) which are well circumscribed and occur in specific domains of cognitive functioning. These require domain-specific neuropsychological tests to be detected.

REFERENCES

1. Ajgett P, Agostony C, Axelssor I, Bresson JL, Goulet O, Hernell O, et al. Iron metabolism and requirements in early life. Do we know enough – A commentary by ESPGHAN committee on Nutrition. *Journal of Haed, Gut and Nutrition*, 2002, 34, 337-345.
2. Algarin C, Peirano P, Garrido M, Logoltt B, Marelo P. Iron deficiency Anaemic in infency. Lay Lastmy effects on auditory and visual system functioning. *Paediatric Research*, 2003, 53, 217-223.
3. Youdim MB. Brain iron deficiency and excess; cognitive impairment and neurodegeneration with involvement of striatum and hippocampus. *Neurotox Res*. 2008 Aug;14(1):45-56.
4. Beard J. Iron deficiency Alter Brain development and functioning *journal of nutrition*, 2003, 133, 14685-14728.
5. Beard JL, Hendricks MK, Perez EM, murray Kolb LE, Beeg A, Vernon Feagons L. Maternal Iron deficiency Anaemia affects post potom emosion and cognation *American society for nutritional science, journal nutrition*, 2005, 135, 267-272.
6. Bruner AB et al. Randomized Study of cognitive effects of Iron supplementation in non anemia iron deficiency adolescent curts, *Lancet*, 1996, 12, 992-946.
7. Bruner AB et al. Randomized study of cognitive effects of Iron supplementation in Non-Anemia Iron deficiency adolescent curts. *Lancet*, 1996, 12, 992-996.
8. Bruner AB, Joffe A, Duggan AK, Cascila JF, Brandt J. Randomized Study of Cognitive Effects of Iron Supplementation in Non Anaemic Iron Deficient Adolescent girls. *Lancet*, 1996, Vol 346, 12, 992-996.