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Research Paper

Assessment of cognitive function in patients with cerebral malaria

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Abstract

Introduction: Cerebral malaria is one of the most common infections of the central nervous system. The disease is more frequent in children, several neurological disorders are included. Neurological disorders caused by this disease can affect cognitive function in children with this disease . The purpose of this study was to evaluate cognitive function in children with cerebral malaria and compare it with healthy children.

Methods: This cross-sectional study sample included children with cerebral malaria and healthy 7-12 years Sistan and Baluchestan. To collect test data revised IQ children Wexler (WISC_R), Attention test track color (CTT), the index of working memory Fourth Edition Wechsler Intelligence Scale(WMS), visual examination Rey and memory test audio Rey and for data analysis ANOVA test using out.

Results: There was significant differences between groups on measures of verbal Intelligence ($p < 0.001$), performance intelligence ($p < 0.003$), general intelligence ($p < 0.001$), attention ($p < 0.001$), working memory ($p < 0.001$) , immediate visual memory ($p < 0.001$), delayed visual memory ($p < 0.001$), immediate auditory memory ($p < 0.001$) and delayed auditory memory ($p < 0.001$), respectively.

Conclusion: cerebral malaria can cause defects in cognitive function in children with the disease.

Keywords: cerebral malaria, cognitive function, memory, attention.

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Introduction

Malaria disease has widespread prevalence in the world which could have great impact on people health and economic cost for communities particularly in developing countries ((1);
(2). According to the World Malaria Report of WHO, 219 million cases and 660,000 deaths of malaria were reported in 2010 which was more prevalent among aged group less than 5 years (3). In 2011, totally 3239 malaria cases reported in Iran included 1710 indigenous and 1529 imported cases that had relative decreasing trend than 2010(3). Most of malaria cases were residing in southern parts of the country including Hormozgan, Sistan & Baluchestan and Kerman provinces (4-8). In these regions, there are five malaria vectors including Anopheles stephensi, Anopheles culicifacies s.l., Anopheles superpictus s.l., Anopheles fluviatilis s.l., and Anopheles dthali where A. stephensi and A. culicifacies s.l. regarded as the most important vectors (8-11). The most important Plasmodium species are Plasmodium vivax (88%) and Plasmodium falciparum (12%) (5). Cerebral malaria in children can lead to seizures, severe anemia, hypoglycemia, loss of consciousness and coma and also cause damage to the brain, causing defects in the cognitive function of children(12-14). In other words, the prefrontal cortex and frontal inflammation caused by parasitic infections, In other words, the prefrontal cortex and frontal inflammation caused by parasitic infections, Frontal and temporal atrophy, impaired blood-brain barrier, Damage to the parietal lobe, hippocampus and brain stem, Nerve damage caused by ischemia / hypoxia and pathophysiological symptoms such as intracranial pressure Which are the outcome of cerebral malaria, Can all be severe defects in the children's cognitive function (15-19). Because childhood is an important period of growth and learning, Cognitive disorder in this period could severely affect the growth, Learning, academic function and overall

daily life of children with cerebral malaria (14). Some research results obtained with cognitive disorders suggest stability of cognitive disorder even after treatment of children with neurocognitive disorders(20-22). Despite extensive efforts in malaria research, a few studies were conducted to association of Cognitive function in children with cerebral malaria in Iran. The main purpose of the present study was Assessment of cognitive function in patients with cerebral malaria.

Methods

In this cross-sectional study, 80 children in the two groups, patients with cerebral malaria (n = 40) and healthy controls (n = 40) in Imam Ali hospital at Chabahar and Razi hospital in Saravan were selected by available for sampling. Inclusion criteria of the patient group: patients with cerebral malaria, Over a period of 6 months after infection, Age 12-7. Children who suffer from psychiatric disorders, including anxiety disorders, depression, psychosis and hyperactivity, as well as certain diseases, such as physical disabilities, diabetes, heart disease or other serious diseases, as well as those who are taking psychiatric drugs, the study were excluded.

Children in the control group were selected by visiting elementary schools of those two cities and matched for age, sex and duration of primary school education in years. Demographic characteristics are shown in Table 1 below.

Table 1: Demographic characteristics

Variable	Children with cerebral malaria	Children in the control group
	(Standard deviation)± mean	(Standard deviation) mean
(year)age	9.5 ±(1.3)	9.6±(1.4)
(year)education	3 ±(1.2)	3±(1.3)
(male،female)sex	(20،20)	(20،20)

After obtaining the written consent of the parents of these children, they are using the Wechsler revised Intelligence Quotient children (WISC_R), Attention test track color CTT, the index of working memory Fourth Edition Wechsler Intelligence Scale, wechsler memory scale or WMS, visual examination Rey, Rey auditory memory test were evaluated.

Wechsler revised Intelligence Quotient children: Wechsler Intelligence Scale Revised (WISC-R), for 6 -13 years old children, was used to assess cognitive function (intelligence) in healthy and sick children. This test assesses the intelligence of children in three scales of full IQ, verbal IQ, and performance IQ using 6 verbal subscales including information, similarities, arithmetic, vocabulary, comprehension, and digit span and 6 performance subscales including picture completion, picture arrangement, block design, object assembly, digit symbol, and maze, totally 12 subscales. Usually ten subscales (5 verbal and 5 performance subscales) are implemented and two others are known as complementary subscales. In this study, all 12 subscales were implemented but 10 original subscales were used to estimate verbal, performance, and full IQs. Classification of intelligence into two main verbal and performance types is due to its diagnostic value and not due to existence of two different intelligence types. During 1982-1985, the test was translated into Persian in Shiraz University and its psychometric properties were reported. Eleven tests out of twelve (except vocabulary test) were translated into Persian and those questions improper with Persian culture were identified and after preliminary survey were substituted with suitable equivalents. For each age group with a 4 months difference, raw scores of subscales were converted to scale scores, and verbal, performance, and full IQs with a mean of 100 and standard deviation of 15. The tests and IQs reliability was calculated using test-retest method; the median reliability coefficient of this test was 0.73. The correlation coefficient of subtests with each other and verbal, performance, and full IQs was used as the standard measure of validity (23,24).

Trails test color or CTT: The purpose of this test is that evaluate the speed of attention and Visual search and space and version for children Has been developed for ages 7-16 years. This test has two forms 1 and 2 that number 1-25 written inside them and on the page dispersed. Participants must find the numbers on the page and connected to each other. In the form 2, each numbers in the circle is written in two different colors that the participants must change in which the color of the numbers. During the work, the time spent participants recorded by the experimenter. The

reliability of the test Equal to 0.45-0.68 and the correlation between the form 1 and 2, it has been reported 0.69(25).

wechsler memory scale Fourth Edition or WMS: The indicator calculate by Using subscale of sequence of letters and numbers and The reliability is good. Test-retest reliability of 0.82 and split half reliability of 0.85 was reported(26).

Visual memory test Rey: Visual memory test ray was used to assess visual memory. This test was developed in 1942 and includes images of shapes and lines, and two cards (A ,B). the standardization of the test was done by Sadeghi (26) and panahi (27). Criterion validity was 0.59 and test-retest reliability was 0.60 (26.27).

Auditory-Verbal memory test Rey: Evaluate the immediate and delayed auditory memory (recall, recognition) and retest reliability was moderate in the period of one year ,0.55 (28). Jafari and colleagues using the Pearson correlation coefficient, earned positive correlation 0.73 between the two versions of the test(29). Data were analyzed using SPSS-18 software.

Finding

Considering to the effects of age and education on cognitive functioning of subjects, both groups were matched for age and education, and no significant difference was found between the two groups in terms of age and education. The mean and standard deviation of the variables in the two groups are presented in Table 2 and 3. The data in Table 3 displays scores (WISC-R) in children with cerebral malaria and healthy counterparts for each subscale and ultimately significant measures of verbal intelligence, practical intelligence and total intelligence ($p < 0.01$), revised Wechsler IQ test results for children represents the effect of cerebral malaria in children's cognitive levels.

Table2: Mean and standard deviation of attention and aspects of memory in the two study groups

Variable	**Sick** (n=40) Mean (sd)	**Healthy** (n=40) Mean(sd)
Attention form1	259.60 ±(128.56)	262.50 ± (81.9)
Attention form2	±378.78(182.43)	325.80± (75.61)
Working Memory	13.32± (4.65)	29.30± (4.89)
Immediate auditory memory	32.8± (3.88)	44.9± (5.65)
Latency auditory memory (Reminders)	8.83± (1.11)	11.36± (1.80)
Latency auditory memory (Recognition)	12.66± (1.04)	14.48± (0.62)
Immediate visual memory	23.43± (4.27)	29.89± (4.80)
Latency visual memory	13.21± (3.75)	19.46± (4.84)

Table 3: Mean verbal, performance, and full IQs and 12 subscales of Cerebral Malaria children and their normal counterparts.

Subscale	**Sick** (n=40) Mean(sd)	**Healthy** (n=40) Mean(sd)	**T**	**p-value**
Information	(1.82)±7.37	(1)±11.65	-6.92	0.001
Similarities	(1.66)±8.9	(1.12)±10.75	.47	0.04
Arithmetic	(1.62)±6.07	(1.17)±9.75	-8.45	0.001
Vocabulary	(1.64)±8.55	(1.56)±11.77	-0.62	0.03
Comprehension	(1.54)± 7.72	(1.14)±11.90	-6.48	0.001
Digit span	(1.64)±6.85	(1.15)±9.45	-5.04	0.001
Picture completion	(2.11)±6.95	(0.98)±10.9	-5.21	0.001
Picture arrangement	(2.03)±7.1	(0.90)±10.50	4.54	0.001
Block design	(1.37)±7.37	(0.84)±10.57	-0.78	0.04
Object assembly	(1.64)±8.35	(0.91)±11.70	2.22	0.02
Digit symbol coding	(2.31)±7.92	(1.23)±11.05	-2.71	0.008
Maze	(2.07)±7.25	(1.27)±11.40	-2.98	0.004
Verbal intelligence	(6.71)±84.27	(6.38)±107.42	-5.56	0.001
Performance intelligence	(7.17)±82.40	(4.80)±108.10	0.22	0.003
Full intelligence	(6.08)±83.27	(5.65)±108.70	-3.37	0.001

The results of multivariate analysis of variance attention, working memory, immediate and delayed auditory memory are in Table 4. According to Table 4,between the performance of children in the two groups in tasks related to attention, memory, active, immediate and delayed auditory memory (recall and recognition) and immediate and delayed visual memory is significant difference 0.001.

Table 4: The result of Multivariate analysis variance of attention and various aspects of memory In two groups of children with cerebral malaria and healthy counterparts

Variable	F	Sig	Statistical power	Effect
Attention form1	12.08	0.001	0.18	0.93
Attention form 2	17.91	0.001	0.24	0.98
Working memory	57.93	0.001	0.50	1.00
Immediate auditory memory	96.37	0.001	0.61	1.00
Latency auditory memory (Reminders)	42.60	0.001	0.41	1.00
Latency auditory memory (Recognition)	56.45	0.001	0.48	1.00
Immediate visual memory	32.54	0.001	0.35	1.00
Latency visual memory	35.69	0.001	0.34	1.00

Result

The research examined cognitive function in children with cerebral malaria were compared with healthy children.The results showed that cognitive functions such as attention, working memory, immediate auditory memory, auditory memory latency (recall and recognition), immediate visual memory, delayed visual memory, verbal IQ, performance IQ and general IQ of children with cerebral malaria are significantly weaker than healthy children.These findings are aligned with the results of Studies of cognitive functions in children with cerebral malaria compared with healthy counterparts. Dugbartey study of working memory(30), auditory memory, immediate and delayed visual memory in children with cerebral malaria were compared with healthy children and their research results indicate that the performance was weaker in pediatric patients than in healthy children. The research findings in the field of active memory, auditory memory, immediate and delayed visual memory is aligned. Holding in his study suggested defects in immediate auditory attention and memory (31) and Al Serouri visual memory and executive function deficits in children(32). Which agrees with the findings of the present research. Boivin reported that children with cerebral malaria, most of the attention, working memory, visual memory and performance function are faced with problems(33-34, 16). Fernando evaluated auditory memory, performance function and general IQ (35) Carter assessed working memory, visual memory (17) and Idro assessed attention and general intelligence in children (36)and their research results indicate a defect in this practice. John in his findings to the deficit in attention, working memory and performance function of their children (13). Kihara deficits in auditory memory, performance function, working memory and attention (37) and Birbeck attention deficit and visual memory (38) and Idro injury in attention, memory, delayed auditory, visual memory, executive function, and general intelligence have reported. In addition to the assessment of attention and memory, to evaluate the levels of cytokines in children with cerebral malaria have been discussed in this context represents a relationship between elevated levels of (Tumor necrosis factor-a) TNF-a increase in the cerebrospinal fluid impaired attention and memory performance of these children (39). Due to the significant role of the nervous system, cognitive function and IQ, Potchen using ct scans (Computerid tomography scan) to assess brain damage in these patients, and major changes in the frontal lobe, including inflation, temporal, parietal and occipital and thalamus and basal core inflation

was observed in the brain of sick children (40). Gamanagatti also studied the magnetic Rzvnas based image processing (Magnetic emission tomography) MRI may indicate damage to specific areas of the brain, including the hippocampus and the prefrontal cortex (41).

Generally many factors such as parasitic infections, prolonged seizures, hypoglycemia caused by the disease, the pathophysiological processes such as intracranial pressure and cerebral blood flow in these patients, it can cause brain damage (10-9, 12). And each of these brain injuries are associated with a number of cognitive impairment. Damage to the frontal cortex, prefrontal and basal ganglia are associated with malfunction of attention and IQ. Damage to these areas could be considered a defect, malfunction, and general verbal IQ in patients with cerebral malaria is also explained. . (42-44, 40, 34, 13). Deficiency of Attention in children can cause problems in memory and intelligence. On the other hand, the temporal lobe and hippocampus damage is associated with impairment of memory and general and performance intelligence (45,13). However, only in the hippocampus-dependent memory function is active, and other areas of the brain that is involved, But the damage caused by ischemia / hypoxia in the hippocampus, retrieving information from memory and cause malfunction of the active memory (11). And damage in the temporal lobe, associated with defects in auditory memory (46);The temporal lobe seizures sclerosis (sclerosis) Gychgahy middle and associated memory impairment (47) And for this reason is that children with cerebral malaria in accumulation potential and have difficulty retrieving audio information, Auditory memory span is short and they forget their heard soon (31). In addition, auditory memory, visual memory of the children because of damage to the occipital lobe, it is difficult (48). Damage to the occipital lobe can cause disturbances in the process, interpret and the Generally visual data. Damage to this area, as well as the power of visualization and visual reminders to reduce and as a result, the visual reminder that the child has been disrupted. In addition, Parietal lobe damage have been more difficult to understand and organize the images generated (8). That is why the performance of these children in complex visual-spatial tasks, is very weak. So what was proposed, many children with cerebral malaria because of damage to different parts of their brains, the number of defects in cognitive functioning experience. These defects effect learning, academic performance, and other daily functions. Although this research was to compare the cognitive function of patients with cerebral malaria in different stages of disease and cognitive function after treatment was provided, this is a limitation of the study, but the findings of the study Carter (17) and Kihara (37) suggests that cognitive problems children may be stable and will remain so for several years after the illness. (37,17). It is suggested that future research, in addition to addressing the cognitive function of children with cerebral malaria in different stages of the disease, In order to develop rehabilitation protocols focus on children's cognitive functions and evaluating the effectiveness of various approaches to improve cognitive performance measures to be taken.

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