Attention Deficit Hyperactivity Disorder and Anxiety in Children With Malignancy

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Received: 2 Apr. 2016; Revised: 10 Aug. 2016, Accepted: 05 Oct. 2016

Abstract- Attention deficit hyperactivity disorder (ADHD) and Anxiety is the most common childhood psychiatric disorder. Based on studies, these disorders are more prevalent in some chronic disease. This study aimed at investigating the prevalence of ADHD and anxiety in children with malignancy and anxiety in their parents and comparing the results with those of the control group. One hundred, 3-15-year-old children with malignancy and 100 healthy children without malignancy or any chronic disease were included in this case-control study as case and control groups, respectively. Subjects were selected from children who were referred to the pediatric ward of Amir Kabir Hospital of Arak, Iran, in the form of simple probability and based on inclusion and exclusion criteria. ADHD and Anxiety were diagnosed by Conner's Parent Rating Scale-48 (CPRS-48) and Hamilton Anxiety Rating Scale (HARS) and were confirmed by psychologist consult. Data were analyzed by Student t-test in SPSS18. ADHD was observed in 23 cases (23%) with malignancy and 5 controls (5%) (P=0.001). In the case group, 57 children (57%) and 45 of their parents (45%) were suffering from anxiety while in the control group the figure was observed in 12 children (12%) and 11 of their parents (11%) (P=0.001). ADHD and anxiety are more common in children with malignancy as compared with children without malignancy and anxiety is also more common in their parents. Therefore, implementing interventions and psychiatric counseling are recommended for these children and their parents.

Acta Med Iran, 2016;54(11):718-723.

Keywords: Attention deficit hyperactivity disorder; Anxiety; Children; Malignancy

Introduction

Malignancies are uncommon in individuals younger than 19 years old. However, malignant neoplasms are considered as the second leading cause of death in children aged between 3 and 15 (1). Pediatric cancers are significantly different from adult cancers (1), especially histologically and regarding common tumor sites (1). Cancer is one of the diseases causing emotional stress in patients and their relatives (2-4). Some cancers such as pheochromocytoma are developed in children by releasing physiological stress-inducing adrenergic neurotransmitters. While the other varieties of cancer result in different psychological and physiological reactions due to their effects on interleukins, metabolism disorders and mental effects resulting from the awareness of prognosis (4,5). Based on the evidence, psychological disorders such as anxiety are significantly associated with malignancies in affected children and their parents. In their study on psychological and behavioral disorders in children aged between 4 and 15 suffering from posterior fossa brain tumor, M Varela *et al.,* (6) indicated that anxiety and aggression disorders are more frequent in children with malignancy compared to the control group. In a similar study, Abby R (7) also indicated that GAD (Generalized Anxiety disorder), depression, prolonged grief and decreased the quality of life are highly frequent in the parents of children with malignancy. The aforementioned cases are of great importance since it has been indicated that with regard

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to their effects on patients and their parents, a variety of psychological disorders in children with malignancies and their parents can have different effects (sometimes adverse ones) on the acceptance of the treatment in parents and children and consequently their response to the treatment and also the clinical course of the disease (8,9). According to studies, other than anxiety, a psychological disorder with a probable significant relationship with malignancy is Attention deficit hyperactivity disorder (ADHD) (10,11). ADHD is the most common childhood neurobehavioral disorder which includes attention deficit, motor restlessness and impulsive behavior based on the criteria of the diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) (12). It affects 5-10% of children in school age (13). The causative agent of ADHD in children is not specifically known, but some evidence relates it to underlying genetic defects and central nervous system disorders (14). According to studies, this disorder can be significantly associated with a variety of childhood chronic disease (15-17), depression (17), behavioral, emotional, language, and hearing disorders (18-19) and even diseases such as epilepsy (15,16) and abnormal EEG in children (20). And even similar to malignancies, response to the disease and the clinical course of the disease can be affected by these disorders (21-23). Kahalley *et al.,* (10) indicated that the prevalence of ADHD in children with acute lymphoblastic leukemia (ALL) and brain tumor is significantly higher than that of the general population. Since one of the risk factors of ADHD is environmental stress (12) and similar to other psychological disorders such as anxiety, ADHD can be related to pediatric malignancy and affect its course and prognosis, the evaluation of this disorder and other psychological disorders, especially anxiety in children with malignancy and their parents can be useful for the treatment of the underlying disease (malignancy) and also appropriate clinical encounter with the associated disorders using appropriate psychiatric interventions (8,9). As a result, this study aimed at investigating the prevalence of ADHD and anxiety in children with malignancy and anxiety in their parents and comparing the results with those of the control group.

Materials and Methods

This case-control study was performed on 200 male and female children in the age bracket of 5-16-year-old who were referred or admitted to the pediatric ward of Amir Kabir Hospital in Arak, Iran, in 2013. Based on the inclusion criteria, 100 children with different malignancies (hematologic, brain and other malignancies) who were under treatment as inpatient or outpatient were included in the study as the case group and 100 other healthy children who had referred as an outpatient due to the common cold, abdominal pain, *etc.* were included in the study as the control group. Malignancy was defined as confirmed diagnosis of any type of congenital or acquired malignancies for at least 2 years.

Clinical interviews were carried out with the children and their parents to study the inclusion criteria. It was done so to study the confounding factors that based on the studies may contribute to ADHD in children, such as the history of drug use, smoking, alcohol consumption by mothers during pregnancy, traumatic brain injury in childhood, etc. (12,24).

The clinical interview included questions regarding history of major depressive disorder (MDD), anxiety disorders, schizophrenia, bipolar disorder (BD), somatoform disorders, ADHD (in the case group, before developing CKD), congenital and chromosomal abnormalities such as Down syndrome and Fetal alcohol syndrome, substance abuse, mental retardation, epilepsy, asthma, diabetes, CHF (chronic heart failure), immune deficiency, organ transplantation and history of chronic medication use in children and a family history (first-degree relatives (parents and siblings)) of major psychiatric diseases such as anxiety disorders, schizophrenia, depression, ADHD, etc.

Subjects who had any of the above cases as well as children with birth weight less than 1,500 gr or Very low birth weight (VLBW), pervasive development disorder, autistic disorders (ASD), Tourette's disorder, anorexia or bulimia, a history of suicide attempts in the children and their families, major and chronic maternal diseases in pregnancy, the use of drugs, alcohol and smoking by the mother during pregnancy, a history of moderate to severe head trauma, low socioeconomic status, parental consanguinity and separation or death and history of any other chronic physical and psychiatric illness, were excluded. Furthermore, children whose parents were unwilling to participate in the study were excluded. Schizophrenia, MDD, pervasive development disorder, autistic disorders, Tourette's disorder and bipolar disorder were defined according to DSM-IV criteria as a history of each (25-29). Anxiety disorders were defined based on the criteria of DSM-IV, in the form of the history of different types of phobia, post-traumatic stress disorder (PTSD), panic attacks, obsessive-compulsive disorder (OCD) and GAD (28); mental retardation (MR)

was defined as the IQ of 70 or less (29); epilepsy was defined epilepsy as a history of recurrent seizures for which no cause can be identified in clinical studies (16), and chronic drug use was defined as a history of at least one year of continuous use of one or more types of medications. History of moderate to severe head trauma was defined as a trauma that causes GCS (Glasgow Coma Scale) <12 and symptoms such as dizziness or persistent confusion, behavioral changes, loss of consciousness, neurological symptoms or coma (30). Moreover, the low socioeconomic status was considered as family income less than 5,000,000 Rials and parental education lower than GCSEs.

The matching method was used for selecting the control group, and children were matched in two groups regarding age, gender, developmental level, economic status, the number of family members, place of residence (in terms of floor and area) with a standard deviation of ±2. After parents were provided with a complete description and a written consent was taken from them, they were asked to fill out a checklist of demographic and clinical information of children including age, sex, duration of malignancy, the number of hospitalizations due to malignancy (for the case group), Conner's Parent Rating Scale-48 (CPRS-48) based on the diagnostic criteria of DSM-IV for checking the condition of children regarding ADHD and Hamilton Anxiety Questionnaire (HARS) for the assessment of anxiety in their children and themselves. Conner's Parent Rating Scale (CPRS) was standardized by Conners *et al*., in 1999. It has two 93-item and 48-item versions. The present research uses the 48-item version. This version of Conners Questionnaire evaluates 5 factors of conduct, psychosomatic-impulsivity, hyperactivity, anxiety and learning problems and has 4 choices scored from 0 (never) to 3 (very high). The score of each article is converted into t scores with the average of 50 and standard deviation of 10. If the t scores of 12 standard deviations are higher than the average, the individual has a problem (31). Abdekhodaie Z *et al*., (32) reported the sensitivity and specificity of this form of Conner Questionnaire for the diagnosis of children with ADHD at 90.3% and 81.2%, respectively. HARS is one of the scales designed by Max Hamilton in 1959 (33,34). This test has 13 items each of which includes a set of symptoms which are scored from 0 (no symptom) to 4 (very severe and debilitating). The overall score varies from 0 to 56. The scores of 20-24,25-29 and higher than 30 are indicative of mild, moderate and severe anxiety, respectively (33,34). Clark DB *et al*., (34) conducted a study to assess the reliability and validity of the Hamilton Anxiety Questionnaire. The present research was conducted on 256 individuals aged between 12-18 who were selected from the patients of two clinics and the general population. The reliability and validity of this questionnaire in the evaluation of individuals regarding different degrees of anxiety were calculated powerful and efficient in the present research. It should be mentioned that ADHD diagnosis for children with this disorder was confirmed by evaluating its differential diagnoses such as hyperthyroidism (by measuring TSH and FT4) and lead poisoning (Blood Lead Level (BLL) >5-10 µg/dl) (35). The collected data were analyzed with SPSS software (Statistical Package for the Social Sciences, version 18.0, SPSS Inc, Chicago, Ill, USA) and descriptive statistics methods for frequency determination. Moreover, student t-test and x2 were used for quantitative and qualitative variables, respectively. *P*.values less than .05 were considered significant. This study was confirmed by the ethics committee of Arak University of medical sciences, and in all stages of this study, we were loyal to Helsinki declaration principles and a written consent was obtained from all of the participants and they were free to exit the study at their will.

Results

The mean age of children in the case and control groups was calculated at 6.67±3.04 and 6.69±2.92, respectively (*P*=0.95). There were 57 (57%) boys and 43 (43%) girls in the case group and 53 (53%) boys and 47 (47%) girls in the control group (*P*=0.67). In the case and control groups, 23 (23%) and 5 (5%) children were affected by ADHD, respectively. (OR=5.7, *P*=0.001).

In the case group, 57 children were affected by anxiety which 11 (11%), 7 (7%) and 39 (39%) children suffered from mild, moderate and severe anxiety, respectively while in the control group, between 12 children with anxiety, 3 (3%), 5 (5%) and 4 (4%) children suffered from mild, moderate and severe anxiety, respectively. (OR=9.7, *P*=0.001). Among 200 parents in the case and control groups, 45 (45%) and 11 (11%) parents were affected by anxiety, respectively (*P*=0.001). (Table 1) Research results indicated that the sex distribution and mean age of children with ADHD and anxiety in each of case and control groups have no significant relationship with the considered disorder (ADHD or anxiety) (Table 2). According to results, no significant difference was observed between ADHD and duration of malignancy and the frequency of hospitalization (*P*=0.42 and *P*=0.79, respectively).

Moreover, it was indicated that there is no relationship between the incidence of anxiety in the parents of children with malignancy and duration of malignancy (P=0.3) and the frequency of hospitalization (P=0.13).

Table 1. The results of HARS in the parents of both groups

Group	Number of parents	Total cases with anxiety	Mild anxiety (20-24 score)	Moderate anxiety (25-29 score)	Severe anxiety (30<score)	OR[3]	*P.value*[4]
Case group[1]	200	45 (22.5%)	22 (11%)	16 (8%)	7 (3.5%)	0.001	6.6
Control group[2]	200	11 (5.5%)	7 (3.5%)	3 (1.5%)	1 (0.5%)		

1: Parents of children with malignancy, 2: Parents of children without malignancy, 3: Odds-Ratio, 4: *P*.values less than .05 were considered significant

Table 2. The sex distribution and mean age of children with ADHD and anxiety in case and control groups

Group	ADHD			Anxiety		
	Sex		Age	Sex		Age
	Boy	Girl	SD[4]± average age	Boy	Girl	SD±average age
Case group[1]	14 (60.8%)	9 (39.1%)	7.23±3.23	31 (54.3%)	26 (45.6%)	7.17±3.04%)
P.value[2]	0.81		0.3	0.68		0.55
Control group[3]	2 (40%)	3 (60%)	6±3.74	6 (50%)	6 (50%)	6.87±3.28
P.value	0.64		0.58	0.12		0.82

1: children with malignancy, 2: children without malignancy, 3: *P*.values less than .05 were considered significant, 4: Standard Deviation

Discussion

Based on the results of the present study, the prevalence of ADHD in the case group (23%) was significantly higher that the control group (5%).

In their study on the prevalence of ADHD in children with ALL and brain tumor, Kahalley L *et al*., (10) indicated that the prevalence of ADHD in these children (9%) is significantly higher than the general population of children (3%) in the U.S. In a similar study, Patel SK *et al*., (11) also indicated the high prevalence of ADHD in children with brain tumor. But unlike the results of our study, Krull KR *et al*., (36) did not find any difference between the prevalence of this disorder in children with leukemia and the general population in their study on ADHD in 161 children with leukemia. The difference between our study and others lies in the type of malignancy; in the majority of studies, children were selected among children with brain tumors and hematologic malignancies while children with other malignancies were also investigated in our study. However, with regard to the results, it seems that malignancies are significantly associated with the incidence of ADHD regardless of the type of malignancy. In the present research, the prevalence of anxiety was calculated at 57% and 12 % in case and control groups, respectively. This difference was significant. M Varela *et al*., (6) in their study for the evaluation of psychological disorders in children aged between 4-15 sufferings from posterior fossa brain tumor, indicated that anxiety and aggression disorders are more frequent in children with malignancy compared to the control group. In a similar study by Adduci A *et al*., (37) in 2012, it was indicated that the varieties of anxiety disorders in children with a brain tumor are significantly prevalent compared to control group members. Similar to what was noted regarding ADHD, the results of our study and similar studies indicate that the prevalence of anxiety in children with malignancies is higher regardless of their type. According to our study, there was a significant relationship between the prevalence of anxiety in the parents of children with malignancy (45%) and the parents of children without malignancy (11%). In this regard, in a review study, in 2012, for investigating the mental condition of parents of children with malignancy, Abby R (7) indicated that anxiety, depression, prolonged grief and decreased the quality of life are highly frequent in the parents of children with malignancy.

With regard to the results of previous studies and the present study, it seems that there is a significant relationship between all 3 main variables discussed in this study, i.e. ADHD, anxiety in children with malignancy and their parents with malignancy which demonstrates the necessity of the examination and monitoring of children with malignancy and their parents for the aforementioned disorders using counseling and psychiatric intervention. Otherwise, the association of these disorders and malignancy can have a damaging effect on children's therapeutic process and follow-up treatment by their parents (8,9). However, due to the importance of the relationship between ADHD,

anxiety and other psychiatric disorders and pediatric malignancy (6-11) and the fact that these results cannot be generalized to the entire population, a further future study on other age ranges and in other treatment centers is recommended.

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