DOI: 10.5350/BTDMJB201208301

Psychiatric Disorders and Learning Problems in Children and Adolecents with Sickle Cell Disease

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ÖZET

Orak Hücre Anemili çocuk ve ergenlerde psikiyatrik bozukluklar ve öğrenme problemleri

Orak Hücre Anemisi (OHA) kronik bir süreç ve ağrılı krizleri de içeren ve hayatı olumsuz etkileyen komplikasyonlarla seyreden bir hastalıktır. OHA'lı çocuk ve ergenler uyum problemleri ve bozulmuş psikososyal işlevsellik açısından risk altında olarak görünmektedir. Mevcut literatür OHA tanılı çocuk ve ergenlerin normal kontrollere göre daha düşük hayat kalitesi ve daha yüksek sıklıkta nöro-psikiyatrik problemler gösterdiğine işaret etmektedir. Nöro-psikiyatrik problemler arasında depresyon, anksiyete bozuklukları, öğrenme bozuklukları, eksternalize davranış bozuklukları, enüresis ve dikkat güçlükleri sıklıkla bildirilmektedir. Bu yazı OHA'lı çocuk ve ergenlerde psikiyatrik bozukluklar ve öğrenme problemleri üzerine literatürü gözden geçirmeyi amaçlamaktadır.

Anahtar kelimeler: Orak Hücre Anemisi, çocuk, ergen, psikiyatrik bozukluklar

ABSTRACT

Psychiatric disorders and learning problems in children and adolecents with Sickle Cell Disease

Sickle cell disease (SCD) is characterized by a chronic course and disabling complications including recurrent pain attacks. Children and adolescents with SCD appear to be at risk for adjustment problems and impaired psychosocial functioning. The available research indicates that children and adolescents with SCD have a lower quality of life and a higher frequency of neuro-psychiatric problems than that of normal controls. Among the neuro-psychiatric problems, depression, anxiety disorders, learning disorders, externalizing behavior problems, enuresis and attention difficulties are commenly reported. This article aims to review the current literature on psychiatric disorders and learning problems in children and adolescents with SCD.

Key words: Sickle Cell Disease, children, adolescents, psychiatric disorders

Bakırköy Tıp Dergisi 2012;8:95-100

INTRODUCTION

Sickle cell disease (SCD) is a chronic, autosomal recessive disorder characterized by the predominance of the protein hemoglobin S (HbS) in red blood cells. SCD primarily affects people of African, Caribbean, Asian, Middle Eastern, and Mediterranean descent (1). SCD is characterized by a chronic course and disabling complications including an increased risk of infections. Recurrent pain chrisis that requires emergency management may be considered as the hallmark of SCD (1,2). Children and adolescents with SCD face many challenges of living with a chronic condition that requires lifelong medical management (2). As observed in children and adolescents with other chronic illnesses, the current literature suggests that children and adolescents with SCD may be at risk for adjustment problems and impaired psychosocial functioning (3,4).

The available research indicates that children and adolescents with SCD have a lower quality of life and a higher frequency of neuro-psychiatric problems when compared to the normal controls (2,5). Among the neuro-psychiatric problems, depression, anxiety disorders, learning problems, externalizing behavior problems, enuresis and attention difficulties are commonly reported (6-10). This article aims to review the current literature on psychiatric disorders and learning problems in children and adolecents with SCD.

Quality of life

Health has been defined as being not only the

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Geliş tarihi / *Date of receipt:* 13 Aralık 2011 / December 13, 2011

Kabul tarihi / *Date of acceptance:* 15 Şubat 2012 / February 15, 2012

absence of disease and infirmity but also the presence of physical, mental, and social well-being (11). Health-related quality of life (HRQOL) refers to the physical, psychological, and social domains of health seen in areas influenced by a person's experiences, beliefs, expectations, and perceptions (12). Number of studies to date has examined HRQOL in chronic diseases of childhood and adolescence including obesity, cancer, and HIV infection (13,14,15). HRQOL in children and adolescents with SCD have also been studied in a handfull of studies. The majority of these studies have reported a lower HRQOL when compared to the normal controls (16,17,18). In a more recent study, Dale et al reported that both children with SCD and their parents rated overall HRQOL and all subdomains of HRQOL lower than healthy children and their parents (2). There is also evidence that some differences may exist between the reports of children and parents on HRQOL. Panepinto et al. found that, compared with children, parents reported worse HRQOL in overall perception of health, physical functioning, behavior, and self-esteem domains (19).

Depression

Majority of the available studies have shown that children and adolescents with SCD have a higher risk of depressive symptoms (6,7,20,21). These include both major depression and other forms of psychiatric diagnosis with depressive symptoms. In a recent study, approximetely half of children and adolescents with SCD were diagnosed with either dysthymia (90%) or major depressive disorder (10%) (6). In that study, the age at onset of depressive disorders appears to be younger among patients with SCD when compared with the normal population. The mean age for dysthymic disorder and major depressive disorder were reported as 9 and 14 years of age, respectively (6). Like the children with other chronic illnesses, depression in children and adolescents with SCD is usually accompanied with impaired functioning on multiple domains. Adolescents with SCD have been reported to have significant problems in social relationships, isolation, and school failure, with 29% meeting the criteria for depression based on symptom scales (7).

Although the risk factors of depression in SCD are not completely known, there is evidence that disease related factors may have an influence. There appears to be a positive correlation between the frequency of pain episodes and depressive symptoms (22). Jerrel et al. also has found that the children and adolescents with SCD with depression had a higher frequency of vaso-occlusive pain attacks and acute chest syndrome visits per year and developed more complications with related organ damage (6). As shown for other chronic medical conditions, parental psychiatric characteristics have been found to be associated with the emotional symptoms in children with SCD. Unal et al. has found a relation between anxiety, depression, and marital adjustment levels in mothers and depression in children (22).

Anxiety Disorders

As observed in other chronic diseases, children and adolescents with SCD usually experience anxiety symptoms (7,20,21,22). The unpredictable painful nature of SCD, frequent hospitalizations, fear of worsening of the condition, worries about the future social life as an individual and the stigma associated with SCD appear to contribute to an increased risk of anxiety disorders (4,23). The predicators of anxiety symptoms may differ between childhood and adolescence. Younger children with SCD may experience seperation anxiety symptoms, especially on seperation from their mothers (24). This may partly be explained by the mothers' role in the health care of the children. Mothers' own worries about their child and overprotective parenting styles may also contribute to the separation anxiety of the child. Regarding to the adolescence period, body image and peer relations may be considered as the main domains of life. Since adolescents with SCD usually have a shorter stature than their peers, they may feel embarrasment in peer relations and, in turn, may withdraw from social acitivities (25). As the adolescent grow older, this anxiety on body image may disrupt their romantic relations. In addition to these psychosocial factors, disease related factors have also been suggested to be linked with anxiety symptoms in SCD. Mahdi et al. has found that the frequency of vasooclussive attacks are related with an increased risk of anxiety symptoms (26).

Externalizing Behavior Problems

Most of the studies generally suggest a higher prevalence of internalizing problems but no increased

risk of externalizing problems in children and adolescents with SCD (27). However, methodological issues of these studies, including the psychiatric scales used, might have limited the identification of externalizing problems in children with SCD. In an early study by Brown et al. children and adolescents with SCD have been found to have a higher frequency of externalizing behavioral problems than their healty siblings rated by caregivers (28). In a more recent study, Hijman et al. has shown that the children with SCD had more severe externalizing problems than the normal population according to teacher rated data (8). The etiopathogenesis of externalizing problems in children with SCD has not been studied extensively. However, there is increasing evidence that externalizing behavioral problems, especially the symptoms associated with impulsivity, may be related with cerebral infarcts on the frontal lobes (29,30,31).

Enuresis

Enuresis is commonly reported among children with SCA. The prevalence of enuresis is estimated between 29-50% in SCD which is much higher than the normal population data (32-35). Etiological explanations of the high rates of enuresis in SCD is largely unknown. However, some disease related factors have been suggested to be related with a higher frequency of enuresis in SCD. Babela et al. showed a positive correlation between a higher frequency pain attacks and enuresis (34). In contrast, a more recent study did not find a relation between pain attacks and enuresis (32). There is evidence that enuresis has a broad negative impact on children with SCD. Children with SCD who had enuresis have been reported to experience higher levels of total psychosocial problems (36).

Neurocognitive deficits and learning problems

The available research has shown that the children and adolescents with SCD have a higher risk of learning problems and academic underachievement (37). Academic underachievement appears to reflect the interaction of neurocognitive deficits associated with SCD and the school attainment problems related with frequent hospitalizations (10,38,39,40). Neurocognitive deficits in SCD may be broadly clasiffied as global intellectual disabilities and specific neurocognitive impairments. Among the spesific neurocognitive impairments, problems on attention, executive functions, memory, language and visuomotor functions have been studied in different studies (10,40-43).

One of the most devastating complications of SCD, which is directly related with neurocognitive impairments, is cerebral infarction. It is shown that cerebral infarcts are present on magnetic resonance imaging (MRI) scans in one third of children and adolescents with SCD by the age of 18 years (44-48). Both overt and silent infarcts evident on neuroimaging have been described in SCD. Overt infarct, cerebral infarction accompanied by neurological symptoms, is estimated to occur in 11% of children with SCD-SS (49). In contrast to the overt infarcts, silent infarcts have been defined as cerebral infarcts shown with MRI in the absence of clinical neurologic symptoms. Silent infarcts occur more commonly than overt infartcs, with a prevalence of 21.8% in children and adolescents with homozygous SCD (44).

Various studies have investigated intellectual function or general intelligence (IQ), in children with SCD. These studies mainly included the children above 6 years of age (10). However, a limited number of studies have also focused on younger children (47,50). One of the studies on younger children has reported delays in the developmental milestones (50). On the other hand, most of the studies on older children with SCD have reported varying degrees of impairment on IQ and subscales of IQ (51,52,53). In the light of the available research, it is suggested that impairment in intellectual development may appear in infancy and increase with age (10). IQ in children with SCD varies with the degree of neurological compromise. Children with evidence of clinical or silent infarcts were found to demonstrate lower total IQ scores and certain IQ subscores compared to normal population (40). There is also evidence that there may be differences on IQ between children with clinical and silent infarcts. Armstrong et al. have shown that, when compared with children with silent infarcts, the children with clinical infarcts demonstrated more deficits on certain IQ scores (43).

It is well known that executive functions are important for almost all of the cognitive functions. Majority of the studies to date have shown a higher frequency of impairments on executive functions in children with SCD when compared to the normal population (10). Among

the executive functions, working memory deficits appear to be more prominent (40). Brandling-Bennett et al. reported a decreased working memory span (54). White et al, more specifically, reported a decreased word length span (55). Deficits on working memory were also found to be related with cerebral injury and especially with frontal infarcts (54,55)

Attention difficulties are commonly reported in children and adolescents with SCD (8,10,56). Among attention problems, particularly sustained attention was suggested to be impaired in children SCD (10,29). Although not completely proven, deficits in attention are often related to the presence and severity of cerebral injury. Frontal lobe abnormalities, especially anterior infarcts, appear to underlie in the attention deficits (38,56,57). There is also evidence linking diffuse lesions to disruption of attentional processes on orienting tasks in SCD (58).

The available literature on memory functions in SCD is relatively limited. Schatz and Roberts have shown that children with SCD showed difficulties for digit span-backward (59). There is also evidence that deficits on visual-spatial memory are more frequently reported than deficits on verbal memory functions (41). As the other cognitive deficits, deficits on memory have been suggested to be related with neurological integrity including the presence and the severity of cerebral infarcts (10).

Management of psychiatric disorders in SCD

Medical advances in the treatment of SCD have transformed it from a condition associated with very early morbidity and mortality into a life-long, chronic condition (7). However, the studies on the treatment of psychiatric disorders in SCD are limited. Moreover, the majority of children and adolescents with SCD do not reach psychiatric evaluation and treatment. It is estimated that only one-third of patients with SCD receive treatment from a mental health professional (27). Patient and family education is the hallmark of interventions. For the management of psychiatric problems, the utilization of psychological interventions including cognitive-behavioral therapy and medical treatment including psychotropic medications may be needed. Spesific education services must be warranted for the children with intellectual disabilities. Childs' developmental needs and spesific learning problems must be established before the initiation of education. The children with cerebral infarcts, frequent hospitalizations and premorbid psychiatric symptoms must be regularly evaluated by a child and adolescent psychiatry specialist.

A limited number of studies investigated the safety and efficacy of psychotropic medications in children and adolescents with SCD. There appears to be a bidirectional relationship between emotional symptoms and chronic pain in SCD. It is suggested that children with SCD who experience chronic pain are usually depressed, and alleviating the depressive symptoms may have a salutary effect on the pain (6). There is evidence that the combination of antidepressants or anticonvulsants with opioids may be associated with fewer acute vaso-occlusive pain visits (60). Several antidepressants have been found to be effective in the management of disparate pain disorders, including amitriptyline, imipramine,venlafaxine, bupropion and duloxetine (61,62). However most of these studies included adult patients. The research on the selective serotonin reuptake inhibitors (SSRIs), which are considered as firstline medications for the treatment of depression and anxiety symptoms in the normal population of children and adolescents, is unfortunately limited in SCD. Jerrel et al. in their recent study did not reach a conclusive finding on the efficacy of SSRIs due to the high rates of incompliance in their cohort (6).

When initiating a treatment with antidepressants, a careful evaluation by a child psychiatrist is needed to avoid the potential adverse reactions of the drug and the unwanted reactions with the other medications used. This evaluation includes an initial hematologic examination and, in needed cases, the consultation of a pediatric hematology specialist. Similar to the initial treatment, follow up of the patients may warrant timely hematologic examinations and consultation of a pediatric hematology specialist.

Similar to the treatment of other psychiatric disorders in children with SCD, the literature on the treatment of enuresis is limited. Primary caregivers use a wide range of interventions for nocturnal enuresis, however, there is a lack of the empirically supported treatments for enuresis (63). In an early study by Figueroa, intranasal desmopressin acetate has been shown to be effective in children and adolescents with SCD (35). Imipramine (a tricyclic antidepressant), has also been shown to be effective in reducing symptoms (63).

CONCLUSION

Children and adolescents with SCD experience a high frequency of neuro-psychiatric problems. Neuro-psychiatric problems in SCD are usually underdiagnosed and undertreated, although they cause an additional burden on the quality of life of these patients. The collaboration of different disciplines including general practitioners, pediatric hematologists and child or adolescent psychiatry specialists is crucial for the early diagnosis and effective treatment of these conditions. Future studies are needed to clarify the treatment options of psychiatric problems in children and adolescents with SCD.

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