Chronic conditions in adolescents (Review)

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Abstract. The health problems related to the nervous system are on rise in young infants leading to high mortality amongst this age group. A chronic medical condition (CC) is present in this age group to the tune of 10-20%. We searched the electronic database PubMed for pre-clinical as well as clinical controlled trials reporting variable chronic conditions especially in pediatric patients. Most of these reports revealed that type 1 diabetes mellitus is the most common CC in young infants. In female patients, metabolic control is often disturbed during CC in this age group. Poor metabolism regulation often results in long-term complications, including cognitive disorders. In cognitive disorders, memory loss and learning problems are the most among adolescents. Executive problems are observed to be associated with low physical activities. The review article concludes that knowledge about factors influencing treatment adherence is crucial in chronically ill infants. Further, we should focus on protective factors in order to prevent health risk behavior.

Contents

1. Introduction

Mortality rates are higher among adolescents than among younger children (1,2) and mental health problems among adolescents are increasing day by day (3). The increase in mental health problems is related with poor school achievements and high unemployment rates. It has been shown that positive school environments promote adolescent health and prevent health-risk behavior (4).

The experimental behavior could be considered a normal part of adolescent development. However, sometimes it leads to risky behavior that might compromise health, quality of life, or life itself (5). For instance, early sexual activities, unsafe sexual practices, drug abuse and antisocial behaviour could put health at risk. Protective factors, on the other hand, can be defined as conditions that improve the resistance to risk factors and disorders (6) and they can be identified at multiple levels in adolescents: the individual, the family and the community (7). The concept 'social determinants of health' encompasses these levels as well as the national level (8). Worldwide, the strongest determinants of adolescent health are national wealth and access to education. Improving access to education and employment for young people as well as reducing the risk of transport-related injury are suggested as the most effective interventions in order to improve adolescent health worldwide. Moreover, safe and supportive families and schools together with positive and supportive peers are crucial to help adolescents develop their full potential.

2. Chronic conditions in adolescents

A chronic illness, defined as a disability interfering with normal life and/or demanding treatment for ≥3 months during a year (9). Asthma, type 1 diabetes mellitus (T1DM), epilepsy and inflammatory bowel disease are all examples of chronic illnesses prevalent in paediatric patients. Neurodevelopmental conditions are also common in children and adolescents. The worldwide prevalence of attention-deficit hyperactivity disorder (ADHD) among school children has been estimated to about 5% (10) and about 1% of Swedish school children are diagnosed with autism spectrum disorders (ASD) (11) and Tourette syndrome (9) respectively. However, neurodevelopmental problems commonly co-exist in children and adolescents and when this overlap is taken into account, it has been reported that approximately 7-10% of young people suffer from a neurodevelopmental problem (11). The overall prevalence of chronic conditions in childhood and adolescents should thus be estimated to 15-20%. Some of these conditions require daily and lifelong medical treatment. Other conditions entail social problems, resulting in difficulties exploring life, while other adolescents with chronic conditions participate in

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risk-taking behavior (10). In fact, increasing data indicate that adolescents with chronic conditions are engaged to the same extent or even more in health-risk behavior compared with their healthy counterparts (12,13). Further, there is evidence that health-risk behavior tend to cluster together (14,15). Due to this, young people with chronic conditions have double disadvantage during their adolescence (16). Moreover, adolescents with disabilities are less exposed to protective factors (17) and children with chronic conditions are more exposed to bullying (18), have fewer contacts with peers and more emotional problems than healthy counterparts (19). Furthermore, a study in a recent past indicated an association between chronic conditions in children and lower family socioeconomic status, compared to healthy peers (20).

3. Type 1 diabetes in adolescents

Getting T1DM during adolescence is complicated and related to poorer long-term metabolic control, compared to patients getting diabetes <10 years of age (21,22). Also, metabolic control often deteriorates during adolescence (23). However, two distinct trajectories of metabolic control across adolescence have been identified: moderate control with slight deterioration (representing a majority of adolescent patients) and poor control with rapid deterioration (<10% of patients). Adolescents with poor and rapidly deteriorating metabolic control reported lower paternal monitoring and frequency of help with diabetes management, lower functional autonomy, and lower self-control than others. Patients in this group were also more likely to report diabetes-related emergency room visits and diabetes-related hospitalizations.

The metabolic deterioration during adolescence is especially prevalent in girls (24). However, there is a gender difference in HbA1c already at diagnosis (25) and at follow-up where girls present higher values than boys. One reason for this phenomenon in adolescent girls can be increased GH-secretion, which induces insulin resistance (26). Other reasons for poor metabolic control in adolescents have been speculated to be irregular meal (27) and exercise patterns (28), poor adherence to treatment regimens (29) as well as risk-taking behavior.

Risk-taking behaviours are baneful in patients with T1DM. Tobacco smoking in patients with T1DM is associated with an increased risk for premature death by cardiovascular disease (30). Alcohol inhibits gluconeogenesis in the liver, which might result in severe hypoglycaemia. Ingestion of carbohydrates and measuring of blood glucose before sleep can prevent this (31). Further, cannabis smoking can first lead to excess snacking and then to loss of appetite. Drug use, in general, also alters brain functions, increasing the risk for mistakes with diabetes management. Adolescents with T1DM should be encouraged to refrain from smoking, binge drinking and use of other drugs.

Sexual activity in adolescents with T1DM must be specially acknowledged. Focus should be put on avoiding hypoglycaemia after intercourse as well as optimizing metabolic control in case of pregnancy. Poor metabolic control during pregnancy increases the risk for congenital malformations and foetal death (32). Contraceptives should be advocated in the group of sexually active adolescents with T1DM. Condoms, newer oral contraceptives (OCs) with lower oestrogen doses and newer progesterones as well as long-acting reversible contraceptives (including intrauterine devices and implantable rods) are recommended.

4. Long-term complications from T1DM

Patients with T1DM and good metabolic control have a double risk for death from any cause or from cardiovascular disease, compared to controls without T1DM (33). In patients with poorer metabolic control this risk is even higher. With HbA1c ≥83 mmol/mol the adjusted hazard ratio is 8.51 for death from any cause and 10.46 for death by cardiovascular disease as compared to controls without T1DM (34). Recently it has been shown that young adults with mean HbA1c >78 mmol/mol had a significantly higher proportion of retinopathy, microalbuminuria and/or macroalbuminuria compared to the group with HbA1c below 57 mmol/mol. Other studies show that HbA1c exceeding 70 mmol/mol is associated with long-term complications, such as cardiovascular disease and nephropathy (35) while these complications are not seen when long-term mean HbA1c is kept below 60 mmol/mol (36).

The main complications of T1DM are micro- and macrovascular diseases, manifested as retinopathy, nephropathy, neuropathy, and cardiovascular disease (37). These might result in visual impairments and blindness, renal failure and hypertension, pain, muscle weakness, autonomic dysfunction, cardiac disease, peripheral vascular disease and stroke. Recently cognitive dysfunctions, based on neuropsychological testing, were reported to be five times more common in adults with T1DM, compared to adults without diabetes (38). Cognitive problems are thus discussed as one of the major complications to T1DM as well.

5. Executive functioning problems and ADHD

Executive functions serve to organize and control thought and behavior (39) and are often defined as the 'conductor' of the brain. Key elements of executive functions include planning and organization abilities, anticipation, initiation of activity, different aspects of attention, impulse control and self-regulation, utilization of feedback, selection of efficient problem-solving strategies, mental flexibility and working memory (40). Functional magnetic resonance imaging and positron emission tomography have related brain networks involved in executive functioning to the prefrontal cortex of the brain.

Impaired executive functioning is one of the characteristics of ADHD (41). Executive functioning problems are also commonly occurring in individuals with impaired intellectual abilities (42), in ASD (43) as well as in patients with anxiety and depression (44). These neurodevelopmental disorders commonly co-exist in children and adolescents, which is why the acronym ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations) has been developed. The concept of ESSENCE advocates a holistic and multidisciplinary approach to patients presenting with early neurodevelopmental symptoms.

Executive functioning problems are presented on a spectrum, ranging from mild problems to more severe, compatible with the diagnosis of ADHD (45). There are 18 symptom criteria

of ADHD, according to the DSM-IV (46) and DSM-5 (47). The 3 subtypes/presentations of ADHD are: the combined, the inattentive and the hyperactive/impulsive type/presentation. At least 6 out of 9 symptoms in each domain have to be present in order to fulfill the diagnostic criteria for ADHD. The new DSM-5 states that in young people from the age of ≥17 and ≥5 symptoms are required. The symptoms should be present before 12 years of age, be clinically significant in ≥2 different environments and cause functional disabilities during ≥6 months. The heritability of ADHD is around 76%, suggesting a strong genetic role in ADHD aetiology (48). Thus parents of patients with ADHD are likely to carry the same condition. Moreover, boys are more frequently diagnosed with ADHD during childhood (49) and it is discussed that girls' executive problems frequently are unnoticed and undiagnosed (50). In adolescents with ADHD, time perception is often affected. Moreover, adolescents and adults with ADHD are at heightened risk of drug abuse (51) and antisocial behavior (52).

Clinical guidelines for the treatment of children and adolescents with ADHD recommend the use of multimodal treatment consisting of behavioral interventions, such as parent management training and teacher consultations as well as pharmacological treatment (53). Behavioral interventions include increased support from adults in many daily life situations; reminders, help to organize tasks, get started, follow and complete tasks as well as help to find alternative solutions when required (54). This support is required both in schools and during leisure time (55). The most common pharmacological treatment is stimulant-medication (55). The latter has been shown to prevent risk-behavior such as criminality (56).

6. The brain and ADHD

The brain development is often altered in patients with ADHD. This observation was further confirmed by imaging studies of ADHD patients that revealed involvement of the frontal lobes in developmental delay (57). The development of parietal lobes, basal ganglia, corpus callosum and cerebellum are also altered. Functional magnetic resonance imaging studies reveal a hypoactivation of frontoparietal networks, involving executive functions, and hypoactivation of ventral networks, involving attention, in children with ADHD (58). However, there were also indications of hyperactivation of regions in the ventral network, which might support the symptom of distractibility in ADHD. Moreover, children with ADHD have been found to have a delayed striatal development (59). In youths and adults with ADHD striatal activation is also low (60), yielding a suppressed reward system. However, the striatal activity is increased with stimulant-medication, which also improves cortical development in adolescents with ADHD (61).

7. Diabetes and neurodevelopmental/neuropsychiatric conditions

Mild cognitive problems are reported in both children (62) and adults (63) with T1DM. Working memory and other executive functions are particularly affected (64). These cognitive dysfunctions have been related to an early onset of the disease and to a history of hypoglycaemic seizures but not to long-term metabolic control (65,66). However, there are studies in adults reporting an association between chronic hyperglycaemia and cognitive dysfunctions (67), while another study reveals a lack of correlation between severe hypoglycaemia or ketoacidosis and cognitive problems in children with T1DM (68). The diathesis theory suggests that the young brain may be harmed by hyperglycaemia early in life, which confers a vulnerability to insults, such as hypoglycaemia, later in life (69). Testing with brief cognitive tests several times a day during 4-6 weeks in school children with T1DM have revealed decreased mental efficacy during spontaneously occurring acute hypo- and hyperglycaemic episodes (70).

Magnetic resonance imaging studies have shown that patients with T1DM have morphological changes in the grey and white matter of the brain. However, the CNS changes in adolescents are subtle and their functional significance uncertain (71). In this context it is noteworthy that ketoacidosis at onset of T1DM has been found to result in morphologic and functional brain changes, associated with adverse moderate neurocognitive outcomes (72).

A number of studies report an increased risk of psychiatric disorders (73), including ADHD (74), in adolescents with T1DM. This is found particularly six months after disease onset but also later in life. However, the association between ADHD and diabetes is debated and it has been demonstrated that ADHD is associated with type 2 but not with type 1 diabetes (75). Although conflicting results in the relationship between ADHD and T1DM, executive problems will yield specific difficulties for patients with T1DM. The treatment of T1DM requires regular insulin injections and dose adjustments in relation to carbohydrate content of the meal as well as planned or accomplished physical activity. This is demanding and requires good cognitive skills. Earlier studies of children with T1DM demonstrate an association between good executive functions, treatment adherence and consequent good metabolic control (76). Good metabolic control has also been associated with lower impulsiveness when compared to patients with poor metabolic control (77).

8. Conclusion

Chronic conditions in adolescents are associated with few protective factors and clustered health-risk behavior. The combination of chronic conditions and low numbers of protective factors are often hazardous and associated with an increased risk of clustered health-risk behavior. Moreover, in cases with the presence of ADHD, the pattern of few protective factors and clustering of health-risk behavior among adolescents with chronic conditions is aggregated. Further, ADHD is common among adolescents with other chronic conditions, particularly neurological conditions.

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