CHILD AND ADOLESCENT PSYCHIATRIC APPROACHES IN SOLID ORGAN TRANSPLANTATIONS

Manual For Clinicians

Editors

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PREFACE

A person is a biopsychosocial human being. When evaluating it in terms of health, it is essential to evaluate it both biologically, psychologically, and sociologically. In this context, solid organ transplants also require a biopsychosocial approach. Considering the patient as a whole not only increases the success of the treatment but also positively affects the patient's quality of life. This multidisciplinary approach becomes more important in childhood. It has been our main aim to evaluate the patients by considering the well-being of both the family and the child.

Various psychiatric problems can be seen in children and young people who need solid organ transplantation. These problems may make it difficult for the child to comply with the treatment, and may interrupt the medical treatment practices. Recognizing the needs of children with special needs in terms of mental health before and after solid organ transplantation and knowing how to behave and what to pay attention to will increase compliance with medical treatment.

Therefore, this book has emerged as a result of this approach. As far as we know, there is no book in the world that deals with the basics of the psychosocial approach to children who will have solid organ transplants. We think that we will fill this gap with this book.

Since the importance of knowing the normals of the child's development in patient management is known, we have reserved a long place on this subject. Then it focused on mental examination and ethical issues. Afterward, compilations were made specific to diseases. In addition, information about psychiatric drugs was given to clinicians.

We hope it will be useful for all clinicians and wish you a good reading.

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CHAPTER 1

HISTORICAL BACKGROUND OF PEDIATRIC KIDNEY AND LIVER TRANSPLANTATION IN TURKEY

Mehmet HABERAL[1]

Organ transplant for children remains one of the most complex and challenging areas within current medical practice. The practice of transplant in the pediatric population has revolutionized the life of children with end-stage organ failure. Pediatric transplant as a subspecialty is growing around the world with the establishment of new transplant programs and prioritization of organs for children.

In 1953, the first temporarily successful transplant of a human kidney was performed by Jean Hamburger in Paris. A 16-year-old boy received the kidney of his mother as living donor transplant. (1) Then in 1954, a milestone was made with the first long-term successful kidney transplant by Joseph Murray. Joseph Murray, a plastic surgeon, performed the first successful kidney transplant on the Herrick brothers, adult identical twins. (2) In February 1967, 6-year-old Tommy Hoag became the first Children's Hospital Los Angeles (CHLA) patient to undergo a kidney transplant with a kidney donated by his father.

History of Pediatric Kidney Transplant in Turkey

A first attempt of a solid-organ transplant in Turkey began with two heart transplants in 1968. By the early 1970s, we started to conduct experimental studies on liver transplant and on November (3), 1975, we performed the first

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day throughout the country, but deceased donors are still far below the desired rates. Efforts to increase awareness continue through the media, schools, and many public and private institutions. Improvements in legislation, education, and coordination are key factors for increasing the quality and the quantity of transplant activities in Turkey.

Since 3 November 1975 until 1 January 2022, our team has performed 3288 kidney transplants (380 pediatric and 2908 adult patients), and since 1988, 701 liver transplants (334 pediatric and 367 adult patients). In over 40 years of kidney and liver transplant history in Turkey, 46876 (2502 pediatric patients) kidney and 18203 (2612 pediatric patients) liver transplants have been performed nationwide.

In conclusion, transplant is currently the best option for children with chronic organ failure. Although pediatric organ transplant is active in some parts of many developing countries, it is still inactive in many others and mostly relying on living donors. The lack of deceased donor programs in most of these countries is one of the main issues to be addressed to adequately respond to organ shortages. Still, pediatric kidney transplant outcomes are markedly improved and younger children today experience better long-term graft survival and anticipate even more advances in the future of pediatric kidney transplant.

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CHAPTER 2

MENTAL PROBLEMS COMMONLY EXPERIENCED IN PEDIATRIC ORGAN TRANSPLANTATION

Esra BASKIN[1]

Solid organ transplantation in children and adolescents is a life-saving treatment method with increasing success in recent years for patients with organ failure (1). Survival rates have increased in pediatric solid organ transplantation over time (2). Today, children and their families who have organ failure due to kidney, liver, bowel, heart, and lung diseases are directed to organ transplantation. Kidney transplants are the oldest successful solid organ transplants and continue to have the best long-term survival. Currently, pediatric kidney transplants have a 5-year survival rate of over 90%. Kidney transplant has many advantages over other solid organ transplants. Kidneys are paired organs and people can usually function well with a single organ, and using living related kidney donation provides better immunological matching and therefore reduces the risk of rejection. Two recipients can receive organs from one cadaver donor, helping to reduce the waiting list compared to other types of solid organ transplants. Additionally, the kidneys are less immune active than some other organs.

Immunosuppression is the main component in graft and patient survival of solid organ transplant recipients. Traditionally, immunosuppressive protocols for the pediatric kidney transplant consisted of induction with lymphocyte-depleting agents for high-risk children or interleukin 2 receptor antagonists (IL-2-RAs) for lower risk children. To date, no large randomized studies have examined the effect between induction and no induction of IL-2-RA or lymphocyte-depleting agents

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process may be different. Hyperactivity in ADHD, antisocial attitudes in conduct disorder, opposition to every action in defiant disorder, inability to achieve organ regulation due to sleep and appetite deterioration in depression, interaction difficulties and restlessness in autism spectrum disorder could complicate the clinical follow-up of the patient, especially when they are hospitalized, making it difficult for the healthcare team. Sudden discontinuation of psychiatric treatments used during and after surgery may exacerbate psychiatric symptoms. In addition, medication toxicity or exacerbation of symptoms can be observed due to the interactions of psychotropic and immunosuppressive medications. For this reason, it is very important to be aware of the mental health problems that may develop in addition to surgery, medical follow-ups and immunosuppressive therapy during the organ transplantation process, in terms of treatment success. Scales measuring mental health problems have also been developed to support this treatment success. For this purpose, the validity and reliability study of the Pediatric Transplant Rating Instrument (p-tri) was also performed in our center (41).

Pediatric organ transplantation is a life-saving as well as a challenging process for both the child and the family, every stage of which must be taken seriously. Keeping in mind that mental disorders can be seen as comorbid in people with diseases that may require organ transplantation in childhood, working with mental health professionals at every stage of the process (before and after organ transplantation) will affect the success of treatment.

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CHAPTER 3

THE PERSPECTIVES OF PSYCHOSOCIAL DEVELOPMENT AND CHILDREN HAVING CHRONIC DISEASES

Zulal TÖRENLİ KAYA[1]

Chronic diseases are defined as health problems that last longer than three months or are not likely to improve, that negatively affect the functionality of the person in many areas and cause limitations in the short and long term (1, 2). Since children with chronic diseases may be adversely affected in terms of physical, cognitive, social, and mental development, it is important to consider the patients from the biopsychosocial/holistic perspective (3). When they are evaluated psychologically, the feelings such as fear, anxiety, panic, anger, aggression, withdrawal, hopelessness, and guilt; unconscious defense mechanisms such as denial and regression; attitudes such as excessive fondness and dependence on parents, using the disease, refusing the seriousness of the disease and treatment, opposing the treatment team and family, and sometimes blaming them are frequently seen in these children and adolescents, due to long-term illness and hospitalization process (4). It is important to consider that these emerging psychological reactions will differ according to the age and developmental level of the child.

When explaining the illness to a child with a chronic illness, the focus should be on making explanations suitable for the child's cognitive and mental development. For a child below a certain level of development, it can be very difficult to establish the relationship between illness and bodily functions. Young children know very little about their bodies other than what they observe.

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SUGGESTIONS TO PHYSICIANS

Physicians who carry out the treatment process with children and adolescents with chronic diseases should first understand the developmental level of the child, how s/he perceives the disease and what kind of causality s/he establishes about the disease (3). In order to achieve an effective approach, the physician should gather information about the child's cognitive and mental development before giving information, establish a dialogue that s/he can comprehend, and constantly evaluate the child's understanding to avoid possible misconceptions (5). The physician should use a simple and understandable language suitable for the child's developmental level and should support the narrative with visual materials if necessary (3).

In addition to improving medical problems, it is important for the physician to be aware of the child's psychological needs and to adopt supportive communication with the child and her/his family. While communicating, the physician's attitudes such as ignoring the patient's clues, changing the subject, avoiding responsibility, giving early and unrealistic assurances about the treatment, treating the patient as an "organ" rather than as a mental and physical whole, and running away from the patient are inappropriate. In addition, these attitudes also inhibit the child's need to obtain information and ask questions (11). For this reason, the physician's hearing and understanding of what the child is saying is as important as the child's understanding of what is said (5).

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CHAPTER 4

CHILD PSYCHIATRIC ASSESSMENT AND ETHICAL ISSUES IN SOLID ORGAN TRANSPLANTATIONS

Burcu AKIN SARI[1]

Solid-organ transplants are an increasing form of treatment all over the world. During organ transplantation, clinicians primarily aim to save the patient's life. Since the organ to be transplanted is valuable, the person to whom this procedure will be performed is determined as a result of detailed research. Tissue compatibility, gene studies, possible outcomes of immunosuppressive therapy are examined and decisions are made accordingly. In addition, the mental health of the person to be transplanted is also a subject of investigation, because mental health is one of the most important factors affecting the success of these surgeries(1). In adult cases, psychiatrists first assess whether there is any condition that may impair the patient's compliance with treatment. For this purpose, psychopathology, history of addiction, material and moral support are questioned.

In childhood organ transplants, the family is as important as the child in the psychiatric evaluation. Due to the difficulties of this period in adolescents, the clinician examines both the adolescent and the family in detail. The main topics in child psychiatry evaluation are (2):

» Knowledge and willingness about organ transplantation
» History of family and child's level of adherence to treatment during medical illness
» Psychiatric and substance use assessment and history of the child and the parents

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To overcome all these ethical problems is to inform the patient and his/her family in detail. It is thought that ethical problems will be minimized, as the family, who is informed about the possibilities of non-transplant treatment, what to do before, after, and during the transplant, how to continue the use of medication, the positive aspects of the transplant process and the possible risk factors, will make their own decision.

In summary, while evaluating the child and adolescent who will be transplanted, a multi-dimensional evaluation should be made, a multisystemic approach should be adopted, mental health should be taken into consideration, and different evaluations should be made for each patient by considering the ethical issues while evaluating the patients.

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CHAPTER 5

INTELLECTUAL DISABILITY AND SOLID ORGAN TRANSPLANTATIONS

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Intelligence is defined as all the abilities of human beings to think, reason, perceive objective facts and judge (1). It is determined by genetic, environmental, and social factors and follows a dynamic, ever-changing course throughout life. It is an indispensable condition for a person to be an individual who can stand alone in the society.

Intellectual Disability (also defined as mental retardation, failure to thrive) (ID) is a disorder that starts before the age of 18 and includes both intellectual and adaptive dysfunctions in conceptual, social, and practical areas. To be diagnosed according to the DSM-5 diagnostic criteria, the following three criteria must be met (2):

A. Deficits in intellectual functions such as reasoning, problem-solving, designing, abstract thinking, judgment, learning in school, and learning from experience, validated by both clinical assessment and an accepted measure of intelligence applied to the individual.
B. Deficiencies in adaptive functioning failing to meet developmental and socio-cultural criteria for personal independence and social responsibility. Unless an ongoing basis is provided, adaptive deficits limit functionality in one or more areas of daily life, such as communication, social participation, and independent living in diverse environments such as home, school, work, and society.
C. Intellectual and adaptive deficits begin during the developmental stage.

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studies (16). For this reason, it is generally stated in studies that ID should not constitute a contraindication.

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CHAPTER 6

ATTENTION DEFICIT AND HYPERACTIVITY DISORDER AND ORGAN TRANSPLANTATIONS

Ali BACANLI[1]

Organ transplantation has become an important treatment option, increasing long-term survival for many childhood end-stage organ diseases. After the increase in survival, it has become important for patients to feel healthy in psychosocial terms as much as their physical health, and studies conducted on this issue have revealed that cases with organ transplants show lower performance in terms of psychosocial functionality compared to the healthy population (1). Moreover, in order to find the answer to why the patients, who are applied the same treatment protocols, give different treatment responses, it is necessary to evaluate in detail both biological factors and psychosocial factors.

While there is a widespread literature on risk factors related to physical health that affect the processes before and after organ transplantation, there is less study on risk factors related to mental health that affect all these processes. However, it should not be forgotten that psychiatric diseases such as Attention Deficit Hyperactivity Disorder (ADHD) that will be mentioned in this section can negatively affect many areas such as doctor-patient relationship, treatment compliance, hospitalization process, organ acceptance and quality of life after transplantation. Although cross-sectional psychiatric evaluations focusing on psychological and behavioral symptoms in the last few months before transplantation are carried out in many centers where organ transplantation is

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CHAPTER 7

AUTISM SPECTRUM DISORDERS AND SOLID ORGAN TRANSPLANTATIONS

Hande AYRALER TANER[1]

Autism spectrum disorders (ASD) are neurodevelopmental disorders characterized by early-onset social communication and interaction difficulties and repetitive behaviors. It is known to be known that the genetic component is dominant. However, disorders related to early brain development and neuronal reorganization form the basis of this condition (1). Patients diagnosed with ASD are a very heterogeneous group. Diagnoses such as attention deficit hyperactivity disorder (ADHD), anxiety disorders, sleep disorders, disruptive behavior disorders, depressive disorders, obsessive compulsive disorder, bipolar affective disorder, schizophrenia are more common than those without ASD (2). These comorbid diagnoses can differentiate the clinical presentation of the disorder. In a study conducted in the United States and published in 2021, it was reported that ASD are seen in one of every 44 children. However, it has been reported that it is seen approximately 4 times more in boys than in girls (3). In a study in Turkey in which autism spectrum disorders were screened, it was found to be seen in 1 in 117 children (4).

Autism Spectrum Disorder Diagnosis

These children have difficulties in establishing relationships, difficulty in emotional responsiveness, inadequacy in verbal and non-verbal communication, as well as stereotypical motor movements, commitment to sameness, and limited

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and special education support; should not hesitate to get support from child psychiatry when needed.

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CHAPTER 8

ANXIETY DISORDERS AND SOLID ORGAN TRANSPLANTATIONS

Meryem Özlem KÜTÜK[1]

Organ transplantation improves the quality of life for the patients, provides many children and young people with the opportunity to attend school and to participate in life again (1). Anxiety disorders are one of the most commonly encountered mental health problems in children and adolescents during this difficult process. In this review, we attempt to provide guidance to all the field workers about anxiety disorders that might be observed during the process of organ transplantation in children.

Anxiety is derived from the Latin root "angere" meaning suffocation or being obstructed. Anything that is regarded as a danger by an individual results in this disturbing feeling and it is an important component of the stress response. Anxiety is a normal warning prompting individuals to take essential measures for the approaching threat in order to be protected from it; as a reaction to this stimulus, the organism develops a "fight" or "flight" response (2–4).

In fact, anxiety and fear are natural parts of general developmental steps; however, if they cause a significant hindrance or deterioration in an individual's daily functioning then it will fulfill the criteria for a mental health problem. Therefore, a low level of anxiety is productive, but a high level is harmful. Anxiety can be defined as being worried, bothered, or concerned; individuals express it as "an apprehension that something bad will happen" or "an unexplained state of fear".

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For cardiovascular disease (CVD) patients, TCAs can significantly affect the heart rate and the rhythm, and they are not recommended in anxiety disorders seen in this group of patients. SSRIs are safer on the cardiovascular system and can be used as the first choice for anxiety disorders of CVD patients (96–98). In patients using anticoagulants like warfarin, we recommend being careful about bleeding risks as SSRIs alter platelet aggregation-activation and lengthen the bleeding time.

Venlafaxine is known to cause ECG changes and blood pressure elevations. Therefore, regular blood pressure monitorization is recommended during its use (99).

Moreover, children can experience sleep disturbances before and after transplantation because of anxiety disorders. In recent years, melatonin, diphenhydramine, and hydroxyzine are frequently used in children and adolescents with sleep problems (78,100,101).

One important aspect to remember in all organ transplant patients is that drugs that inhibit the enzyme CYP3A4 like fluvoxamine, sertraline, and paroxetine can increase the blood concentrations of certain immunosuppressants like tacrolimus or cyclosporine if they are used together (102).

Lastly; in the period of organ transplantation, there is a high level of metabolic chaos in the body, the risk of experiencing drug-related side effects is high so during admissions to intensive care units oral intake might be restricted; in order to limit the duration of possible side effects during this period and to enable a fast drug exchange, agents with short half-lives like sertraline and midazolam should be preferred instead of fluoxetine or diazepam with long half-lives (103,104).

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CHAPTER 9

MOOD DISORDERS AND SOLID ORGAN TRANSPLANTATIONS

Tuğba ESEROĞLU SÖYLEMEZ[1]

The diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM), published by the American Psychiatric Association, are widely adopted and used all over the world. While "Mood Disorders" was a classification covering depressive disorders and bipolar disorders in DSM-IV-TR, these two disease groups were divided into separate sections in DSM-5 updated in 2013. However, since these two diseases were considered together in studies conducted with organ transplant patients following DSM-IV-TR criteria and the number of publications on pure bipolar disorder was very limited, "Mood Disorders" in DSM-IV-TR was preferred as the title of this chapter.

DSM-5 describes 8 diseases under the category of "depressive disorders" (1). These are:

- Disruptive Mood Dysregulation Disorder
- Major Depressive Disorder
- Persistent Depressive Disorder (Dysthymia)
- Premenstrual Dysphoric Disorder
- Substance/Medication-Induced Depressive Disorder
- Depressive Disorder Due to Another Medical Condition
- Other Specified Depressive Disorder
- Unspecified Depressive Disorder

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CHAPTER 10

PSYCHOTIC CONDITIONS AND SOLID ORGAN TRANSPLANTATIONS

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PSYCHOTIC DISORDERS AND ORGAN TRANSPLANTATION

Psychotic disorders can sometimes begin in childhood or adolescence (1). In a study evaluating 110 cases of childhood-onset psychosis between 2003 and 2005, it was found that the frequency of psychotic disorders increased with increasing age and was more common in males. It was reported that 35.5% of the cases were diagnosed with unspecified psychotic disorder, 24.5% with schizophreniform disorder, 22.7% with mood disorder with psychotic symptoms, 10% with schizophrenia, 2.7% with schizoaffective disorder, 4.5% with other psychotic disorders. Another remarkable finding was that all of these situations had many negative effects on the child's functionality and development (2). Psychotic symptoms can also be seen in autism spectrum disorder or mental retardation. However, psychotic symptoms may also occur due to other medical conditions. This is called "Psychosis Due to Another Medical Condition " (3).

However, not all psychotic symptoms mean psychosis. It has been reported that psychotic symptoms can be seen from time to time in healthy individuals (4). Although symptoms such as psychosis, disorganized behavior and formal thought disorder firstly bring to mind psychotic disorders, especially schizophrenia, there may be many reasons for this (3). Sub-threshold psychosis symptoms can

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risk of arrhythmia, and the combination of clozapine with mycofenalate mofetil may increase the risk of agranulocytosis (51).

Treatment of delirium is accomplished by correcting the underlying medical condition. Delirium treatment is multidisciplinary. First of all, landscaping should be done, benefiting from daylight, ensuring the balance of sleep and awakening day and night are among the most important points. It is useful to have objects such as clocks and calendars around to provide time orientation. Reducing the noise and personnel changes in the environment and making the environment as similar as possible to the environment that the child is used to will help to alleviate the symptoms (43). Various psychopharmacological treatments can also be used until the underlying condition is identified or the deterioration in the condition is corrected. Haloperidol, risperidone, olanzapine and quetiapine are frequently used agents (36). Haloperidol is the most commonly used agent in the treatment of pediatric delirium, and side effects such as dystonia and prolonged qt distance were found in 6% of the cases (52).

Psychotic conditions can be seen before and after organ transplantation and may impair treatment compliance. In organ transplant patients, psychosis may develop for any other reason, as well as psychosis or delirium may be seen due to the immunosuppressive drugs used and the medical conditions experienced. Particular attention should be paid to the level of family support in children and adolescents diagnosed with psychosis before organ transplantation, and it should be ensured that the family can deal with all medical care of the child throughout the process. It will be useful to follow these patients closely in order to detect problems that may arise during the process. With this; recognizing earlier the symptoms of delirium that may develop due to the underlying disease, especially in the pre-transplant waiting period or in the post-transplant intensive care unit, performing the necessary environmental arrangements and correcting the underlying medical condition will shorten the hospitalization period of the patients and will make a significant contribution to reducing mortality.

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CHAPTER 11

APPROACH TO PSYCHOPATHOLOGIES IN CHILDREN: RECOMMENDATIONS TO CLINICIANS

Duygu KABA[1]

Children with organ transplants often feel alone, powerless, and frightened as they are removed from their safe home environment and instead forced to live in a frightening, and uncomfortable such as a hospital or intensive care unit. Emergencies, hospitalization, and surgical processes – that is, situations they cannot control – can cause great stress, even trauma that negatively affects the mental state of children, in addition to the physical pain and distress caused by the disease itself (1). These children may use behaviors such as aggression, introversion, regression, and non-cooperation with the treatment team instead of words when communicating their negative emotions (2). These behavioral problems may continue later in life, even after the child is discharged (3).

It is known that children with chronic diseases have an increased risk of psychiatric disorders (4). So it is much more difficult for children who have a mental illness to cope with this difficult process. However, healthcare professionals may not know how to approach a child with mental illness who is hospitalized or admitted to the outpatient clinic. However, if this crisis is not managed properly, these children's self-esteem may be negatively affected. This can lead to disruptions in the developmental processes of children, the emergence of new mental problems, and the worsening of existing mental problems. Therefore, in this section, the approach to the most common psychopathological conditions in children will be explained to clinicians.

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delirium (15); however, delirium is more difficult to detect in these children and early childhood (11). Parents' inability to bond with their child compared to the past (not being able to console their child, decreased eye contact of the child, etc.), developmental regression in the child, and temporary loss of acquired skills should remind delirium (16). It can be evaluated in infants according to their ability to focus and maintain attention (whether they make eye contact and whether they show interest in objects or maintain this interest) (17). To be able to recognize the acute and fluctuating course of the cognitive state, the basal cognitive status of children with transplantation, especially in the preschool period or those with special needs, when they apply to the hospital should be evaluated with psychometric tests (18). Additionally, various scales developed for screening delirium in children with both typical development and special needs can also be used (19).

Children who are transplant candidates or recipients often experience additional distress as they lag behind their daily activities.These children often express their sadness and anxiety about not being able to go to school. Findings show that hospital schools opened to compensate for this deficiency increase the morale of children and even speed up the treatment process and reduce the length of stay in the hospital (20). Organizing and expanding hospital schools to meet the play, activity, and education needs of children with special needs in organ transplant centers will be beneficial in terms of supporting the mental health of children (21).

Consequently, the healthcare team at the transplant center must move beyond a narrow focus on treating the child's illness. They should be sensitive to their emotional and social needs, including children with special needs. Opportunities such as various activities and educational support should be provided by providing age-appropriate communication and empathy with these children in transplantation centers; the negative psychological consequences of hospitalization should be minimized (22).

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CHAPTER 12

DRUGS COMMONLY USED IN PSYCHOPHARMACOLOGY AND POSSIBLE DRUG INTERACTIONS IN SOLID ORGAN TRANSPLANT CANDIDATES OR RECIPIENTS

Duygu KABA[1]

Due to various stressors, drugs used, and physiological changes, mental problems that require psychotropic drug treatment can be seen in the organ transplantation process. However, organ dysfunction in the pre-transplant period can affect the pharmacokinetics of some psychotropics. After transplantation, drug interactions with the immunosuppressant can lead to reduced drug efficacy or vice versa toxicity (1). In this section, although the literature is limited, frequently used psychotropics in organ transplant candidates or recipients and possible drug interactions will be mentioned.

ANTIDEPRESSANTS

In these cases, antidepressant agents, especially selective serotonin reuptake inhibitors (SSRIs), are frequently used in anxiety disorder or depressive disorder. Citalopram, escitalopram, and sertraline are frequently preferred in the initial treatment because of their low side effects and interaction profiles (2). Although there are conflicting findings in the literature that citalopram and escitalopram prolong the QT interval at high doses; it has been reported that these drugs should be used in low doses in patients with arrhythmias, liver failure, a phenotype of slow metabolizers by cytochrome CYP2C19, or using another CYP2C19 inhibitor drug, such as cimetidine (3).

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atomoxetine is via the CYP enzyme system (mainly CYP2D6) (17). While no dose adjustment is required for both drugs in renal failure, atomoxetine should be used in low doses in hepatic failure (18).Since both atomoxetine and methylphenidate may increase blood pressure and heart rate and prolong the QT interval; use in children with serious heart problems, arrhythmia or cardiomyopathy requires cardiology consultation and close follow-up (18). There are cases reporting that methylphenidate is beneficial for depression or immunosuppressant-related an amotivational conditions in adult transplant patients (19), but the clinical experience of its use in combination with immunosuppressants in children is quite limited.

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