ECRONICON OPEN ACCESS

EC NEUROLOGY
Research Article

The Effect of Parent-Child Play Therapy in Decreasing Depression and Anxiety among Patients with Acute Lymphoid Leukemia (ALL) and Acute Myeloid Leukemia (AML) Under Chemotherapy and Radiotherapy

Maryam Sedghi*, Samaneh Asgharian, Jeyran Shafieian and Neda Seyfollahi

Young Researchers Club, Ardabil Branch, Islamic Azad University, Ardabil, Iran

***Corresponding Author:** Maryam Sedghi, Young Researchers Club, Ardabil Branch, Islamic Azad University, Ardabil, Iran.

Received: July 18, 2020; **Published:** September 30, 2020

Abstract

Background and Objective: Children diagnosed with cancer show depression and anxiety symptoms that could lead to many problems in the process of treatment. The objective of play therapy is to decrease depression and anxiety, their symptoms and creating positive outcomes in the health of these children.

Methodology: This study is an interventional study. The statistical population in this study included all children between the age of 6 and 15 who were diagnosed with cancer that were hospitalized in hospitals of Ardabil during 2019. The sample in this study was collected through convenience sampling. After calculating the depression and anxiety scores for the children, 30 children were chosen as the statistical sample and randomly divided into two groups of control and intervention. Then, the play therapy sessions (8 two-hour sessions) were carried out on the intervention group and ultimately, the depression and anxiety tests were conducted on both groups, after the eight sessions of play therapy. The data analysis was carried out by MANOCVA.

Findings: The findings from this research suggested that the depression and anxiety scores were improved in the intervention group, comparing to the control group.

Conclusion: In this study, play therapy led to a significant decrease in the depression and anxiety of the intervention group, comparing to the control group. Playing could be used as an effective intervention by the members of the healthcare system for the hospitalized children so that they are prepared for carrying out the painful treatment methods and the stress of being hospitalization.

Keywords: *Children Diagnosed with Cancer; Depression; Play Therapy*

Introduction

Cancer is considerable in any age, while the death rate due to the cancer is higher among the children between the age of 3 - 14, comparing to the other patients [1]. Children's cancer include a group of malignancies that have their own epidemiology-pathology and death rate. This disease has a higher diversity comparing to this disease among adults and it is considered as the most common death cause among the ages of 1 - 16 in the western countries [2]. Leukemia claims around 8 percent of the cancers in human population and around 7 percent of the deaths, due to the malignancies, so that it holds the fifth rank in the world and the second rank in Iran. In the meanwhile, acute myeloid leukemia is reported to be the second most common leukemia (18.5 percent) in Iran [3]. Prevalence of AML is roughly 2.3 per 1,000 persons and this rate increases by the increase in the age, so that it is estimated that the rate increases to 1.7 by the age of 65 and up to 16.2 after that. The death rate due to AML is 0.5 under the age of 10 and 20 per 100,000 persons, in the ninth decade of life [4]. This type of cancer, that is the most common type of acute leukemia among the adults, begins from the bone marrow and leads to formation of a lot of abnormal white cells and if it is left untreated, it deteriorates rapidly. The treatment of leukemia is very complex and it highly depends on the age, health condition, type of leukemia and its spread [5]. Blasts or cancerous blood cells are abnormal in AML and they do not turn into healthy white blood cells. The blasts accumulate in the bone marrow and blood and leave lesser space for healthy white blood cells, red blood cells and platelets. At this stage, infections, severe bleeding and as a results anemia could happen [6]. During the

past two decades, special attention has been paid to the regulatory role of microRNAs. MicroRNAs are a large subcategory of noncoders that impact the gene expression and the change in their expression could affect their important biological processes such as proliferation, differentiation, and apoptosis [7]. In the meantime, AML is phenotypically and genotypically a heterogenic disease, that accompanies the accumulation, propagation and resistance towards apoptosis of myeloid hematopoietic precursor cells and also inhibiting their differentiation in the bone marrow and peripheral blood, and leukemic cells lead to disruption of the maturation of normal myeloid, erythroid and megakaryocytic precursor cells [8].

Blood malignancies such as leukemia, lymphoma and multiple myeloma are formed due to the disruption in the blood cells production. Neoplastic proliferation of blood cells leads to accumulation of malignant cells and as a result the suppression of normal cell in the bone marrow, and this disruption in the bone marrow function leads to symptoms in various parts of the body [9]. Leukemia is among the most common white blood cell neoplastic diseases that happens due to the abnormal proliferation of immature leukocytes and its precursors in the bone marrow. This disease leads to the accumulation of malignant cells in the bone marrow and as a result suppression of natural hematopoietic elements and this process is considered as the bone marrow failure. Lack of platelets and normal white and red blood cells and also presence of blast cells in the peripheral blood and their accumulation in various tissues of the body such as lymph nodes and spleen play a great role in formation of this disease [10].

Scientists believe that acute depression is pretty common among children. Around two percent of the children between the ages of 6 and 12 and four percent of the adolescents are diagnosed with depression [11]. According to the criteria of TR-IV DSM for major depression disorder in children and adolescence, despite the increasing rate of these disorders among the children, they are not included in the list of mental disorders for children and adolescence, since they are not inclusive in this age group. However, International Mental Health Research Center of Australia has proposed a child behavioral assessment checklist that categorizes behavioral problems in two general and eight specific groups. In this categorization, anxiety and depression disorders among the children is included in the specific disorders' category [12]. Depression treatment among children is quite similar to the adults. 1. Drug therapy, 2. Electroshock therapy, 3. Psychotherapy, 4. Family therapy [13]. Creating cognitive changes and other methods in psychotherapy in order to alleviate depression are quite useful [14]. Also, studies have shown that anxiety is the most common emotional disorder among the patients diagnosed with cancer that emerges in several forms: situational anxiety that is due to the terrifying aspects of the disease, the anxiety related to the treatment, exacerbation of anxiety disorders [15]. In cases which the patient diagnosed with cancer considers cancer as a threat to their lives, they become quite anxious and anxiety gradually turns to an important clinical problem, since the meaning of the meaning of the accidents is an important factor in making individuals anxious. Among its symptoms could be referred to sweating, heart palpitations, restlessness, reassurance seeking, changes in thinking (perception, concentration, worrying) and physical symptoms such as muscle tension or fatigue [16].

Intraoperative radiation therapy (IORT) is among certain radiotherapy methods during which high dosages of 10 to 20 Gy are radiated on the tumor texture immediately after the surgery [17]. Radiation on the tumor texture after the surgery is used to assure the complete removal of microscopic tumors (remaining from the surgery) and preventing tumor recurrence [18]. Generally, IORT could be carried out through using photon and electron beams. Based on the treatment methods and equipment, IORT clinical techniques are divided into three general categories including Intraoperative Electron Radiotherapy (IOERT), Low-Energy X-Ray IORT (IORT- Low kV) and High-dose-rate intraoperative radiation therapy (IORT-HDR) [17]. In IOERT method, a narrow electron beam is used to radiate on the tumor texture. IOERT is most common, comparing to the other methods, due to the more uniform distribution of electron beam and the low depth of the electron beam penetration [19]. The pain due to the electron beam is distributed within the few centimeters of the beam landing area due to the short range of the beam and does not penetrate the deeper tissues. This feature leads to protection of the healthy tissues under the tumor texture. In order to implement IOERT, common linear accelerators or specific mobile accelerators designed for this purpose could be used [20]. Chemotherapy is among the common cancer treatments that is used especially in spread cancers and leads to longer recovery periods in patients diagnosed with cancer [21]. Combine chemotherapy treats many of the malignancies and leads to the increase in

the lifespan and better inequality of patients diagnosed with cancer. However, some of the oral manifestations in the patients diagnosed with leukemia are due to some chemotherapy or radiotherapy complications and these symptoms are pretty common and well-known. Among these symptoms could be referred to oral mucositis, dry mouth, and viral, bacterial and fungal infections along with pain.

There have been many different approaches in psychotherapy of children. However, regardless of their specific orientations, almost all of them follow one shared belief: using game or game environment is the inevitable specification of diagnosis and treatment in the children. Among the treatments that are applied on the children and have ad proper and considerable results is play therapy [22]. Games is a proper method for treating the children, for children face problems in oral expression of their feelings. Children could decrease their barriers through game and show their feelings better [23]. Play therapy among techniques for treating various children disorders such as depression, anxiety and behavioral problems and it is effective in many cases [24]. One of the approaches in play therapy is release play therapy that was introduced by David Levy in 1938. This method is a structured approach in play therapy and it is used for the children who have experienced a special stressful situation. Levy did not believe in the significance of interpretation and based his approach on the influence of game in abreaction effect. In this approach, the main role of the therapist is to change the scenes and recreate the experience which leads to the anxiety of the child, by the selected toys. Recreation of the damaging event helps the child to release the pain and stress that the event creates in them. During the time the child is playing, the therapist expresses the verbal and nonverbal feelings of the child in a reflective manner [25]. On the one hand, there is no integrated treatment pack for identification and treatment of these issue in different research literature and it seems that a lot of research has to be conducted in the treatment techniques for such children. Hence, considering the high prevalence of psychological disorders in cancer and the large gap between the prevalence and treatment, the lack of interventions is deeply felt. This research tries to study the effectiveness of play therapy in decreasing depression and anxiety in patients diagnosed with ALL and AML, treated by chemotherapy and radiotherapy.

Methodology

This study is an interventional study. The statistical population in this study included all the children between the age of 7 and 15 diagnosed with cancer and admitted to hospitals in Ardabil and had a record in 2019. After gaining the permissions from Ardabil University of Medical Sciences, the research sampling was carried out through objective-based and convenience sampling methods among the children hospitalized in Ardabil hospitals. In this study, 30 children diagnosed with cancer were chosen through convenience sampling. The properties of studied units (inclusion and exclusion criteria): Inclusion criteria included: 1. Age between 6 and 15 2. Bing hospitalized and having records in Ardabil Hospitals 3. Certainty about the cancer diagnosis 4. Normal IQ based on record 5. Having depression and anxiety symptoms considering the clinical interview criteria 6. Consent of parents and child to the presence of the child in the study. Exclusion criteria: 1. Children who were not able to participate in the play therapy sessions due to severe sickness 2. Children who were hospitalized lesser than a week (due to the low number of the sample) 3. Presence of fractures or problems that would interfere with activities.

To measure the studied variables, the following instruments were used:

- **Beck depression scale:** Beck's depression scale was first introduced by Beck, Mendelson and Moko Rabaf in 1961, and it was revised in 1971 and published in 1978. In 1996, Beck and his collogues carried out a fundamental revision in order to cover a wide range of symptoms and also to coordinate more with the depression disorders diagnostic criteria of DSM-IV. Also, in order to show the decrease in the appetite and sleep, two of its items were revised in this revised form. This questionnaire, which includes 21 items, is answered in a four-degree scale from zero to three. These items are on issues such as sadness, pessimism, sense of weakness and failure, sense of guilt, sleep disorders, lack of appetite, hating self, etc. so that 2 items are on emotions, 11 items are on cognition, 2 items are on overt behaviors, 5 items are on physical symptoms and 1 item is on interpersonal symptomatology. Accordingly, this scale determines the different degrees of depression from weak to severe and its score range is from minimum of zero and maximum of 63 (scores between 0 and 10 are the lack of depression, 11 to 17 are weak depression,

18 to 29 are mild depression and 30 to 36 are severe depression). Nowadays, this scale is used as a self-assessment scale and the participant must read the items of each group and cross the answer that item that expresses their feelings, comparing to the other sentences. These items assess the lowest to the most severe disorders in that regard, respectively. The participant could gain a score between zero and three in any aspect (zero is the lack of depression symptoms and 3 is the severity of the disorder in that aspect). By summing the scores of the individual, the first limits of the references could be referred to and the depression severity of the individual could be determined. Among these studied could be referred to Tashakori and Mehryar in 1994 that calculated its reliability coefficient to be 0.78 in Iran. In other studies, such as the study of Partoi in 1975, Vahabzade in 1973 and Chegini in 2002, the validity of Beck's scale was reported to be higher and varied between 0.70 to 0.90. In 2000, Beck, Stir and Brown reported the internal consistency of this instrument to be between 73% to 92% with a mean of 86% and alpha coefficient of 86% for the patient group and 81% for the non-patient group. Rajabi., *et al*. reported the Cronbach's alpha of 87% for the whole scale, validity coefficient of 83% and retest coefficient of 49%, with a three-week time difference [26].

- **Beck's anxiety scale:** Beck's anxiety scale was introduced by Beck in 1988. This scale includes 21 anxiety symptoms. The participant has to respond to the items in the form of "Never", "Weak", "Mild" and "Severe", and these choices are scored as 0, 1, 2 and 3, respectively. In this scale, scores between 0 and 23 show weak anxiety, 24 to 28 are mild anxiety and scores higher than 29 are disease anxiety. Beck., *et al*. (1998) scale is a self-report questionnaire that is prepared for measuring the anxiety severity in adolescents and adults. Carried-out studies suggest that this scale has a high validity and reliability. Its internal consistency coefficient (alpha coefficient) was 0.92, its after one-week retest reliability was 0.75 and its items' correlation varies between 0.30 and 0.76. Five content, Same times, structure, diagnostic and factor reliabilities was carried out for this test and all showed that this instrument has a high efficacy in measuring anxiety severity. This scale includes 21 items and the participant chooses one of the four choices for each item, to show their anxiety. The four choices of each item are scored in a four-part scale from 0 to 3. Each of the test items describes one of the common symptoms of anxiety (mental, physical and phobic symptoms). Hence, the total score of this scale is between zero and 63 [26].

General approach of the treatment

The treatment program in this study is a combination of family play therapy and child therapy and the activities with cognitive-behavioral and humanistic approaches were selected. All the games are carried out by the cooperation of the mother and the child and the mother benefits from the carried-out activities. The type of the selected activities such as relaxation, positive imagination, storytelling, etc. are designed to have positive influence on the mother, as well, and to target her psychological emotions and sufferings. Child therapy is a therapy through which the therapist educates the parents and supervise their performance so that they learn how to have unguided play sessions with their children. According to Van Flit [27] humanistic, behavioral, interpersonal, cognitive, developmental and systematic theories are used in child therapy. Family play therapy is also a creative treatment approach in which the children enter a treatment process in the family system [28]. And includes the parents as the participants in the treatment (in this approach, the parents and the children - all family members - are considered as the references). This type of play therapy is family oriented and the child is the parents'' facilitator and the parents are the child's facilitator. Through teaching the game language to the child, the communication between the child and the parent is facilitated. This type of game is designed for the parents and the child to have a higher awareness towards each other [29].

Data analysis method

To describe the data, descriptive statistics methods such as frequency, percentage, mean and standard deviation were used and for the data analysis and studying the independent variable effect (play therapy) on the dependent variables (anxiety and depression), inferential statistics methods such as and MANCOVA and ANCOVA were used.

Research Findings

Samples in this study included 30 children diagnosed with cancer in Ardabil County, and their frequency and personal information are provided in the table below. 26.7 per cent (4 individuals) of the subjects in the control group had a background of the disease for years, 40 per cent (6 individuals) for 2 years, 13.3 percent (2 individuals) for 3 years, 6.7 percent (1 individual) for 5 years, 6.7 percent (1 individual) for 6 years, and 6.7 percent (1 individual) for more than 6 years. 33.3 percent (5 individuals) of the subjects from the experiment group had a background of the disease for years, 26.7 percent (4 individuals) for 2 years, 6.7 percent (1 individual) for 3 years, 13.3 percent (2 individual) for 5 years, 13.3 percent (2 individual) for 6 years, and 6.7 percent (1 individual) for more than 6 years. Also, 26.7 percent (4 individuals) of the subjects in the control group had a bad financial situation, 26.7 percent (4 individuals) had a medium financial situation, and 46.7 percent (7 individuals) had an excellent financial situation. 13.3 percent (2 individuals) of the subjects in the experiment group had a bad financial situation, 60 percent (9 individuals) had a medium financial situation, and 26.7 percent (4 individuals) had a good financial situation.

Group		Control Group		Experiment Group	
Statistical Index		Mean	Standard Deviation	Mean	Standard Deviation
Variable					
Depression	Pretest	43.86	8.07	25.40	11.76
	Posttest	43.13	6.36	12.20	6.88
Anxiety	Pretest	49.26	7.59	31.06	10.81
	Posttest	50.73	6.37	14.73	5.89

Table 1: *Mean and standard deviation of depression and anxiety in two groups of control and experiment.*

As it could be observed from the table above, the pretest and posttest score of the control group mean and (standard deviation) of the depression 43.86 (8.07) and 43.13 (6.36), anxiety 49.26 (7.59) and 50.73 (6.37). The pretest and posttest score of the experiment group mean and (standard deviation) of the depression 25.40 (11.76) and 12.20 (6.88), anxiety 31.06 (10.81) and 14.73 (5.89).

	Test Name	Value	F	df Hypothesis	df Error	P	Eta Square	Statistical Power
Model	Pillai Effect	0.466	10.903	2	25	0.000	0.466	0.982
	Wilk's Lambda	0.534	10.903	2	25	0.000	0.466	0.982
	Hoteling Effect	0.872	10.903	2	25	0.000	0.466	0.982
	Largest Error Root	0.872	10.903	2	25	0.000	0.466	0.982
Group	Pillai Effect	0.903	116.847	2	25	0.000	0.903	1
	Wilk's Lambda	0.097	116.847	2	25	0.000	0.903	1
	Hoteling Effect	9.348	116.847	2	25	0.000	0.903	1
	Largest Error Root	9.348	116.847	2	25	0.000	0.903	1
Depression	Pillai Effect	0.519	13.465	2	25	0.000	0.519	0.955
	Wilk's Lambda	0.481	13.465	2	25	0.000	0.519	0.955
	Hoteling Effect	1.077	13.465	2	25	0.000	0.519	0.955
	Largest Error Root	1.077	13.465	2	25	0.000	0.519	0.955
Anxiety	Pillai Effect	0.399	8.300	2	25	0.000	0.399	0.939
	Wilk's Lambda	0.601	8.300	2	25	0.000	0.399	0.939
	Hoteling Effect	0.664	8.300	2	25	0.000	0.399	0.939
	Largest Error Root	0.664	8.300	2	25	0.000	0.399	0.939

Table 2: *MANCOVA significance test results on the variables of depression and anxiety.*

MANCOVA results in the table above suggested that there is a significant relationship between the pretest score of any of the variables of depression and anxiety with the combination of depression and anxiety posttest scores ($p < 0.000$) In other words, there is a significant difference between the experiment and control groups in the variables of depression and anxiety. Studying the value of eta indicated that 90 per cent of the variance of the combined variable is determined by the group membership of the studied individuals.

	Dependent Variable	SS	DF	MS	F	P	Eta Square	Statistical Power
Model	Depression	152.829	1	152.829	7.720	0.012	0.219	0.738
	Anxiety	216.167	1	216.167	11.105	0.003	0.299	0.894
Group	Depression	1587.898	1	1587.898	75.541	0.000	0.744	1
	Anxiety	2366.387	1	2366.387	121.565	0.000	0.824	1
Depression Pretest	Depression	516.918	1	516.918	24.590	0.000	0.486	0.998
	Anxiety	14.358	1	14.358	0.738	0.398	0.028	0.131
Anxiety Pretest	Depression	0.090	1	0.090	0.004	0.948	0.000	0.050
	Anxiety	325.503	1	325.503	16.722	0.000	0.391	0.976
Error	Depression	546.561	26	21.022				
	Anxiety	506.116	26	19.466				

Table 3: *MANCOVA significance test results on the variables of depression and anxiety.*

Results presented in table 3 suggested that there is a significant relationship between depression and anxiety pretest with combining the scores of depression and anxiety posttest ($p < 0.000$).

Discussion and Conclusion

The objective in this research is to study the effectiveness of parent-child play therapy on the decrease of depression symptoms in children diagnosed with cancer, perceived stressed by their mothers and improving the parent-child relationship. The findings from ANCOVA suggested that the depression symptoms in children who were diagnosed with cancer and had gone through parent-child play therapy were lower, comparing to the control group. Hence, it could be concluded that parent-child play therapy could decrease the depression symptoms in children who were diagnosed with cancer. The results from this study are in accordance with the results from Tew [30], Hatami., *et al*. [31] and Zare'pur., *et al* [32]. By emphasizing the awareness techniques and expressing different emotions, Hatami., *et al*. [31] approved the effect of group play therapy on children depression. According to the Wilmshurst [33] and Clark., *et al*. [34], the low emotion expression level and incorrect child upbringing methods are considered among the children depression risk factors. Also teaching parent-child play therapy to the mothers with children diagnosed with diseases could decrease their depression, for the emotions governing the relationship between the parent and child affect the parents' situation and leads to a decrease in the parents' anxiety and rectify the parent-child relationship. Using art-oriented games in a study, Zare'pur., *et al*. [32], targeted the low self-confidence and self-esteem of depressed children diagnosed with cancer and decreased their depression. The common symptoms in all depression disorders include presence of sadness, sense of emptiness, sensitive mood, along with physical and cognitive changes that influence the individual capacity for their performances significantly (DSM-5). The intervention that is used in this study included activities that might have influenced some of the common symptoms in depression and improved them. For instance, in the mental imagery activity, the children were forced to concentrate so that they could imagine more details in their minds. These imageries accompanied the sense of joy, increase in their decision-making capabilities and resealing positive and negative emotions. Also, performing this activity before sleep could probably help children by decreasing their sleep problems, by creating a calm atmosphere. Identification and emotion express games, and also play-

ing with medical equipment, family puppets and animals could reveal the child's emotions and concerns about the disease and family and probably influence the child's mood. During these games, the child could express their concerns freely and receive empathy for them and find solutions, if possible. It has to be mentioned that it was tried to preserve the balance between the positive and negative emotions in choosing them. In this study, correcting the parent-child relationship was another process through which play therapy probably affected the depression symptoms in children who were diagnosed with cancer.

Another finding of this study suggested that parent-child play therapy had decreased the anxiety of children diagnosed with cancer. These results were in accordance with the results from Rey [35], Tew., *et al*. [30] and Sadri [36] and Nainis., *et al*. [37], in which the art therapy was studied in patients diagnosed with cancer. In this study, a significant decrease was discovered in the variable of anxiety. Hummer., *et al*. [22] also showed that the anxiety levels decrease due to the fact that the parent-child method leads to sympathetic interactions between parents and children and their acceptance. Alexon., *et al*. [38] studied the effectiveness of play therapy on the decrease of anxiety in children diagnosed with acute disease. To explain the findings this research, it could be said that since children have not yet reached an abstract thinking so that they can express their emotions and feelings, a method should be found, through which children can reveal their positive and negative feelings so that the reason for their behaviors could be studied. Since playing for children is equivalent of speaking for the adults, playing is a mean for expressing feelings, establishing relationships, describing experiences, revealing wishes and self-boom, and on the other hand, it helps with the communication of the child inner thoughts with the outside world [39]. A pint worth mentioning here is the fact that the children transmit their negative emotions towards their environment to a considerable level during play therapy and the therapist could perceive the child's inner problems and mental concerns, by observing these overt behaviors in the form of games. To explain the result of the decrease in the anxiety, it could be said that due to the fact that in this treatment method, the sense of self-efficacy among the parent and child decreases the anxiety, their bound is improved and the treatment effects tend to increase. Finally, it has to be mentioned that this study had certain limitations, such as: 1. Using convenience sampling due to the limitations in the sampling 2. Lack of 3 or 6-month follow-up 3. Lack of comparing the patients diagnosed with different cancers. Hence, considering the results in this study and other studies based on the effectiveness of psychological interventions on the chronic diseases, it is necessary not to suffice with the medical treatments and provide an effective help with the increase in the mental health and increase in the use of effective approaches in coping with pain in these patients and as a result treating this disease, through establishing consult and psychotherapy centers and using psychological interventions in the hospitals and oncology centers.

Conclusion

In this study, play therapy led to a significant decrease in the depression and anxiety of the intervention group, comparing to the control group. Playing could be used as an effective intervention by the members of the healthcare system for the hospitalized children so that they are prepared for carrying out the painful treatment methods and the stress of being hospitalization.

Acknowledgement

At this moment, we would like to appreciate the help of the Association for Supporting Patients Diagnosed with Cancer in Ardabil Province who helped us through conducting this study, and also the help and support of Ardabil University of Medical Sciences, Shafa Parto Center and Imam Khomeini Hospital.

Bibliography

1. Khazaee S. "Freedom from cancer". *Tehran: Mohaghegh* (2011): 20-40.

2. Movahedi M and Tohidifar MH. "Pediatric Cancers in Nelson Text book of Pediatrics". Yazd Publication (2011): 89-93.

3. Salehi M., *et al.* "Comparison of artificial neutral network and Cox regression model in survival prediction of breast cancer patient". *JIUMS* 21 (2013): 120-128.

4. Greer PJ., *et al.* "Wintrobes Clinical Hematology". Acute and Chronic Myeloid Leukemia 10th edition (2005): 631-641.

5. Zand AM., *et al.* "Effect of age, gender, blood group on blood cancers types". *Kowsar M* 15 (2010): 111-114.

6. Packson N., *et al.* "Why is acute leukemia more common in males? A possible gender determined risk linked to the ABO blood group genes". *Annals of Hematology* 78.5 (1999): 233-236.

7. Miska EA. "How microRNAs control cell division, differentiation and death". *Current Opinion in Genetics and Development* 5.15 (2005): 563-568.

8. Appelbaum FR., *et al.* "Acute myeloid leukemia". *Hematology American Society of Hematology Education Program* (2011): 62-86.

9. Adeyemo TA., *et al.* "Orofacial manifestation of hematological disorders: hemato-oncologic and immuno-deficiency disorders". *Indian Journal of Dental Research* 22.5 (2011): 688-697.

10. Pourshahidi S., *et al.* "The prevalence of oral manifestations in children with hematologic malignancy's". *Elixir Humanity Physiology* 49.8 (2012): 9718-9720.

11. Hosainzadeh M. "Brunner and sudarth's. Medical surgical nursing". Tehran: Boshra Publication (2011): 480.

12. Evans RE and Debora KN. "Psychiatric and mental health nursing". Philadelphia. Published, by Mosby co (2005): 193-197.

13. Pourafkari N. "Kaplan and sadok synopsis of psychiatry". Tehran: Shahrab (2001): 623-635.

14. Monirpour N. "Relationship between negative experiences and sign of depression in sari city adolescences'. [Dissertation] in Master of Science in clinical psychology". Tehran: Iran University of Medical Sciences (2004): 110-142.

15. Bolton P., *et al.* "Interventions for depressions symptoms among adolescent survivors of war and displacement in Northern Uganda: a randomized controlled trial". *The Journal of the American Medical Association* 298.5 (2007): 519-527.

16. Stark DP and House A. "Anxiety in cancer patients". *British Journal of Cancer* 83.10 (2016): 1261-1267.

17. Willett CG., et al. "Intraoperative radiation therapy". *Journal of Clinical Oncology* 25.8 (2007): 971-977.

18. Harrison LB., *et al.* "High dose rate intraoperative radiation therapy (HDR-IORT) as part of the management strategy for locally advanced primary and recurrent rectal cancer". *International Journal of Radiation Oncology Biology Physics* 42.2 (1998): 325-330.

19. Baghani HR., *et al.* "Dosimetric evaluation of Gafchromic EBT2 film for breast intraoperative electron radiotherapy verification". *Physicists in Medicine* 31.1 (2015): 37-42.

20. Calvo FA. Ecancermedical science. Groenwald SL, Frogge M, Goodman M, Yarbro CH. Clinical guide to cancer nursing. Burlington, Massachusetts: Jones and Bartlett Learning LLC (2013).

21. Terezhalmy GT., *et al.* "Cancer chemotherapeutic agents". *Dental Clinics of North America* 40.3 (1996): 709-726.

22. Hamer HJ., *et al.* "Anthroposophic art Therapy in chronic Disease: A Four-year prospective cohort study". *Explore* 3.4 (2007): 365-371.

23. Pedro-Carrol J and Reddy L. "A preventive play intervention to foster children resilience in the after of divorce". Empirically based play interventions for children. Washington DC: American psychological association (2015): 51-75.

24. Hanser S., *et al.* "A group play therapy model for children with ADHD symptomology". *Journal of Child Psychology and Psychiatry* 10.4 (2010): 191-211.

25. Bratton SC., *et al.* "The Efficacy of Play Therapy With Children: A Meta analytic Review Treatment Outcomes". *Professional Psychology Research and Practice* 36.4 (2015): 376-390.

26. Fathi Ashtiani Ali. "Psychological tests". Tehran: Ba'ath Publications (2012): 139.

27. Van Fleet R. "Filial therapy: what every play therapist should know". *Magazine of the British Association of Play Therapist* 65 (2011): 16-19.

28. Mc Monigle CL. "Parents and children's experiences in family play therapy". Thesis for Ms Degree in Human Development. Faculty of the Virginia Polytechnic Institute and State University. Falls church, Virginia (2008).

29. Maxwell A. "Family play therapy: A play therapist handbook". Colorado association for play therapy, spring conference (2012).

30. Tew K., *et al.* "Filial therapy with parents of chronically ill children". *International Journal of Play Therapy* 11.1 (2002): 79-100.

31. Hatami Z., *et al.* "The effect of group play therapy on depressed children". *School Counselor* 7.4 (2012): 26-20.

32. Zare Pour A., *et al.* "The effect of group play therapy on depression in children with cancer". *Scientific Journal of Kurdistan University of Medical Sciences* 14.13 (2009): 72-64.

33. Wilmshurst L. "Abnormal Child Psychology". USA: Rutledge (2009).

34. Clark M., *et al.* "Treatment of childhood and adolescent depression". *American Family Physicians* 86.5 (2012): 442-448.

35. Ray DC. "Impact of play therapy on parent-child relationship stress at a mental health training setting". *British Journal of Guidance and Counselling* 36.2 (2008): 165-187.

36. Sadri A. "The effectiveness of therapeutic model of DIR approach, family-based fluoride on improving coping defiance syndrome in children and reducing maternal stress". Master's Degree in Clinical Psychology, Ferdowsi University of Mashhad (2013).

37. Nainis N., *et al.* "Relieving Symptoms in Cancer: Innovative Use of Art Therapy". *Journal of Pain and Symptom Management* 31.2 (2006):162-169.

38. Axelson DA., *et al.* "Fluvoxamine for the treatment of childhood anxiety disorders". *Journal American Academy Child and Adolescent Psychiatry* (2013): 415.

39. Bratton SC., *et al.* "The Efficacy of Play Therapy With Children: A Meta analytic Review Treatment Outcomes". *Professional Psychology Research and Practice* 36.4 (2005): 376-390.

Volume 12 Issue 10 October 2020