Article

Life perceptions, problems and psychological wellbeing in preadolescent and adolescent patients in treatment for leukemia compared with healthy peers

Marta Tremolada [1*], Ilaria Tamara Chiavetta [1]

[1] Department of Development and Social Psychology, University of Padua, Italy; marta.tremolada@unipd.it; ilariatamara.chiavetta@studenti.unipd.it
* Correspondence: marta.tremolada@unipd.it; Tel.: +39-3474868835

Abstract: There is still little research on psychological wellbeing and reported problems in preadolescents and adolescents under therapy for leukemia, also comparing them with their healthy peers. The present study aims to analyze the life perceptions, psychological well-being and problems' intensity in these patients during the first year of therapy and to compare these reports with those of matched healthy peers adopting a battery of self-report questionnaires. Mann-Whitney tests identified the younger patients more at risk than older ones in their problems' intensity and psychological symptoms. Older patients resulted instead more vulnerable regarding past life perceptions. Wilcoxon test with 2 dependent samples analyses showed that: healthy peers have a better perception of current life and lower percentage of somatization symptoms than patients after 6-months post-diagnosis. On the other hand, healthy peers reported more problems dealing with impulsivity, mood, disorganization, concentration and memory than patients both at 6-months and 1-year from diagnosis. Healthy peers reported also more anxiety and depression symptoms than patients and worse past and future life perceptions than patients at 1-year from diagnosis. The clinical aim is to perform a psychological screening of preadolescents and adolescents in order to prepare ad hoc psychological interventions.

Keywords: children; adolescents; leukemia; in treatment; healthy peers; life perceptions; psychological wellbeing; reported problems

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1. Introduction

Adolescence is a period of time of significant physical and emotional changes and a diagnosis of leukemia during this time could have an important impact on their psychological and physical development. There is still little research on how preadolescents and adolescents feel about their lives in this illness experience and what they think about the future shape of their lives. There is little information what the cancer experience means to adolescents and how it affects their current lives and future plans. Adolescents with cancer represent a major challenge to healthcare professionals because as well as having a serious illness, they are also going through the life stage that defines adolescence. Adolescence is an important period of growth and development that involves significant psychological, social, and maturational adjustments as adolescents move toward adulthood. Healthy professionals must know the preadolescents' and adolescents' psychological well-being, life satisfaction and the intensity of possible reported problems so that they can support them in their everyday life facing the illness and in their decision making regarding their own future.

Quality of life (QOL) during treatment is an important aspect of the care for the adolescent with cancer, but few studies in this area have been done, principally focusing exclusively on childhood cancer survivors (Reinfjell et al. 2017). In one study exploring QOL issues for the adolescent with cancer, authors compared adolescents with cancer on therapy to those off therapy and to healthy controls (Wu et al. 2006). On therapy, adolescent males and females reported poorer overall QOL and physical functioning. Females also reported poorer psychological functioning, cognitive functioning and poorer outlook on life when compared to healthy females. At highest risk were adolescents who were female, older, and nonwhite. Similar findings were reported in younger children, ages 8–12, who had decreased overall QOL and physical wellbeing while on treatment, but the off-therapy cohort had significantly improved QOL which was noted to be better than the healthy controls (Shankar et al. 2005). In an overview of adolescents with cancer, Bleyer reported that the severe toxicities of cancer treatment involved more difficult in coping during adolescence and that QOL during treatment was poor (Bleyer 2002).

Few studies of psychological adjustment following cancer diagnosis and during treatment have focused specifically on the adolescent population. Studies in broader pediatric oncology populations suggest the majority of these patients did not demonstrate significantly elevated levels of anxiety or depression relative to age-matched controls (Goertzel and Goertzel 1991; Pai et al. 2006). A significant minority of pediatric oncology patients, estimated to be 17–30%, demonstrated marked psychological distress, including symptoms of depression and anxiety (Patenaude and Kupst 2005). The extent to which these results can be applied to the adolescent population is unclear, but a report from a study of depression and anxiety symptoms on adolescents shortly after diagnosis indicated a similar pattern (Allen et al.1997). Abrams and colleagues (Abrams et al. 2007) found no significant differences in the depression and anxiety ratings in the cancer group relative to age-matched, healthy controls, though a substantial number of patients in both groups had elevated anxiety and depression scores.

Several studies identified risk factors for those adolescents who will have trouble coping with a cancer diagnosis. Difficulties in parental coping was consistently identified as an important predictor of coping in child and adolescent patients (Frank et al. 1997; Mulhern et al. 1992). Also the type of cancer appeared to play an important role in determining psychological impact as well. Greater uncertainty in the treatment outcome, such as in the use of experimental procedures, was correlated with greater psychological distress (Patenaude and Kupst 2005).

Hopefulness played an important role in coping with the diagnosis and treatment of cancer. The level of hopefulness was correlated with a positive sense of well-being and commitment to treatment and also improved coping and self-esteem, especially with female adolescents (Cantrell and Lupinacci 2004). The relatively high rates of hopefulness were reported in the first six months of treatment. The adolescents identified health and normalcy as the most hoped-for-objects. The adolescent who had positive expectations was able to focus on specific hopes as a way of adapting to their illness and was able to develop a better sense of being which might lead to improved compliance. Also optimism was discovered as a key concept associated with higher QOL in adolescents with cancer (Mannix et al. 2009). Although adolescents with cancer were not more optimistic than their healthy peers, they were significantly less pessimistic. Optimism and pessimism were related to different aspects of well-being. Specifically, a cohesive pattern was found in which optimism predicted positive aspects and pessimism negative aspects of well-being (Sulkers et al. 2013).

The prevalence of symptoms of anxiety and depression found in a longitudinal study (Saevarsdottir et al. 2010) was lower than found in other studies among cancer patients (Iconomou et al. 2004) and the QOL was found relatively good. In another study (Wesley et al. 2013) the minority participants were more likely to endorse physical symptoms and less negative affect compared to White respondents. Higher report of physical symptoms was significantly related to greater negative affect, whereas higher perceived social support from friends was related to higher positive affect. Adolescents tended to report average levels of positive affect and low levels of negative affect compared to healthy populations

Adolescents with cancer experienced significantly more fatigue than peers without chronic health conditions (Daniel et al. 2013). The level of psychological symptoms was significantly higher in adolescents with leukemia comparing with healthy adolescents (Çavuşoğlu and Sağlam 2015). Several studies found that adolescents with cancer had both physical and psychological symptoms, but that they had more psychological and school-related issues (such as interruption in their education, academic failure, not attending school activities), anxiety, somatization, and depression (Li et al. 2013; Ruland et al. 2009).

Children and adolescents on treatment showed levels of self-esteem, depression and anxiety comparable to those of healthy children. However, children and adolescents off treatment reported higher depression and anxiety levels and lower psychological well-being and physical self-esteem than have been reported for healthy Swedish children. The findings suggested that the period after treatment termination was characterized by a higher risk of psychosocial problems than is the actual treatment period (Von Essen et al. 2000).

Aims and hypothesis

The present study aims to analyze the life perceptions, psychological well-being and cognitive functioning in preadolescents and adolescents affected by leukemia during the first year of therapy and to compare these perceptions and symptomatology with those reported by the matched healthy peers. First of all, we started with the administration of self-report questionnaires to the patients with leukemia at two different time points, at 6 months from the diagnosis and at 1 year from the diagnosis. The same procedure was used for the control sample, composed of healthy peers. Subsequently, the data were analyzed by dividing the obtained data into two areas A and B and proceeding to analyze any differences between the two groups of participants regarding their replies to the questionnaires.

The first area of investigation (A) aims to try to understand if the socio-demographic variables are associated with the psycho-social well-being and cognitive functioning of the children and adolescents under therapy for leukemia. So we started by analyzing if the gender (research hypothesis A1) could have some influence on children’s and adolescents’ wellbeing. The literature is consistent in affirming that females are more likely to suffer emotional stress, developing higher psychological symptomatology (Wu et al. 2006; Butler et al. 2008; Tremolada et al. 2016). So we expected to have higher psychological symptoms and more reported problems in females than in males.

Subsequently, the research hypothesis A2 is about the possible influence of age at the time of diagnosis on the psychological well-being and cognitive functioning. Patients diagnosed with cancer in early adolescence seem to declare a worse psychological adaptation of those who received the diagnosis earlier (Zebrack 2011; Kazak et al. 2010).

Subsequently, since the literature does not reveal many studies about possible significant relationships between the family variables and the psycho-physiological well-being in the adolescent patients, it was decided to deepen this topic with the research hypothesis A3. Since the literature revealed that the variables related to family relationships were closely associated with higher levels of personal growth (Barakat et al. 2006; Mattsson et al. 2008), socio-demographic variables relating to the family characteristics were investigated: perceived economic condition, parental schooling years, parent’s workload, parent's age and number of siblings. We didn’t have clear hypothesis on this topic.

For the research hypothesis A4, the economic condition was taken into consideration because the American literature has shown how this variable has a strong influence on the health conditions and life expectancy of an individual. Therefore, generally those who declare precarious economic conditions also perceive a worse state of health (Brinkman et al. 2018). In Italian studies on Adolescents and Young Adults (AYA) cancer survivors (Tremolada et al. 2016; Tremolada et al. 2018; Tremolada et al. 2018) the authors didn’t find significative results on economic condition on psycho-social well-being, so we expected the same trend in this study.

Finally, the type of illness (hypothesis A5) was also taken into consideration in this research because, according to the Maurice-Stam et al. study (Maurice-Stam et al. 2009), the type of illness could also affect the perception of well-being in children. For this reason it is good to underline that the consequences vary according to the type of tumor and therefore the type of therapy and its duration. In addition, age-related life studies at the time of diagnosis showed that older children at the time of diagnosis report more depressive symptoms and higher stress levels later (Zebrack 2011; Kazak et al. 2010).

The second area of investigation (B) concerns the comparison between patients and healthy peers with respect to the answers given in the self-report questionnaires. In particular, studies concerning the quality of life of patients compared to control groups are controversial as reported below. We therefore want to evaluate whether patients in the first year of treatment have a different perception of life compared to healthy peers and in what direction (B1).

The second question of area B concerns the symptomatology situation. The studies in this regard were conducted mainly on survivors and obtained contradictory results. Some of them indicate that there are no significant differences in the quality of life or the presence of stress perceived by a group of patients and control subjects (Kazak et al. 2010). Others (Zebrack and Chesler 2002; Tremolada et al. 2017), show that in the group of survivors the perception of their quality of life is much lower compared to peers, with an increased risk of reporting symptoms of depression, somatic stress and self-esteem difficulties, especially if underwent Hematopoietic Stem Cell Transplantation (Tremolada et al. 2018). Another Italian study underlines a better health related quality of life and psychological well-being in AYA cancer survivors than healthy peers (Tremolada et al. 2016). We expected the same trend with better life perceptions in patients, especially at 1 year form the diagnosis, when their partially came back to their normal life (B2), while at 6 months we expected major reported symptoms in patients than controls.

A further research question of area B concerns the presence of possible differences in the cognitive problems reported by the patients being treated with respect to the control group (B3). In fact, in a study by Maurice-Stam et al., (Maurice-Stam et al. 2009), on a group of young adults recovered from cancer, we highlight first of all a gender difference in the choice of coping strategies: the off therapy girls report a type of coping more oriented to sharing emotions, while the males speak less of the illness, finding itself, in some cases, to choose avoidance strategies. In the same Italian study cited above, (Tremolada et al. 2016), the AYA cancer survivors perceived a best cognitive functioning in their life than healthy peers. In this case we could expect a similar result even among the young patients during therapy.

2. Results

2.1 The impact of socio-demographic variables on patients at 6 months (hypothesis A1, A2, A3, A4 and A5).

In the patient sample, we didn't obtain gender differences in the several self-reported psychological symptoms, perceived cognitive functioning and current/past/future life perceptions.

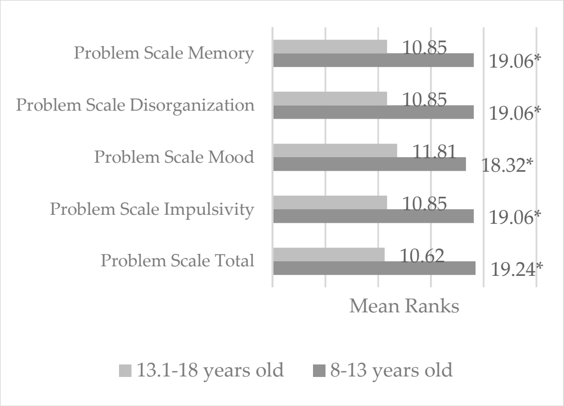
Regarding the research question A2, the Mann-Whitney test was carried out to assess whether there was a significant difference in the scores of the different questionnaire scales according to age groups (8-13; 13.1-18). The values of the test for the total scale of cognitive problems (U = 47.0; p = 0.01), for the impulsivity scale (U = 50.0; p = 0.01), for the mood problems (U = 62.5; p = 0.04), for the disorganization difficulties (U = 50.0; p = 0.01) and for memory problems (U = 50.0; p = 0.01) resulted significant. Examining the middle ranks we found that younger patients were those who reported more problems, as shown in figure 1.

Correlations between the familiar variables and the several scales didn't obtain significance and the perceived economic situation didn't influence these scales adopting the Kruskal-Wallis test. Also type of leukemia didn't influence the given variables adopting the Mann-Whitney test.

2.2 The impact of socio-demographic variables on patients at 12 months (hypothesis A1, A2, A3, A4 and A5).

In the patient sample, we didn't obtain gender differences in the several psychological symptoms, perceived cognitive functioning and current/past/future life perceptions.

Figure 1: Symptomatology and significant cognitive problems according to patients' age after 6 months from the diagnosis



Regarding the research question A2, the Mann-Whitney test was carried out to assess whether there was a significant difference in the scores of the different questionnaire scales according to age groups (8-13; 13.1-18). The values of the test for the past life perception (U = 52.5; p = 0.03) resulted significant. Examining the middle ranks it was possible to see that the older patients were those who reported lower past life perceptions (Mean ranks=11.25) than the younger ones (Mean ranks=17.65).

Regarding the group of patients, the analysis showed that the age of the parent was correlated with the BSI-18 arousal (rho = 0.36 p = 0.05). So as the parent's age increased, the somatization symptoms declared by the children/adolescents became higher. In addition, the parent's job-hours mean was related to the patient's perception of life so that the more workload for the parent was associated with dampen child's perception of life, both past (rho = 0.38; p = 0.05) and future (rho = 0.46; p = 0.01). This could be due to the fact that, after 1 year from the diagnosis, the parents returned to work and the children could feel abandoned. Table 1 shows these results.

Table 1: Analysis of the average ranks for the BSI-18 scale for the variable age at 1 year

	Parental age		**Parental schooling years**		**Parental hours of job/a week**		**Number of siblings**	
	rho	**p**	**rho**	**p**	**rho**	**p**	**rho**	**p**
Current life perception	-0.08	0.67	-0.07	0.73	-0.26	0.18	0.22	0.27
Past life perception	-0.19	0.33	-0.06	0.76	**-0.38***	**0.05**	0.009	0.97
Future life perception	-0.01	0.95	-0.08	0.70	**-0.46***	**0.01**	0.12	0.54
BSI-18 arousal	**0.36***	**0.05**	0.15	0.45	-0.24	0.21	-0.09	0.64
BSI-18 somatization	0.10	0.58	-0.24	0.21	-0.11	0.55	0.17	0.37
BSI-18 depression	0.20	0.29	0.15	0.45	0.05	0.80	0.04	0.82
BSI-18 total	0.36	0.06	0.06	0.75	-0.11	0.57	0.09	0.62

Problem Scale total	-0.002	0.99	0.12	0.55	-0.19	0.33	0.22	0.27
Problem Scale Impulsivity	-0.14	0.48	-0.05	0.80	-0.31	0.10	0.22	0.26
Problem Scale Mood	0.33	0.09	0.05	0.78	-0.11	0.56	0.16	0.42
Problem Scale Disorganization	0.08	0.67	0.02	0.93	-0.03	0.88	-0.05	0.79
Problem Scale Concentration	-0.01	0.96	0.17	0.39	0.13	0.51	0.12	0.55
Problem Scale memory	-0.10	0.60	-0.02	0.92	0.21	0.27	0.15	0.45

2.3. Comparison of scores reported by patients and healthy peers in the different scales examined at 6 months from diagnosis (questions B1, B2 and B3 at 6-months post diagnosis)

In order to answer the research question B1, the Wilcoxon test was performed for 2 dependent samples. There were significant differences in the average ranks comparing the patients with the healthy peers as regards the life perceptions, specifically the perception of current life (Z = -2.62; p = 0.01), with the group of patients reaching an average of 6.57 (SD = 2.03), while the group of healthy peers stood at 7.79 (SD = 1.42). In the other scales of life perception we didn’t obtain any significance both in the past life perception (Z = -1.44; p = 1.50) and in the future life perception (Z = -1.43; p = 0.15).

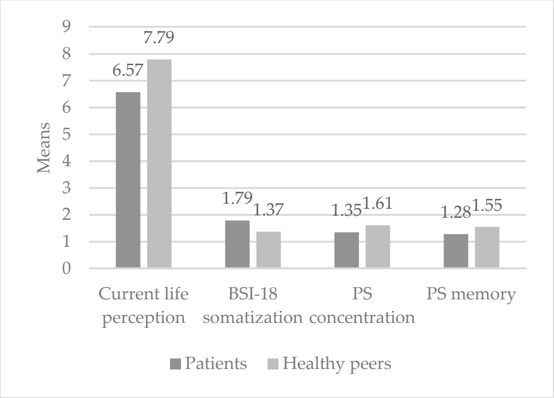
Responding to hypothesis B2, as regards the dependent variable of anxiety symptoms measured with BSI-18, there are no significant differences in the mean ranks between patients and matched healthy peers with regard to the symptoms of arousal (Z = -1.89; p = 0.6). On the other hand, the scores for the physical symptoms were significantly different in the two groups (Z = -2.54; p = 0.01), with an average of 1.79 (SD = 0.84) for the clinical group and 1.37 (SD = 0.33) for the control one. For the symptomatology concerning the depressive symptoms, no significance emerged (Z = -1.12; p = 0.90) and also for the overall symptomatology measured by total BSI (Z = -0.47; p = 0.64).

Finally, to analyze the hypothesis B3, the Wilcoxon test was always used with 2 dependent samples, inserting the scales of the Problem Scale questionnaire (PS) as dependent variables one at a time. In the Problem Scale (PS) questionnaire the difference between the mean ranks relative to the total score between the two groups was not significant (Z = -1.85, p = 0.06). The same trend was obtained for the impulsivity scale (Z = -1.23, p = 0.26), for the mood scale (Z = -0.78; p = 0.43) and for the disorganization one (Z = -1.61, p = 0.10). With regard to concentration difficulties, on the other hand, significant differences emerged between the mean ranks (Z = -2.27; p = 0.02) with a mean of 1.35 (SD = 0.45) for the group of patients and a mean of 1.61 (DS = 0.44) for the control group. Finally, the difference between the averages for memory problems was also significant (Z = -2.71; p = 0.01), with the patients settling at an average of 1.28 (DS = 0.45), lower than their peers of the control group (M = 1.55; DS = 0.37). Figure 2 shows a summary of the only significant differences between patients and healthy peers

2.4. Comparison of scores reported by patients and healthy peers in the different scales examined at 12 months from diagnosis (questions B1, B2 and B3 at 12-months post diagnosis)

In order to answer the research question B1, the Wilcoxon test was performed for 2 dependent samples, where there were found significant differences in the mean ranks between the two patient and healthy groups as regards the life perceptions, specifically the perception of past life (Z = -2.08; p = 0.04), with the group of patients reporting an average of 8.67 (DS = 1.61), while the group of healthy peers an average of 7.86 (DS = 1.86). The same trend was found in the future life perception scale (Z = -1.92; p = 0.05), where the clinical group reported a higher average of scores (M = 8.89; DS = 1.34) compared to that of the control group (M = 8.07; DS = 1.53), this meant that the ill children/adolescents reserved more hope for the future.

Figure 2: Significant differences between patients and healthy peers in the several assessed domains



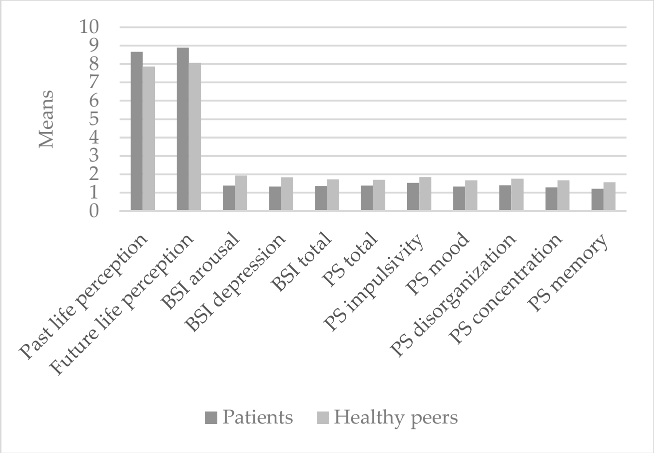
Responding to the hypothesis B2, regarding the possible difference between the two groups regarding the presence of anxiety symptoms measured with BSI-18, there were found significant differences in the mean ranks between patients and healthy peers as regards the arousal symptoms (Z = -3.13; p = 0.002), with the group of patients reporting a mean score of 1.38 (SD = 0.42) while the group of healthy peers of 1.93 (SD = 0.68). The same trend was found for the depressive symptoms (Z = -2.22, p = 0.001), with an average of 1.33 in patients (SD = 0.36) and 1.84 (SD = 0.86) for the peers. The overall symptomatology measured by total BSI was also different (Z = -2.95; p = 0.005), with a mean of 1.36 (SD = 0.29) for the group of patients and 1.73 (DS = 0.52) for the control group. While there was no significant difference between the two groups for symptoms related to somatization (Z = -0.2; p = 0.84).

Finally, to analyze the hypothesis B3, the Wilcoxon test was always used with 2 dependent samples, inserting the scales of the Problem Scale questionnaire (PS) as dependent variables one at a time. Significant differences were found between the ranks of the patient group and that of healthy peers. The trend of the means was always the same, i.e. the group of patients reported significantly lower means in the intensity of problems compared to those of hospitalized children/adolescents. The overall mean score of the Problem Scale (PS) was significantly different between the two groups (Z = -2.78; p = 0.05) with patients reporting an average of PS difficulties of 1.33 (SD = 0.35), while healthy peers stood at 1.70 (SD = 0.31). Impulsivity problems were reported with a mean of 1.53 (SD = 0.42) for the clinical group and a mean of 1.85 (SD = 0.48) in the control one, showing a significantly difference in their mean ranks (Z = -2.09; p = 0.04). The same trend was shown in the mood problems scale (Z = -2.41; p = 0.02), where the patient group reported a lower average (M = 1.33; SD = 0.35) compared to that of healthy peers (M = 1.67; SD = 0.56). A similar trend was also found for disorganization problems (Z = -3.20; p = 0.01), with the group of patients reporting an average of 1.40 (SD = 0.57) and the control group an average of 1.75 (SD = 0.36). Concentration problems were also reported differently in the two groups (Z = -2.65; p = 0.09), with a mean of 1.28 (SD = 0.35) for the group of patients and a mean of 1.67 (SD = 0.53) for the control one. Finally, the reported scores related to memory (Z = -2.69; p = 0.08) were significantly different along the two groups, with patients reporting an average of 1.21 (SD = 0.27) versus an average of 1.56 (SD = 0.45) reported by healthy peers. Figure 3 shows a summary of these results.

3. Discussion

Despite the increase in survival rates, the tumor disease implies a physical, social and psychological cost both for the adolescent patients and for their family. Alongside physical care, it is necessary to improve the quality of adaptation to the pathology, with particular attention to reestablishing the normal development trajectories that may have been compromised or altered.

Figure 3: Significant differences between patients and healthy peers in the several assessed domains



One of the challenges health professionals are required to respond to is to help patients maintaining physical health and psycho-social well-being (Bessell 2001). This study is built, therefore, from the need to fill some gaps in the literature with respect to the adaptation to adolescent tumor disease and, in particular, wants to deepen the implications at the psycho-social level within the first year after the communication of the leukemia diagnosis, therefore in the acute and chronic phase of the therapies.

The international literature analyzes the influence of socio-demographic variables on the quality of life and psychological wellbeing of off-therapy children, in fact Ness and colleagues (Ness et al. 2008), state that the young age at the time of diagnosis, the female gender and low levels of schooling and family income are associated and contribute to the severity of the physical and psychological sequelae reported by the off-therapy children.

However, even if the literature is quite consistent with the idea that the female gender is associated with major psychological and social problems (Butler et al. 2008) even in AYA cancer survivors (Tremolada et al. 2016), no significant differences in any of the three scales have emerged in the present research, that is neither in that of the perception of life (current, past and future), nor in the psychological well-being and not even in the problem difficulties both 6 months and 1 year after diagnosis. It seems that in front of an event like that of the disease boys and girls are more homogeneous in their reports.

Another aspect that affects the levels of perceived stress is the age at the time of diagnosis: those diagnosed with cancer in early adolescence seem to declare a worse psychological adaptation of those who received the diagnosis earlier (Zebrack 2011; Kazak et al. 2010). In this study the patients at 6 months from the diagnosis belonging to the 8-13 years of age range, have shown higher anxiety, impulsivity and more intensive problems in mood, disorganization and memory domains. This result could be due to the fact that children that have a greater age could have more problem solving strategies to cope with the illness and could have more communication exchanges with adults (parents, health professionals, other ill adolescents) comparing with the pre-adolescents. This result isn't in line with the literature and future studies with an ampler sample should clarify better this phenomenon.

On the other hand, as regards the situation at 1 year from the diagnosis, patients between 8 and 13 years old are those who had a significantly better past perception of life compared to the 13.1-18 years old group. In this case, it is very likely that the older children, 5 years before the disease, were preparing to enter the puberty phase, this implies many changes at the hormonal and physical level. In those years, they could have experienced great disturbances that still today remember as a difficult period of their life.

Since the literature revealed that the variables related to family relationships (perceived economic condition, parents' schooling years, parents' age and number of siblings) were closely associated with higher levels of personal growth (Barakat et al. 2006; Mattsson et al. 2008), the factors related to parents and siblings were investigated, with the expectation that they would be predictive of a higher level of perceived well-being and, therefore, of a lower negative impact of the disease. We didn't obtain relevant or strong results, only a possible association between higher parental mean hours of job and lower patients' future life perceptions. This could be an influence due to the family organization that influences hope. Increasing the hours of work of the parent, given that the patient stays much better, decreases the time that the latter can spend with their sons and then the patients could feel abandoned. Also perceived economic condition didn't impact on patients' wellbeing as found in Italian childhood cancer survivors (Tremolada et al. 2016). Also type of leukemia didn't emerge as an important factor, probably due to the major concentration of Acute Lymphoblastic Leukemia than Acute Myeloid Leukemia.

Comparing the patients' self-reports with those of matched healthy peers is the second important focus of our study.

Research on off-therapy children seems to point out that adolescents and young adults out of therapy declare themselves to be in good psychological health, declare a high level of quality of life, are optimistic and make long-term plans for their future (Maurice-Stam et al. 2009; Servitzoglou et al. 2007), with only a small minority presenting experiences of anxiety, depression or symptoms of stress trauma due to the experience of illness. In the following study, at the time point 6-months post-diagnosis, it emerges that the patients perceive a present life worse than that of healthy peers and more somatization problems, but less concentration and memory problems. These data can be easily explained if we consider the short and long-term strong sequelae that such invasive therapeutic protocols, such as those for the treatment of childhood leukemia, may have on a person's physical and mental functioning, even if their concentration and memory remained for them stable. The higher somatization symptoms in patients than healthy peers were also found in studies on childhood cancer survivors (Zebrack et al. 2011) with more limitations in their daily routines (McBride et al. 2011), especially if they underwent HSCT (Zanato et al. 2017). The pre-adolescents and adolescents with leukemia are in the most critical phases of their psychophysical development and sexual maturation that could lead them to overestimate some small physical problems that arise; we also remember that the social adaptation and the personality of an adolescent are strongly influenced also by the perception that he/she has of his/her body and is, in fact, known that adolescents tend to declare a deep dissatisfaction with their body image, especially true aspect between females (Wu et al. 2006).

This significant difference does not result in the comparison between the two groups at 1 year from the diagnosis, a period in which they probably start to feel better even physically for a more maintenance therapy and a partial return to their daily activities such as school. At this time, patients also reported better life perceptions both past and future. They are more hopeful for the future and they re-consider positively also their past life than healthy peers. Probably this positive trend and the re-appropriation of their normality led patients to report less symptoms and less problems in their lives than healthy peers. Patients were also carefully followed by mental health professionals and by the teachers individually or in group so to empower their coping strategies and cognitive functioning during the treatment cycles. The results obtained in the present research, with regard to the analysis of this aspect, are in line with the optimistic literature (Gerhardt 2007), as the children/adolescents in therapy declare less cognitive problems, so much so that they record lower scores than healthy peers in all the Problem Scale subscales.

3.1. Strengths and limits

Being a research project carried out by a single center would be interesting to see what happens in other centers, by enlarging the number of patients we could find further significant factors that could influence patients' psychological well-being. Also it would be interesting to also expand the choice of tests to be used, for example not to use only self-report tests that could be influenced by social desirability. First of all, it is necessary to remember that the questionnaires we administer are only self-report, so they do not allow to make an objective assessment of the real cognitive performance of a person, because they are based on perceptions of their personal abilities. This type of questionnaire can trigger the phenomenon of social desirability, so a person in giving answers, sometimes unconsciously, can overestimate their abilities in such a way as to result in an image of more positive self. Furthermore, the aspect of the interview could be observed to evaluate these aspects.

Although they are exploratory studies and the sample is reduced, there are no Italian studies in this regard and the international literature focuses mainly on other constructs compared to these. In fact, in some situations the study presents results that go against the results of other research projects on the international scene. This could be due to a different cultural aspect that should be investigated with other tools.

The final aim of this project is to perform a specialized assessment of the various psychosocial aspects related to the wellbeing and quality of life of these patients in order to identify those areas that are most problematic for them and then prepare ad hoc psychologist and/or psychotherapeutic interventions, for all those preadolescents and adolescents and their families who are most at risk from the psychological point of view or for all those who feel the need.

4. Materials and Methods

4.1. Procedure

The research project was part of the study: "Family factors predicting the short and long-term adaptation and quality of life in children with leukemia" approved by Hospital of Padua Ethical Committee. Being a longitudinal research design, the psychological assessment developed in 5 crucial moments of the child's illness in which important evaluations were foreseen, at the level of the therapeutic protocol, to see if the child's leukemia had reacted well to the therapies. T1 was located after the first week of steroid therapy (day +8); T2 was following the Re-Induction chemotherapy phase (response therapy with risk band assignment), which corresponded to approximately 6 months from diagnosis; T3 occurred approximately at the time of re-insertion of the child at school, during the Maintenance phase, one year after diagnosis of leukemia.

In particular, our work will focus mainly on the second (T2) and third phase (T3) in which we will analyze the perception of life, psychological wellbeing and cognitive difficulties of the children and adolescents at 6 months and at 1 year from the diagnosis.

4.2. Participants

All patients were Caucasian with a mean age of 12.98 (SD=2.91). Tables 2 and 3 show the socio-demographic characteristics of the children/adolescents involved in the study and their parents respectively 6 months and 12 months after diagnosis. Furthermore, as a control group, healthy children / teens and their families were evaluated with the same battery of instruments both to validate the instruments of international origin and to compare statistically the two populations. The patients were matched by age, gender, family composition and economic situation perceived by the group of healthy peers, obtaining a number of 31 couples at 6 months and 31 couples at 1 year. The children and adolescents in the control group met the following eligibility criteria: no history of life-threatening or chronic illness or injury and an absence of learning or sensory problems and other pathological aspects. The control group of healthy peers was enrolled in secondary schools, youth groups, and university faculties in the same region as the patients (Veneto, northeast of Italy).

4.3. Instruments

4.3.1. Brief Symptom Inventory 18 (Derogatis 2000).

The Brief Symptom Inventory 18 (BSI-18) consists of 18 items grouped into three dimensions of six items, serving as a screening for depression, somatisation and anxiety. Respondents are asked to refer about how they felt the last 7 days, and each item is rated on a 5-point Likert scale from 0 (not at all) to 4 (extremely). BSI-18 was used to assess psychological outcomes in long-term survivors of childhood cancer (Tremolada et al. 2016; Recklitis et al. 2006) and in mothers of children under treatment for leukemia (Tremolada et al. 2013; Tremolada et al. 2012), demonstrating good internal consistency from a Cronbach's alpha of 0.83 to 0.92.

Table 2: Socio-demographic characteristics of patients and healthy groups and their families at 6 months (T3)

Children/teens' socio-demographic characteristics		Control group		Patients	
		Frequency	%	Frequency	%
Gender	Males	13	41.9	12	38.7
	Females	18	58.1	19	61.3
	Total	31	100	31	100
Age groups	8-13 years old	17	54.8	18	58.1
	13,01-18 yaers old	14	45.2	13	41.9
	Total	31	100	31	100
		Mean	SD	Mean	SD
Current age		13.32	2.42	12.98	2.91
Type of leukemia	Acute Limphoblastic Leukemia			22	71.0
	Acute Myeloid Luekemia			9	29.0
	Total			31	100

Family socio-demographic characteristics		Control group		Patients	
		Frequency	%	Frequency	%
Respondent parent's educational level	Primary school	0	0	2	6.5
	Secondary school 1^{st} grade	9	29	14	45.2
	Secondary school 2^{nd} grade	9	29	11	35.5
	Degree	1	3.2	1	3.2
	Post Degree	7	22.6	3	9.7
	Missing	5	16.1	0	0
	Total	31	100	31	100
Respondent parents' job	Job leave/housewife	1	3.2	14	45.2
	Abandonment / loss of work Part-	4	12.9	5	16.1
	time	7	22.6	10	32.3
	Full-Time	17	54.8	2	6.5
	Missing	2	6.5	0	0
	Total	31	100	31	100
Respondent parents' workload	≥ 50 hours/a week	3	9.7	1	3.2
	40-49 hours/a week	5	16.1	8	25.8
	30-39 hours/a week	10	32.3	5	16.1
	20-29 hours/a week	5	16.1	6	19.4
	10-19 hours/a week	2	6.5	3	9.7
	0-9 hours/a week	2	6.5	8	25.8
	Missing	4	12.9	0	0
	Total	31	100	31	100

Table 3.: Socio-demographic characteristics of patients and healthy groups and their families at 12 months (T4)

Children/teens' socio-demographic characteristics		Control group		Patients	
		Frequency	%	Frequency	%
Gender	Males	12	41.4	12	41.4
	Females	17	58.6	17	58.6
	Total	29	100	29	100
Age groups	8-13 years old	14	48.3	14	48.3
	13,01-18 yaers old	15	51.7	15	51.7
	Total	29	100	29	100
		Mean	SD	Mean	SD
Current age		13.56	2.73	13.45	2.96
Type of leukemia	Acute Limphoblastic Leukemia			23	79.3
	Acute Myeloid Luekemia			6	20.7
	Total			29	100
Family socio-demographic characteristics		Control group		Patients	
		Frequency	%	Frequency	%
Respondent parent's educational level	Primary school	0	0	0	0
	Secondary school 1st grade	7	24.1	8	27.6
	Secondary school 2nd grade	12	41.4	16	55.2
	Degree	0	0	1	3.4
	Post Degree	7	24.1	4	13.8
	Missing	3	10.3	0	0
	Total	29	100	29	100
Respondent parents' job	Job leave/housewife	1	3.4	15	51.7
	Abandonment / loss of work	2	6.9	4	13.8
	Part-time	6	20.7	7	24.1
	Full-Time	18	62.1	3	10.3
	Missing	2	6.9	0	0
	Total	29	100	29	100
Respondent parents' workload	≥ 50 hours/a week	3	10.3	1	6.9
	40-49 hours/a week	7	24.1	6	20.7
	30-39 hours/a week	10	34.5	4	13.8
	20-29 hours/a week	3	10.3	3	10.3
	10-19 hours/a week	1	3.4	5	17.2
	0-9 hours/a week	1	3.4	9	31.0
	Missing	4	13.8	0	0
	Total	29	100	29	100

4.3.2. Socio-demographic and medical questionnaire

This questionnaire is used for the collection of information useful for understanding the socio-economic and cultural level of the family. There are questions to investigate the age of the parents, the number of years of schooling and the qualification achieved, the work situation before and after the disease, demographic data of the family (number of people, number of children, housing situation, economic situation, place of residence) availability of time for the child.

These are also medical clinical records with these data: type of leukemia, therapeutic protocol and effects of the therapies; number of days of hospitalization; number of blasts at crucial moments of assessment; the level of risk (SR, MR, HR); degree of toxicity of the disease.

4.3.3. Cognitive Problems Scale

It is a 25-item questionnaire, used in other Italian studies (Tremolada et al. 2013; Tremolada et al. 2012), that investigates the presence and intensity (range from 1 = 'never a problem' to 3 = 'often a problem') of cognitive problems shown by childhood cancer experience survivors or mothers of children under treatment for leukemia in the last 2 weeks. The Cognitive Problems Scale has been administered to 118 Italian parents of children with cancer, demonstrating global internal consistency (Alpha = 0.89). A Varimax rotated confirmatory factor analysis, explaining a good proportion of the total variance (56.63%), identified five subscales: Memory (5 items; alpha = 0.78); Mental Disorganization (8 items; alpha = 0.82); Labile Mood (3 items; alpha = 0.75); Impulsivity (4 items, alpha = 0.73); Concentration (5 items; alpha = 0.67); these five dimensions can be combined into a total score, Cognitive Problems score (25 items; alpha = 0.89). Cognitive Problems Scale is derived from the Childhood Cancer Survivor Study battery, and the wider purpose of this measure is to assess the frequency of possible cognitive problems that may arise in people that are under huge stress.

4.3.4. Ladder of life

The children/adolescents have to evaluate, using a 1–10 point scale, the quality of their present life, their quality of life 5 years before and how satisfying their life will be in the future (5 years later after). With this instrument, we can obtain information about individual perception of the past, the present and the future. It has been administered to 118 Italian mothers of children with cancer, demonstrating good global internal consistency (Cronbach's alpha = 0.73).*4.4. Statistical analyses plan*

To respond to the research hypotheses, several statistical analyses will be carried out. Due to the reduced number of subjects, we decide to run only non-parametric tests. First, to answer the research question A, it will be checked whether there are differences in the scale of the questionnaires used in the patients, according to gender (A1), age groups (A2) and of the diagnosis (A5) using the non-parametric Mann-Whitney test.

Subsequently, through Spearman's non-parametric correlations, we want to verify if there are family-related anamnestic variables (hypothesis A3) associated with the several dependent variables (the different scales of the self-report questionnaires). In conclusion, to assess whether the economic condition (hypothesis A4) can be associated with our independent variables we will use the non-parametric test of Kruksal-Wallis being the economic condition a three-level variable.

To test hypothesis B, the Wilcoxon test will be performed on two dependent samples, which evaluates the possible differences between the percentile averages in the different scales relating to the perception of life (B1) and the symptomatology assessed by BSI-18 (B2), and the cognitive problems with the Problem Scale (B3) between the group of healthy peers and the group of patients.

5. Conclusions

As regards socio-demographic variables that could influence patients' well-being, life perceptions and cognitive difficulties it is possible to conclude that gender, family variables, perceived economic condition and leukemia type do not have this role. On the other hand, age could influence the psychological well-being of patients, with the 8-13 age group more at risk.

Comparing the group of patients with that of healthy peers this study showed that: healthy peers have a better perception of current life and lower percentage of somatization symptoms than patients after 6-months post-diagnosis. On the other hand, healthy peers reported more problems dealing with impulsivity, mood, disorganization, concentration and memory than patients both at 6-months and 1-year form diagnosis. Healthy peers reported also more anxiety and depression symptoms than patients and worse past and future life perceptions than patients at 1-year from diagnosis.

The inclusion of mental health professionals in the multidisciplinary treatment team is helpful in addressing potential difficulties in adjustment after diagnosis. Early involvement in treatment may allow for earlier detection when problems arise and allow the patient and clinician to build the rapport and trust that is needed to address problems later on. Supportive psychotherapy, in the office or at the bedside, may be useful in addressing adjustment problems.

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