IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 12 Ser.7 (December. 2023), PP 23-31
www.iosrjournals.org

Impact Of Psychoeducation On Relapse Rates In Early-Onset Schizophrenia

Sonia Sehim[1], Mohamed Nedjari[2]
[1](Department Of Medicine, Psychiatric Specialty / University Benyoucef Benkhedda Of Algiers 1, Algeria)
[2](Department Of Medicine Psychiatric Specialty / University Benyoucef Benkhedda Of Algiers 1, Algeria)

Abstract:
Background*: In early-onset schizophrenia, there exists a critical period, corresponding to the first five years of the illness, during which vulnerability to relapses and deficits associated with psychosis are highest. This risk appears to be primarily linked to medication non-adherence. Current recommendations for therapeutic management of these conditions include antipsychotic medications as well as non-pharmacological interventions, notably therapeutic education (TE) or psychoeducation. Within this context, we conducted a research study with the objective of assessing the impact of a psychoeducational program on the two-year relapse rate in patients with early-onset schizophrenia, compared to a control group.*
Materials and methods*: this is a prospective, comparative and randomized study, including ninety-two patients suffering from early schizophrenia evolving over five years, during a period of 24 months, from September 2021 to September 2023. The patients were recruited from the consultation or hospitalization department of the specialized psychiatric hospital in Algiers. The participants were randomly divided into two equal groups of 46 patients "psychoeducational group versus control group". All patients receive antipsychotic treatment. Validation of the cases was carried out by referring to the diagnostic criteria of the DSM-5. Two assessments were made, clinical (PANSS) and compliance (MARS). Evaluation parameters: relapse, compliance and psychopathology.*
Results: *The overall sample consisted of ninety-two patients, sixty-five men, and twenty-seven women, with an average age of 27.4±6 years. The majority, were single and lived with their families. Most had an educational level ranging from intermediate to secondary. Half of the patients were on monotherapy. 45.7% experienced a relapse, 35.9% had 2 to 3 relapses, and only 18.4% had no relapse. The average duration of hospitalization was approximately 52 days. Patients were assessed with moderate to severe impairment on the PANSS scale (69.9/210). 58.7% of patients had poor therapeutic adherence, with a MARS score less than or equal to 5. Treatment discontinuations were associated with a lack of insight (29.3%), side effects (19.6%), and psychoactive substance use (16.3%). There were no significant differences in sociodemographic, clinical, and evolutionary data between the two groups. At the end of 24 months, the impact of the psychoeducational program was significant in the psychoeducational group compared to the control group. Regarding relapses, a decrease in the medium-term relapse rate was observed (8.7% in the psychoeducational group versus 37% in the control group). Furthermore, these relapses were significantly correlated with the number of psychoeducation sessions conducted (p=0.031). It is worth noting that the duration of hospital stay after a relapse was reduced in the psychoeducational group compared to the control group, respectively, 37.5 days versus 61 days. Regarding the impact of psychoeducation on assessment scales, a significant improvement in therapeutic compliance was observed in the psychoeducational group, with a MARS score greater than 5 in 82.6% of patients compared to 39.2% in the control group. There was also an improvement in symptomatology with an average PANSS score of 45.7/210, compared to 69.7/210.*
Conclusions: *Psychoeducational measures remain a cornerstone in the health process. Their practices and benefits are widely acknowledged for numerous parameters of psychotic pathology. It is crucial to integrate them as early as possible in the management of this chronic condition to prevent detrimental consequences for the young patient.*
Key words: *Schizophrenia – Therapeutic adherence - Psychoeducation – Relapse.*

Date of Submission: 18-12-2023 Date of Acceptance: 28-12-2023

I. Introduction

Schizophrenia is a chronic and disabling illness that affects 1% of the young general population [1.] Despite recent advances in antipsychotic medications, the impact of exclusively medication-based therapeutic strategies remains limited in improving the overall functioning of schizophrenic patients. In schizophrenia, most

of patients are prone to experiencing multiple episodes of acute symptomatology, leading to severe long-term functional impairment. This observation was confirmed by the CATIE study [2], which demonstrated that 74% of patients discontinue their antipsychotic treatment within 18 months after an acute psychotic episode, thereby increasing their risk of relapse. Since the 1990s, the concept of early-onset schizophrenia or early psychosis has garnered growing interest as it represents a crucial moment during which clinical interventions can significantly influence the course of the disease [3-4]. Research on emerging psychosis suggests that there is a critical period, corresponding to the first five years of the illness, during which vulnerability to relapses and deficits associated with psychosis is highest, and this risk appears to be primarily linked to medication non-adherence [5-8]. Studies also indicate that during this critical period, psychotic illness responds particularly well to therapeutic interventions [9-10]. It becomes, therefore, crucial to treat psychosis early to offer the best chances of recovery to the affected individual. Current therapeutic management consensus for schizophrenia includes antipsychotic medications and non-pharmacological interventions, particularly therapeutic education (TE) or psychoeducation [11]. In this context, TE has been the subject of various national and international recommendations, advocating for the systematic integration of psychoeducation into the therapeutic arsenal for individuals with schizophrenia [12-14]. Indeed, Correl and colleagues' meta-analysis in 2018 [15] demonstrated the superior efficacy of a targeted early intervention, including psychoeducation, for young patients with emerging psychotic disorders compared to conventional care. The authors analyzed data from 2176 patients across 10 randomized trials and highlighted the superiority of early intervention in reducing therapeutic non-adherence, re-hospitalization rates, and the severity of both positive and negative symptoms. It is within this framework that we aimed to conduct this research project, with the objective of evaluating the impact of a psychoeducational program on the two-year relapse rate in patients with early-onset schizophrenia, compared to a control group receiving only usual information about their illness.

II. Material And Methods

Type of study:

This is a prospective, comparative, and randomized study.

Study Population:

We included ninety-two patients diagnosed with schizophrenia evolving over a period of five years in our research study. The participants, of both sexes, were aged between 16 and over 30 years, and the study spanned 24 months from September 2021 to September 2023. Patients were recruited from the inpatient and outpatient department of the specialized psychiatric hospital DRID Hocine, Kouba, Algiers, Algeria. The ninety-two patients were randomly divided into two equal groups of forty-six patients, each one was based on the type of care: one group receiving the psychoeducational program in addition to antipsychotic treatment (the "psychoeducational group"), and the other undergoing a control therapy for the same duration (the "control group"). All patients received antipsychotic treatment.

Exclusion Criteria:

Patients with a schizophrenic disorder lasting more than five years, delusional disorders, and those with neurological disorders were excluded from the study.

Evaluation Tools:

a) Case validation was conducted by referring to the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) [16].

b) For this study, we chose to utilize the Positive and Negative Syndrome Scale (PANSS) developed by Kay et al [17] to assess the severity of clinical symptomatology. The scale consists of 30 items, each with a specific definition, distributed across three subscales: positive, negative, and general psychopathology. The total score can range from 30 to 210; a higher score indicates a more symptomatic manifestation of the illness.

c) To assess adherence behavior, we employed the Medication Adherence Rating Scale (MARS) developed by Thompson [18]. This scale consists of a 10-item self-questionnaire that determines the risk of treatment discontinuation. The threshold score was set at 5. A score higher than 5 indicates good adherence, while a score equal to or less than 5 indicates poor adherence. If the score is less than 5, a hetero-questionnaire of the MARS is proposed to the patient to determine the reasons for discontinuation.

Data Collection Method:

Patients meeting DSM-5 diagnostic criteria were all assessed after receiving information about the study's objectives, the tools used, and its procedures. Patients were recruited for the study only after obtaining their informed consent. Data collection was conducted with respecting the anonymity and the confidentiality of information, particularly for patients in the psychoeducational treatment group. The data collection procedure

involved administering a questionnaire that assessed sociodemographic, clinical, and disease progression characteristics (duration of illness, number of relapses, causes of relapses). The questionnaire was standardized for each patient. Case validation was performed by using specific scales: at the end of the interview, which took approximately 45 minutes to 1 hour for each patient, diagnostic confirmation was carried out according to DSM-5 criteria. Clinical evaluation was conducted by using the PANSS scale (Kay et al), which assesses the intensity of psychotic symptoms, both positive and negative, as well as general psychopathology, rated from 30 to 210 points. Therapeutic adherence was assessed by using the Medication Adherence Rating Scale (MARS).

Statistical Analysis

All data collected from the pre-established questionnaire were entered into the SPSS software version 26. Qualitative variables were expressed as percentages or frequencies, while quantitative variables were expressed as means, standard deviations, and ranges. Pearson's chi-square test was used to compare qualitative variables. The comparison between a qualitative and a quantitative variable was performed using the student's t-test. The significance threshold was set at 5% ($p \leq 0.05$).

Description of the Psychoeducational Program

We utilized the "Antipsychotic Medication Education Module" by R.P. Lieberman [19]. It was translated into the Algerian dialect of Arabic, respecting the local socio-cultural context. The aim of this psychoeducational program is to promote patients' autonomy in managing their antipsychotic treatment. The four competency domains include:

1. Acquiring information about medications (antipsychotics).
2. Knowing how to correctly take medications and evaluate their effects.
3. Understanding the side effects of treatment.
4. Learning to address problems related to medication adherence with healthcare professionals.

The 46 patients in the psychoeducational group were divided into five (5) subgroups, with a maximum of 8 to 10 participants in each subgroup. The educational program consisted of twelve sessions, with one session per week lasting from 1 hour to 1 hour and 30 minutes for each group, depending on the session's theme. The groups were led by, a pair of doctors and sometimes a doctor / psychologist pair. All sessions were conducted interactively.

- Monitoring parameters were statistically comparable in both groups.
- The primary observation parameters for evaluating psychoeducational teaching at the end of the study were relapses and their duration compared to the control group. Each re-hospitalization was considered indicative of a relapse, following a conventional stance in the literature.
- Secondary parameters mainly consisted of comparative reassessments (at inclusion versus the end of the program) of adherence (MARS) and the severity of psychopathology (PANSS).
- The same investigators, outside the psychoeducation sessions, conducted evaluations. Five assessment visits were conducted (at day 0, month* 3, month 6, month 12, month 18, and 24). (*M: month).

III. Result

Inclusion

Descriptive results of the overall sample

Sociodemographic Characteristics and Addictive Behaviors: Our sample consisted of 92 patients, including 65 men and 27 women, with a sex ratio of 2.4. The average age was 27.4 ± 6 years, with a predominant age group between 20 and 29 years. The majority of participants were single and lived with their families. Regarding the level of education, most of patients (76%) were distributed between the intermediate and secondary levels, 22.8% had a university education, and 6.5% had a primary level of education. Half of the patients had a moderate social status. On the professional level, 58.7% were unemployed. Regarding addictive behaviors, we observed that 20.7% of our patient's consumed tobacco, and 7.6% consumed a combination of tobacco and cannabis.

Clinical and evolutionary characteristics more than half of the patients (57.6%) experienced an acute onset of their illness. 70.7% exhibited a productive subtype of schizophrenia, while 28.3% showed disorganized schizophrenia. Nearly one-third of the patients had a pre-morbid schizoid personality. Over half of the patients were on monotherapy with second-generation antipsychotics. The majority (89.1%) had a duration of illness equal to or less than 5 years, with 10.9% having an evolution of less than a year. Regarding relapses, 45.7% of patients experienced a single relapse, 35.9% had 2 to 3 relapses, and 18.4% had no relapses. The average duration of hospitalization at inclusion for the entire sample was around 52 days. Concerning evaluations, the mean total PANSS score for our patients was 69.9 at inclusion, indicating a moderate to severe overall impairment. For the evaluation of adherence at the initial visit, the mean MARS score for the entire sample was 4.2 ± 3.457. At this point, 58.7% of patients exhibited therapeutic non-adherence with a general MARS scale

score less than or equal to 5, while 41.3% of patients were adherent. Evaluations from the MARS hetero-questionnaire revealed, in ascending order, plausible causes of discontinuation of pharmacological treatment: 29.3% of patients had poor insight, 19.6% cited antipsychotic side effects, 16.3% engaged in psychoactive substance use, 12.0% mentioned stressful events, and finally, 9.8% indicated therapeutic resistance.

Descriptive results of the comparative sample

There is no significant difference concerning sociodemographic, clinical, and disease progression variables between the psychoeducational group and the control group. No difference was also noted in clinical evaluations using the PANSS scale and therapeutic adherence assessed with the MARS scale, respectively (p=0.067 and p=0.397) (Table n° 1).

Table n° 1: Sociodemographic, clinical, developmental and assessment characteristics of psychoeducational versus control groups

Variable	Psychoeducational group (n=46)	Control group (n=46)
Mean age	26,3±4	26,2±7
Gender		
Male	60,9% (n=28)	80,4% (n=37)
Female	39,1% (n=18)	19,6% (n=09)
Family situation		
Single	87,0% (n=40)	76,1% (n=35)
married	10,9% (n=05)	17,4%(n=08)
Divorced	02,1% (n=01)	06,5% (n=03)
Level of education		
Primary	32,6% (n=15)	06,5% (n=03)
Average	06,5% (n=3)	43,5%(n=20)
Secondary	26,1 % (n=12)	39,1%(n=18)
Academic	34,8% (n= 16)	10,9 %(n=05)
Socio-professional category		
Civil servant	17,4% (n=08)	17,4% (n=08)
Middle management	06,5% (n=03)	00,0% (n=00)
Senior manager	00,0% (n=00)	02,2% (n=01)
Student	23,9% (n=11)	04,3%(n=02)
Liberal profession	04,3% (n=02)	02,2% (n=01)
On disability	02,2% (n=01)	02,2% (n=01)
Unemployed	45,7% (n=21)	71,7% (n=33)
Substance abuse	14,0%(n=21)	17,3% (n=26)
Premorbid personality		
Schizoid	21%	26%
Mode of onset of disease		
Acute	29%	24%
Insidious	17%	22%
Duration of course of the disease		
6 months – 1 year	10.9%	10.9%
≤ 5 years	89.1%	89.1%
Number of hospitalizations	Mean = 1,4	Mean = 1,5
Duration of hospitalization	Mean =53 days	Mean = 51 days
PANSS Total Score	69.7	70.6
MARS Score		
≥ 5	44.8% (n=21)	37.9% (n=17)
≤ 5	55.2% (n=25)	62.1% (n=29)

After the psychoeducational program

Evaluation of psychoeducational therapy results (Table n° 2)

Table n° 2: Distribution of patients according to attendance and participation in psychoeducational workshops

	Psychoeducational group Effective (n=46)	Percentage
1. Attendance at appointments		
Yes	44	95%
No	2	5%
2. Number of participation in psychoeducational sessions		
< Six	1	2,2%
Six	3	7%
Eight	14	30,1%
> Eight	28	60,7%

3. Participation in the workshops		
Minimal	12	26,1%
Average	32	69,5%
Bad	2	4,4%
4. Themes of participation in the group		
Ask questions	8	17,6%
Mixes easily with the group	12	26,1%
Participate in play	10	21,6%
Participates little	16	34,7%
5. Reasons for poor group participation		
Lack of concentration	3	7%
Timidity	7	13 ,4%
Severity of illness	2	5%
Prefers individual therapy	8	17 ,6%
Bad insight	4	9%
No problem	22	48%

Two-year comparative evaluations of goth groups

In our study, no cases of death or dropout from the psychoeducational program were recorded.

Impact of psychoeducation on relapse rates compared to the control group:

At the end of our program, among the 46 patients in the control group, 17 patients (37%) experienced one or more relapses. In contrast, among the 46 patients in the psychoeducational group, only 4 patients (8.7%) relapsed once (Table n° 3; Fig. n° 1).

Table n° 3: Percentage of relapse at 2 years

	Psychoeducational group (Antipsychotics + psychoeducational therapy) **(n=46)**		**Control group** (Antipsychotics only) **(n=46)**	
	Frequency	**%**	**Frequency**	**%**
Male	1	2%	5	10,9%
Female	3	6,7%	12	26,1%
Total	**4**	**8,7%**	**17**	**37%**

Statistical analysis reveals a significant difference in the number of relapses between the two groups (p=0.004), with a significance level below 0.05. Additionally, in the psychoeducational group, a significant relationship is observed between relapse and the number of completed sessions (p=0.031).

Patients who relapsed had participated in fewer than or equal to six psychoeducational sessions, potentially attributed to the severity of the illness or poor insight. Furthermore, these relapses were significantly correlated with the number of psychoeducational sessions attended (p=0.031).

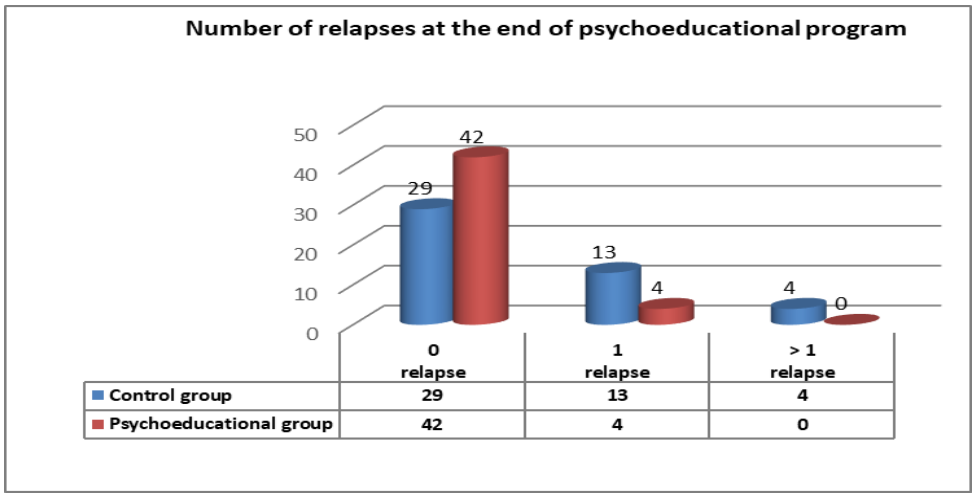

Figure n° 1: Distribution of patients by number of relapses at the end of the psychoeducational program of the two groups

Impact of psychoeducation on hospitalization duration compared to the control group:

At the end of the psychoeducational program, it is also noteworthy that the duration of hospital stay after relapse was reduced in the psychoeducational group compared to the control group, namely 37.5 days versus 61 days. This difference was significant (p = 0.002) (Fig. n° 2).

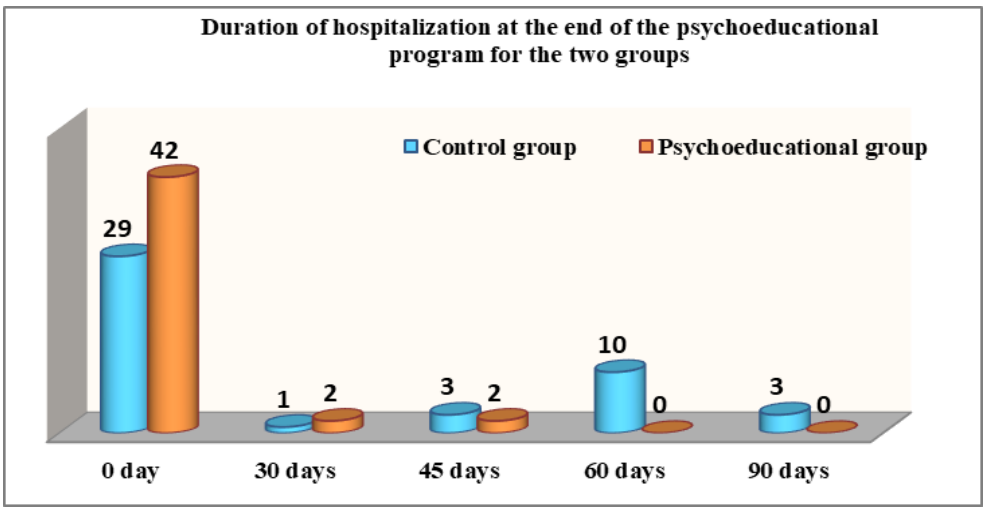

Figure n° 2: Distribution of patients by length of hospitalization at the end of the psychoeducational program of the two groups

Impact of Psychoeducation on Evaluation Scales Compared to the Control Group:

Self-Evaluation Scale "MARS": Significant improvement in adherence to antipsychotic treatment is noted in the psychoeducational group compared to the control group (p=0.000), with an improvement in scores favoring the psychoeducational group (Table no°4; Fig. n° 3).

Table n° 4: Scores of the assessment scales (MARS/PANSS) at the end of the psychoeducational program of the two groups

	Psychoeducational group	Control group
Scores MARS final		
MARS ≥ 5	38 (82,60%)	18(39,20%)
MARS ≤ 5	8 (17,40%)	28 (60,80%)
PANSS		
To the inclusion	69,7 /210	70,6/210
End of the program	45,7/210	71,4/210

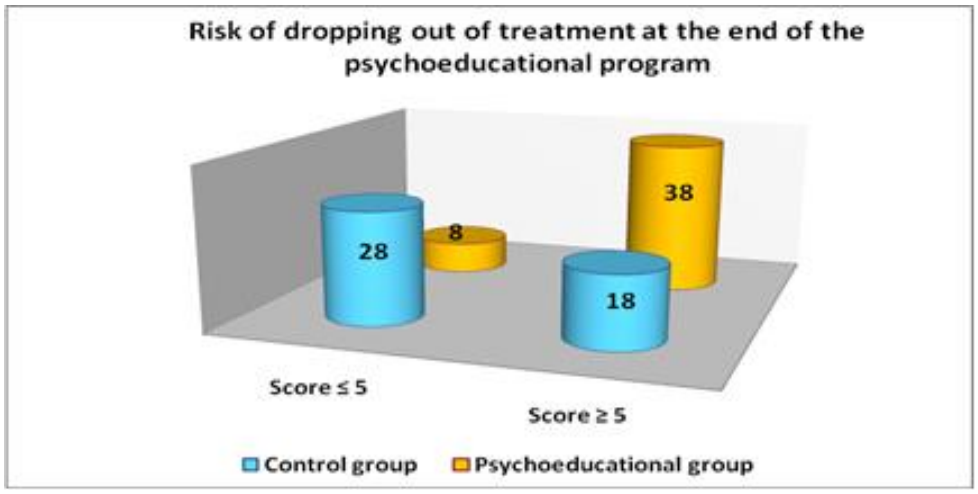

Figure n° 3: Assessment of the risk of treatment abundances at the end of the psychoeducational program of both groups

Hetero-Evaluation Scale "PANSS" (Table 4; Fig. n°4):

First, there was an improvement in the average PANSS global scores for the psychoeducational group at the end of the program compared to the scores at inclusion (45.7/210 versus 69.7/210).

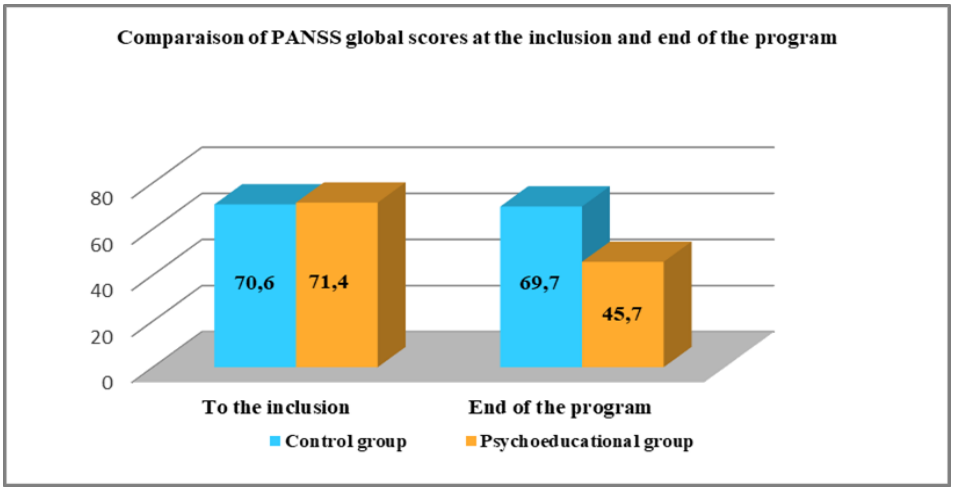

Figure n° 4: Comparison of overall PANSS scores at the end of the psychoeducational program of the two groups

Then, the mean PANSS global score for the control cases was practically similar, 70.6/210 at inclusion compared to 71.4/210 at the end of the program. Finally, concerning the comparison with the control group, the difference was significant in the improvement of the final PANSS mean score for patients in the psychoeducational group compared to the control group (45.7/210 versus 71.4/210; p=0.002).

IV. Discussion

Comparing with other studies in the literature, it can be said that the demographic, clinical, and evolutionary profile of patients in both groups was similar to that commonly described in various studies conducted with patients suffering from early-onset schizophrenia. This is especially true for patients enrolled in studies focusing on psychoeducation and social skills training for the first psychotic episode [20-22].

Statistical analysis of both groups reveals a population of young patients with early-onset schizophrenia, who despite second-generation antipsychotic therapy, experience an average of one to two relapses per year, with hospital stays lasting more than fifty days. Our study also showed a relationship between poor medication adherence and lack of information about the disease and prescribed medications, as well as side effects such as drowsiness, tremors, and fatigue that can interfere with school or work activities. According to various research findings on this topic [21-23], side effects are mentioned by a quarter to two-thirds of patients as the primary reason for poor adherence. The most disabling side effects, especially tremors and sexual effects, have the greatest impact on adherence. For some authors, adherence behavior is influenced more by the difficult or unbearable experience of side effects than by their mere occurrence. Thus, Palazzolo [24] emphasizes the importance of warning patients about the possibility of side effects to alleviate their anxiety and, at the same time, improve their adherence behavior. In our study, the younger the patient, the more likely they were to be non-adherent. Literature data [20-21] support this observation, as several authors have also shown that young age is one of the most important risk factors for low adherence.

Regarding the impact of psychoeducation on relapse rates in our young schizophrenic patients, it was highly effective. Overall, our results are consistent with research studies and meta-analyses published on the impact of psychoeducation in relapse prevention, measuring psychiatric re-hospitalization rates in cohorts of patients with early-onset schizophrenia who attended psychoeducation sessions compared to cohorts of patients undergoing standard treatment [20-22]. This agreement was observed on several evaluated parameters, including relapses and therapeutic compliance. Indeed, we found a significant reduction in the relapse rate in the psychoeducational group compared to the control group.

This reduction in the risk of relapse was observed when the number of session participations was eight or more, with a clear improvement in symptoms. As for treatment compliance, it was also better in the psychoeducational group. Indeed, therapeutic adherence scores evolved positively at each assessment after the psychoeducation program. It should be noted that patients in the psychoeducational group who relapsed did not complete the entire program (less than six sessions).

It is worth noting that the duration of hospital stay after a relapse was reduced in the psychoeducational group compared to the control group, 375 days versus 61 days. Which is consistent with some studies in the literature, including the study by Maurel and al.[25], which sought to demonstrate the benefits of a psychoeducation module focused on self-management of treatment on the average number of days of hospitalization per year in 144 patients with schizophrenia. At the beginning of the study, all patients were hospitalized for about 100 days per year. At 1 year, the "psychoeducational module" group managed to reduce the average number of days of hospitalization per year to 30 (compared to an unchanged score of 100 for the control group) with an average reduction in the PANSS score (50/210 in the "psychoeducational module" group, compared to 70 for the control group). At two years, the progression continued, as the study group decreased to an average of 20 days of hospitalization per year, compared to 80 days for the control group.

We also observe the positive evolution of PANSS scores through evaluations from the beginning to the end of the psychoeducation program, attesting to the effectiveness of overall care on the symptoms presented by patients. Faced with this result, it seems legitimate to think that acquiring knowledge about the disease and its favorable evolution in most cases helps improve certain items evaluated by the PANSS, such as anxiety and especially awareness of the disease.

These findings are in perfect agreement with several results from various literature studies [20-23]. Several research teams have evaluated the impact of psychoeducation on relapse rates, with significant differences in symptoms, evaluation scales, and re-hospitalization rates. First, Mac Gorry's team [20], a pioneer in the management of first psychotic episodes, evaluated the impact of a psychoeducational program in 266 patients aged of 16 to 17 with early-onset psychotic disorders over a 12-month period. They highlighted a significant decrease in the relapse and re-hospitalization rate at 1 year and an improvement in knowledge of the disease. Then, the study by Mac William in 2010 [23] tested knowledge of the disease and assessed therapeutic adherence using the Drug Attitude Inventory before and after six weeks of a psychoeducational program over 24 months.

The results favored patients who participated in multiple psychoeducation sessions by increasing knowledge of the disease and treatment from the first episode. The Valencia team in 2012 [21] prioritized an integrative psychoeducation approach, comparing two groups: one benefiting from treatment education in addition to pharmacological treatment and the other receiving pharmacological treatment alone over a one-year follow-up. The result favored the psychoeducational group in terms of relapse. Finally, Petrakis' study in 2013 [22] assessed the impact of psychoeducation on caregivers of patients with early-onset psychosis, finding short-term improvements in treatment compliance and medium-term reductions in relapses.

Declaration of Interests

The author declares no conflicts of interest related to this article.

V. Conclusion

In conclusion, educational measures remain a cornerstone in the health process. They are cost-effective and can be combined with other types of therapeutic interventions. Their practices and benefits are widely recognized for many parameters. They should be systematically integrated into the care plan for schizophrenic patients from the early stages of the disease to better manage and minimize the impact of this chronic condition on young patients.

References

[1]. Gut-Fayand A. Therapeutic Education Of The Patient And Early Schizophrenia. Ann Med Psychol Xxx (2015) Xxx-Xxx.
[2]. Lieberman Et Al. Effectiveness Of Antipsychotic Drugs In Patients With Chronic Schizophrenia. New England J Med 2005, 22 ; 353(12):1209-23.
[3]. Eckman And Al. Technique For Training Schizophrenic Patients In Illness Self-Management: A Controlled Trial. American Journal Of Psychiatry 1992 ; 149(11):1549-55.
[4]. Marion-Veyron R, Medbouhi N, Baumann Ph And Al. The First Psychotic Episodes: The Importance Of Case Managementfirst Episode Psychosis And Case Management. Elsevier : Psychiatric Evolution 2013, Volume 78, Number 1: 41-51
[5]. Birchwood P Todd, C Jackson. Early Intervention In Psychosis. The Critical Period Hypothesis. Br J Psychiatry Suppl 1998 ; 172(33):53-9.
[6]. Robinson D, Woerner M G, Alvir J M, And Al. Predictors Of Relapse Following Response From A First Episode Of Schizophrenia Or Schizoaffective Disorder. Arch Gen Psychiatry 1999 ; 56(3) :241-7.
[7]. Mcglashan, T. H. A Selective Review Of Recent North American Long-Term Followup Studies Of Schizophrenia. Schizophrenia Bulletin 1988, 14(4), 515.
[8]. Lieberman Ja, Perkins D, Belger A, And Al. The Early Stages Of Schizophrenia: Speculations On Pathogenesis, Pathophysiology, And Therapeutic Approaches. Biological Psychiatry 2001, 50 (11), 884-897.
[9]. Malla A, Norman R, Schmitzn And Al. Predictors Of Rate And Time To Remission In First-Episode Psychosis: A Two-Year Outcome Study. Cambridge University Press. Psychological Medicine 2006, Volume 36, Issue 5: 649 – 658.
[10]. Lieberman J A, Alvir Jm, Koreen A And Al. Psychobiologic Correlates Of Treatment Response In Schizophrenia Neuropsycho-Pharmacology, 1996, Volume 14, Pages 13–21.
[11]. Catana A; Baudoux-Meunier A; Charpeaud T And Al. Therapeutic Education Among Schizophrenia Patients: Schiz'educ Program. Annales-Medico-Psychologiques-Revue-Psychiatriquevolume 173, Issue 1, February 2015, Pages 97-100.

[12]. French Psychiatric Federation. Schizophrenic Beginners: Diagnosis And Therapeutic Modalities. Consensus Conference Of 23 And 24 January 2003. Paris : Ffp; 2003
[13]. Hasan A, Falkai P, Wobrock T. World Federation Of Societies Of Biological Psychiatry (Wfsbp) Guidelines For Biological Treatment Of Schizophrenia, Part 1 : Update 2012 On The Acute Treatment Of Schizophrenia And The Management Of Treatment Resistance
[14]. The American Psychiatric Association. Practice Guidelines For The Treatment Of Patients With Schizophrenia. Books, 3nd Edition; 2021 ; P23-24.
[15]. Correl And Al. Comparison Of Early Intervention Services Vs Treatment As Usual For Early-Phase Psychosis, Jama Psychiatry. 2018 Jun 1 ; 75 (6):555-565.
[16]. American Psychiatric Association. Diagnostic And Statistical Manual Of Mental Disorders (Dsm-5). 5th For The Schizophrenia Spectrum. Ed. Washington,Dc: American Psychiatric Association; 2013. P : 109-155.
[17]. Kay Et Al Kay And Al. The Positive And Negative Syndrome Scale (Panss) For Schizophrenia. Schizophrenia Bulletin 1987.
[18]. Thompson K, Kulkarni J, Sergejew Aa. Reliability And Validity Of A New Medication Adherence Rating Scale (Mars) For The Psychoses. Schizophr Res 2000; 42:241–7.
[19]. Liberman. R. P. Module D'éducation Au Traitement Neuroleptique. Québec, 1986.
[20]. Mc Gorry P.D., Young Ar, Phillips. The « Close-In » Or Ultra Hight-Risk Model: A Safe And Effective Strategy For Research And Clinical Intervention In Prepsychotic Mental Disorder. Schizophr Bull 2003; 29; 771-90.
[21]. Valencia M, Juarez F, Ortega H. Integrated Treatmentt To Achieve Functionnal Recovery For First-Episode Pschosis. Schizophr Res Treat, Volume 2012 ; 1-9 [L'article Id 962371]
[22]. Petrakis M, Oxley J, Bloom H. Carer Psychoeducation In First-Episode Psychosis: Evaluation Outcomes From A Structured Group Programme. Int J Soc Psychiatry 2013 ; 59(4) :391-7.
[23]. Mc Williams S, Egan P, Jackson D, Et Al. Caregiver Psychoeducation For First-Episode Psychosis. Eur Psychiatry 2010; 25(1) :33-8.
[24]. Pallazzolo J, Brousse G, Favre P, Llorca P-M. The Information Of The Schizophrenic Patient : Actuality. L'encephale 2005; Volume 31, Issue 2 : 227-234.
[25]. Maurel M, Drai D, Kaladjiane A And Al. A Randomized Controlled Study On The Impact Of Pharmacoeducation On A French Patient Population With Schizophrenic And Schizoaffective Disorders. Can J Psychiatry. 2010 May ; 55(5) :329-37.