PHARMACOTHERAPEUTIC ADHERENCE AND QUALITY OF LIFE IN PAEDIATRIC OUTPATIENTS WITH EPILEPSY

[1, 2]Virág, Ľ. – [3]Murgaš, M. – [1]Kuželová, M.

[1]Comenius University in Bratislava,Faculty of Pharmacy,
Department of Pharmacology and Toxicology,
[2]Pharmacy Čajka, Nitra,
[3]Outpatient Department of Paediatric Neurology, Nitra

The aim of this study was to obtain data about pharmacotherapeutic adherence, quality of life and its relations in paediatric outpatients.

The present survey was conducted at the Outpatient Department of Paediatric Neurology in Nitra. QOLIE-AD-48 questionnaire was used to assess quality of life and pharmacotherapeutic adherence prospectively. Ninety five patients met the inclusion criteria. The study was approved by the Ethics Committee of the Faculty of Pharmacy, Comenius University in Bratislava.

Questionnaires were returned by 74 (77.9%) paediatric patients. The mean quality of life score was 75.2. The quality of life score was lower in children who had higher seizure frequency, were medicated by polytherapy, who experienced adverse effects, with lower age during first seizure, with stigma, and also in those who experienced non-adherence. Adherence was poor in 15 (20.3%) patients. Non-adherence was significantly more frequent in patients 14–18 years old, in those with insufficient seizure control, in those with adverse effects, and also in patients with lower quality of life ($p < 0.05$).

Non-adherence with medication was detected in practically 30% of our adolescents. Therefore, assessing medication adherence and counseling patients about it should be important components of daily clinical practice mainly in risk patients.

Keywords: Adherence – Antiepileptic drugs – Children – Quality of life

INTRODUCTION

Adherence is generally defined as the extent to which patients' treatment-related behaviours (e.g., taking medication, following a diet, modifying habits, or attending clinics) correspond to health professionals' advice[1]. For individuals with epilepsy, adherence to medication is crucial in preventing or minimizing seizures and their cumulative impact on everyday life. Non-adherence to antiepileptic drugs (AEDs) can result in breakthrough seizures many months or years after a previous episode and can have serious repercussions on an individual's perceived quality of life (QOL)[2,3]. Adherence levels for children and adolescents are highly dependent on the level of support from parents [4]. Teenagers with epilepsy appear to adhere less to medication [5]. Adherence is difficult to measure accurately. In epilepsy adherence has been measured by self-report, drug-level monitoring and prescription refill monitoring. Each method has disadvantages[6]. Self-reporting is the simplest measure. Despite the common use of self-report measures to determine treatment adherence, few measures have been validated specifically for the study of epilepsy [7]. A notable exception is the QOLIE-AD-48 which measures health-related QOL for adolescents with epilepsy and has been found to be reliable and valid [8]. Due to the paucity of published studies on the impact of non-adherence among paediatric outpatients with epilepsy, this study investigates the factors associated with non-adherence to AEDs, as well as the relationship between non-adherence and patient QOL.

METHODS

The present study was a prospective survey conducted at the Outpatient Department of Paediatric Neurology in Nitra, Slovakia. The study period was of 4 years (2005–2009). Over this period 293 patients with diagnosis of epilepsy were treated. The study included children and adolescents from 11 to 18 years of age.

The QOL was measured with the Slovak version of the Quality of Life in Epilepsy Inventory for Adolescents 48 (QOLIE-AD-48). Ms. Joyce Cramer provided the original version of QOLIE-AD-48 [9]. The translation process produced Slovak version of QOLIE-AD-48. The final version was compared with the original version and the differences were sent to the authors of the QOLIE-AD-48. The scores of QOL were transformed to a range of 0 – 100; higher scores mean better QOL.

The inclusion criteria were: age between 11 and 18 years, ability to answer the questions by himself/herself, and presence of active epilepsy within the past 2 years. Patients were excluded if they had had brain surgery, used a concomitant medication with central nervous system effects, or had another progressive neurological or psychiatric illness.

The subjects were informed in a letter attached to the questionnaire that their answers would be used for research purposes, that their identity would not be revealed at any stage, and that the researcher would consider the information confidential.

The voluntary nature of participation was also emphasized. All patients and parents signed an informed consent approved by the ethics committee of the Faculty of Pharmacy of Comenius University in Bratislava.

Questionnaire of known reliability and validity was used to assess treatment adherence (QOLIE-AD-48). The collected data consisted of items on the following topics: adherence to medication taking according to their self or parental report, the subjective reason for non-adherence (including irregular taking, errors of dosage and partial or total omission) and quantification of non-adherence. Drug adherence was considered as satisfactory if the patient took the medication in correct dosage, regularly and as planned for him/her either by his /her own or given by the parents based on their responses to the questions about the above-mentioned items.

Frequencies and description statistics were computed. The connections between the above-mentioned factors to medication adherence and QOL were analyzed by Spearman correlation test, Mann-Whitney test and Pearson chi-square test. Statistical analysis was performed using a level of significance of 5% ($p < 0.05$).

RESULTS AND DISCUSSION

Ninety five patients met inclusion criteria. Questionnaires were returned by 74 (77.9%) paediatric patients. Fifty-two (70.3%) participants had not had a seizure in the previous three months. Fifty-five (74.3%) children had been treated with monotherapy. The most common AEDs prescribed were valproate (58.1%), carbamazepine (29.7%) and lamotrigine (14.9%). Of the 74 AED-treated paediatric patients, 31 (41.9%) experienced at least one symptom that was judged to be an adverse effect (AE).The most common (52.5%) were central nervous system disorders (fatigue, tremor, headache, diplopia), followed by gastrointestinal (37.5%) and skin disorders (15%).

Mean QOLIE-AD-48 total score was 75.2. Mean scores ranged from 33.9 for the Attitudes toward Epilepsy domain to 90.3 for the School Behaviour domain. Table 1presents descriptive statistics for the QOLIE-AD-48 Slovak version. As for gender, there were no significant differences in QOL between boys and girls (75.7 ± 15.2 *vs.*73.8 ± 17.5), but in the Epilepsy Impact domain, girls reported significantly differently with respect to perception of the effects of epilepsy($p < 0.05$).

Compared with those without manifestation of seizures, children with active epilepsy in this sample showed significantly lower QOL overall ($p < 0.05$). There was a high correlation ($r = 0.86$) between poorer QOL scores and detection of adverse effects of AEDs. The QOL was significantly reduced in patients with manifestation of cognitive AEs ($p < 0.05$). The QOL total score was lowered in children: who had

78

lower age during first epileptic seizure ($p < 0.01$), with higher seizure frequency ($p < 0.05$), who were medicated by polytherapy ($p = 0.09$), and also in those who experienced AEs ($p = 0.08$).

Table 1. Descriptive statistics for the QOLIE-AD-48 Slovak version

Subscale	No. of items	Mean score[a]	SD	Cronbach´s alpha coefficient[b]
Epilepsy Impact	12	83.6	13.4	0.80
Memory/Concentration	10	75.9	14.8	0.81
Attitudes toward Epilepsy	4	33.9	21.3	0.69
Physical functioning	5	89.6	12.6	0.70
Stigma	6	77.8	16.8	0.73
Social Support	4	88.2	18.3	0.76
School Behaviour	4	90.3	15.4	0.62
Health Perceptions	3	81.7	19.1	0.47
Total score	48	75.2	19.3	0.72

[a] All subscales scores were linearly transformed to range from 0 to 100 points, with higher values representing better functioning.
[b] Cronbach´s alpha coefficients should exceed 0.70.

Pharmacotherapeutic adherence was satisfactory in 79.7% and was poor in 20.3% of the paediatric patients according to their self report. Adherence to treatment was significantly different in children (less than 14 years old) and adolescents ($p < 0.05$). These data are depicted in Table 2. We also detected a negative correlation between seizure frequency and adherence ($p < 0.01$).

Table 2. Factors affecting adherence to treatment in paediatric patients with epilepsy

	Adherence n = 59 (%)	Non-adherence n = 15 (%)	
Age 11 – 13 (n = 28) 14 – 18 (n = 46)	26 (92.9) 33 (71.7)	2 (7.1) 13 (28.3)	χ^2 =4.80 $p < 0.05$
Seizure activity No seizures (n = 52) Seizures (n = 22)	46 (88.5) 13 (59.1)	6 (11.5) 9 (40.9)	χ^2 =8.25 $p < 0.01$
Importance to take drugs as prescribed Important (n = 66) Not at all important (n = 8)	57 (86.4) 2 (25.0)	9 (13.6) 6 (75.0)	χ^2 =16.62 $p < 0.01$

Manifestation of adverse effects			
Yes (n = 31)	21 (67.7)	10 (32.3)	χ^2 =4.74
No (n = 43)	38 (88.4)	5 (11.6)	p <0.05
Quality of life			
Total score 80 – 100 (n = 24)	23 (95.8)	1 (4.2)	χ^2 =4.40
Total score <80 (n = 50)	38 (76.0)	12 (24.0)	p <0.05
Stigma of epilepsy			
Yes (n = 10)	3 (30.0)	7 (70.0)	χ^2 =17.69
No (n = 64)	56 (87.5)	8 (12.5)	p <0.01

Sixty per cent of non-adherent patients did not adhere to the treatment due to personal judgment about the advantages and disadvantages of the proposed therapy, or denial of illness as their coping style. Also, children with manifestation of AEs had more non-adherence than those without AEs (32.3% *vs.* 11.6%, p < 0.05). Non-adherent patients scored significantly lower than those who are adherent on the QOLIE-AD-48 scores (p < 0.05).

Optimal QOL is one of the main goals of AEDs therapy. Improving QOL was recognized as an essential component of management of paediatric patients with epilepsy[10]. Up to now there are no published in the English literature data concerning the QOL in children and adolescents with epilepsy in Slovakia. The QOLIE-AD-48 Slovak version presents psychometric properties similar to those of the original version and it could be a valid instrument for assessment of QOL in paediatric patients with epilepsy in Slovakia.

Previous studies revealed that the most important for patients with epilepsy were social and psychological aspects of daily life: frequency of seizures, effect of AEDs [11,12]. Frequency of seizures was described as one of the most relevant determinants of poor QOL scores [13,14]. We revealed that the following significant factors influenced on QOL of our patients: frequency of seizures, duration of disease, polytherapy, manifestation of AEs, stigma of epilepsy and non-adherence. The most important parameter determining QOL was the severity and frequency of seizures.

Non-adherence to medication is widespread in chronic disease and is a major problem facing medical practice [6].Current estimates of non-adherence in epilepsy are similar to those in other chronic illnesses and range from 30% to 50%[15]. Non-adherence estimates in paediatric epilepsy range from 14% to 43% on the basis of the measurement method (eg, self-report, blood levels) [16]. In our study, pharmacotherapeutic non-adherence was detected in 20% of our paediatric patients. A recently published study reported that non-adherent patients with epilepsy had a threefold increased risk of mortality compared with adherent patients [17]. Therefore, assessing medication adherence and counselling patients about it are important components of daily clinical practice.

Adherence levels for children and adolescents are highly dependent on the level of support from parents. Kyngas reports that this support is a strong predictor for adherence in teenagers with epilepsy [5]. A number of studies have demonstrated that approximately from one third to one half of adolescents with epilepsy fail to adhere to

their therapy recommendations [4,5,15]. According to our findings about 30% of our adolescents had problem with drug adherence. The reasons why teenagers are less likely to adhere are complex. This age group may feel increased levels of stigma associated with taking AEDs, or may simply be at an age when parental responsibility for ensuring adherence has been relinquished to the adolescent who may simply forget to take the medication [18].

The association of medication non-adherence and seizure control has been documented in previous literature [6]. Similarly, non-adherent patients in our study were more likely than adherent patients to experience a loss in seizure control and those that experienced a loss of seizure control were likely to have their treatment changed in some way (p <0.01). The failure to consider adherence as a reason for apparent medication failure may result in an unnecessary increase in AED dosage or an addition of another AED in an attempt to control seizures [19]. This may unnecessarily expose the patient to more medication-related AEs and iatrogenic complications. In order to assist physicians in identifying non-adherent patients, a standardized epilepsy management protocol should be developed that assists physicians in correctly identifying the causes of treatment failure [20].

CONCLUSION

Pharmacotherapeutic adherence of our sample of adolescents with epilepsy was poor. The frequency of seizure, stigma and manifestation of AEs were statistically significantly related to adherence and also to QOL. Non-adherence to medication may be the single greatest factor in poor seizure control and can be quickly and easily assessed. Therefore adherence assessments should be routine.

More longitudinal prospective multicentric clinical studies are needed to evaluate the Slovak version of the QOLIE-AD-48 in clinical practice. Further studies are also required to better understand long-term effects of epilepsy, its treatment and pharmacotherapeutic adherence on patient´s QOL.

LIMITATIONS

Our study has several limitations. It is cross-sectional and no group comparisons were made; the number of subjects was small; the sample was highly homogenous because of the study criteria, and only one measure was used, all of which may limit future use of the data.

There are also limitations inherent in collecting self-reported data. Adherence was measured using patient report, and patients may have overestimated their adherence. Future research is warranted to augment patient-reported data on non-adherence with one of the well-known measures.

REFERENCES

1. McDONALD, H.P. – GARG, A.X. – HAYNES, R.B.: Interventions to enhance patient adherence to medication prescription: scientific review. JAMA 288, 2002, p. 2868-2879.
2. BAKER, G.A. – JACOBY, A. – BUCK D.: Quality of life of people with epilepsy: a European study. Epilepsia 38, 1997, p. 353-362.
3. EATOCK, J. – BAKER, G.A.: Managing patient adherence and quality of life in epilepsy. Neuropsych Dis Treatment 3, 2007, p. 117-131.
4. ASADI-POOYA, A.A.: Drug compliance of children and adolescents with epilepsy. Seizure 14, 2005, p. 393-395.
5. KYNGAS, H.: Predictors of good compliance in adolescents with epilepsy. Seizure 10, 2001, p. 549-553.
6. JONES, R.M. – BUTLER, J.A. – THOMAS, V.A. – PEVELER, R.C. – PREVETT, M.: Adherence to treatment in patients with epilepsy: Associations with seizure control and illness beliefs. Seizure 15, 2006, p. 504-508.
7. CRAMER, J.A. – GLASSMAN, M. – RIENZA, V.: The relationship between poor medication compliance and seizures. Epilepsy Behav 3, 2002, p. 338-342.
8. PASCHAL, A.M. – HAWLEY, S.R. – ROMAIN, T. – ABLAH, E.: Measures of adherence to epilepsy treatment: Review of present practices and recommendations for future directions. Epilepsia 49, 2008, p. 1115-1122.
9. CRAMER, J.A. – WESTBROOK, L.E. – DEVINSKY, O. – PERRINE, K. – GLASSMAN, M.B. – CAMFIELD, C.: Development of the Quality of Life in Epilepsy Inventory for Adolescents: The QOLIE-AD-48. Epilepsia 40, 1999, p. 1114-1121.
10. PRIVITERA, M. – FICKER, D.M.: Assessment of adverse events and quality of life in epilepsy: design of a new community-based trial. Epilepsy Behav 5, 2004, p. 841-846.
11. SZAFLARSKI, J.P. – SZAFLARSKI, M.: Seizure disorders, depression, and health-related quality of life. Epilepsy Behav 5, 2004, p. 50-57.
12. CRAMER, J.A. – BLUM, D. – REED, M. – FANNING, K.: The influence of comorbid depression on quality of life for people with epilepsy. Epilepsy Behav 4,2003, p. 515-521.
13. VICKREY, B.G. – BERG, A.T. – SPERLING, M.R. – SHINNAR, S. – LANGFITT, J.T. – BAZIL,C.W.: Relationships between seizure severity and health-related quality of life in refractory localization-related epilepsy. Epilepsia 41,2000, p. 760-764.
14. GUEKHT, A.B. - MITHROKINA, T.V. AEVA, F.V. – MICHLAKOVA, L.E. – LOKSHINA, O.B. – FEYGINA, A.F. – GUSEV, E.I.: Factors influencing on quality of life in people with epilepsy. Seizure 16, 2007, p. 128-133.
15. KYNGAS, H.: Compliance with health regimens of adolescents with epilepsy. Seizure 9, 2000, p. 598-604.
16. MODI, A.C. – MORITA, D.A. – GLAUSER, T.A.: One-Month Adherence in Children With New-Onset Epilepsy: White-Coat Compliance Does Not Occur. Pediatrics 121, 2008, p. 961–966.
17. FAUGHT, E. – DUH, M.S. – WEINER, J. – GUÉRIN, A. – CUNNINGTON, M.C.: Nonadherence to antiepileptic drugs and increased mortality: findings from the RANSOM Study. Neurology 71, 2008, p.1572–1578.
18. ANDERSON, G.D. – KIM, H. – WARNER, M.H.: Impact of taking antiepileptic drugs at school in a group of children and adolescents. Epilepsy Behav 1, 2000, p. 17-21.
19. BUELOW, J.M. – SMITH, M.C.: Medication management by the person with epilepsy: perception versus reality. Epilepsy Behav 5, 2005, p. 401-406.

20. HOVINGA, C.A. – ASATO, M.R. – MANJUNATH, R. – WHELESS, J.W. – PHELPS, S.J. – SHETH, R.D. – PINA-GARZA, J.E. – ZINGARO, W.M. – HASKINS, L.S.: Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: Survey of patients with epilepsy and physicians. Epilepsy Behav 13, 2008, p. 316-322.

PharmDr. Ľubomír Virág
Faculty of Pharmacy
Comenius University
Odbojárov 10
832 32 Bratislava
lubomirvirag@gmail.com

ADHERENCIA K FARMAKOTERAPII A KVALITA ŽIVOTA DETSKÝCH PACIENTOV S EPILEPSIOU

[1,2]*Virág, Ľ.* – [3]*Murgaš, M.* – [1]*Kuželová, M.*

[1]Univerzita Komenského v Bratislave, Farmaceutická fakulta,
Katedra farmakológie a toxikológie,
[2]Lekáreň Čajka, Nitra,
[3]Neštátna detská neurologická ambulancia, Nitra

Cieľom práce bolo získať informácie o farmakoterapeutickej adherencii, taktiež o kvalite života detských pacientov s epilepsiou a ich vzájomných vzťahoch.

Hodnotenie sa realizovalo v ambulancii detského neurológa v Nitre. Kvalitu života a farmakoterapeutickú adherenciu sme prospektívne sledovali použitím dotazníka QOLIE-AD-48. Inkluzívne kritériá spĺňalo 95 pacientov. Protokol štúdie schválila Etická komisia Farmaceutickej fakulty Univerzity Komenského v Bratislave.

Vyplnené dotazníky odovzdalo 74 (77,9 %) pacientov. Priemerné hodnoty skóre kvality života sa pohybovali na úrovni 75,2. Znížená kvalita života sa identifikovala u detí s vyššou záchvatovou frekvenciou, s kombináciou antiepileptík, s manifestáciou nežiaducich účinkov, s nižším vekom pri 1. epileptickom záchvate, s pocitom stigmatizácie vplyvom epilepsie, a taktiež u detí s non-adherenciou. Nedostatočná adherencia sa zistila u 15 (20,3 %) pacientov. Non – adherencia sa signifikantne častejšie objavila u pacientov vo veku 14 – 18 rokov, s nedostatočnou záchvatovou kontrolou, s nežiaducimi účinkami a so zníženou kvalitou života (p<0,05). Nedostatočná farmakoterapeutická adherencia sa zaznamenala takmer u 30 % adolescentov nášho súboru. Preto hodnotenie adherencie a podpora jej udržania by mala byť dôležitou súčasťou každodennej klinickej praxe najmä u rizikových pacientov.