# DEPRESSION AND QUALITY OF LIFE IN PATIENTS WITH EPILEPSY - SINGLE CENTRE EXPERIENCE

Željka Petelin Gadže<sup>1</sup>, Katarina Ivana Tudor<sup>1</sup>, Maja Živković<sup>2</sup>, Andreja Bujan Kovač<sup>1</sup>, Biljana Đapić Ivančić<sup>1</sup>, Sibila Nanković<sup>1</sup>, Vlatko Šulentić<sup>1</sup>, Ira Brezak<sup>3</sup>, Petra Nimac Kozina<sup>1</sup>, Barbara Sitaš<sup>1</sup>, Borislav Radić<sup>1</sup>, Monika Mudrovčić<sup>4</sup>, Dragana Mijatović<sup>5,6</sup>, Zdravka Poljaković<sup>1</sup>, Saša Jevtović<sup>2</sup>, Ana Vuksanović<sup>7</sup> & Sanja Hajnšek<sup>8</sup>

<sup>1</sup>Department of Neurology, University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Referral Centre of the Ministry of Health of the Republic of Croatia forEpilepsy,

Affiliated Partner of the ERN EpiCARE, Zagreb, Croatia

<sup>2</sup>Department of Psychiatry and Psychological Medicine, University Hospital Centre Zagreb, School of Medicine,

University of Zagreb, Zagreb, Croatia

<sup>3</sup>Croatian Association for Behavioral - Cognitive Therapies, Zagreb, Croatia

<sup>4</sup>University Hospital for Infectious Diseases "Dr. Fran Mihaljević", Zagreb, Croatia

<sup>5</sup>Istrian Health Center, Umag Section, Umag, Croatia

<sup>6</sup>School of Medicine, University of Rijeka, Rijeka, Croatia

<sup>7</sup>School of Medicine, University of Zagreb, Zagreb, Croatia - student

<sup>8</sup>School of Medicine, University of Zagreb, Zagreb, Croatia - retired

#### **SUMMARY**

**Background:** Patients with epilepsy commonly report depressive symptoms. The main aim of this study was to evaluate the relationship between epilepsy, antiepileptic drugs (AEDs) and depression. We also wanted to evaluate possible association between depressive symptofigms in patients with epilepsy with the quality of life (OoL).

Material and methods: This was a prospective cross-sectional study carried out at the tertiary teaching hospital (University Hospital Centre Zagreb, Croatia) with Ethics committee approval. Questionnaires evaluating depressive symptoms and QoL were administered to consecutive patients treated in the Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy. Depressive symptoms were evaluated using Hamilton Rating Scale for Depression (HAM-D17). Quality of life was assessed using Quality of life in epilepsy-31 inventory (QOLIE-31)

**Results:** 108 patients (63% women, 37% men; mean age 39.54±15.91 years, range 18-80 years) with epilepsy were included. 14.8% of patients had focal, 35.2% generalised and 40.7% both types of epilepsy. Majority of patients (65.74%) were on two and more AEDs and quarter was on monotherapy (25%); 42% were on newer, 19% on older and 39% on both AEDs. Mean total score on HAM-D17 was 9.94±8.18 (men - mean total score 10.16±8.85, women - mean total score 9.81±7.84). There were no significant differences on HAM-D17 regarding gender and age. We didn't find statistically significant differences regarding AEDs (older vs. newer AEDs, or both types AEDs) and results on HAM-D17, nor between the type of epilepsy and results on HAM-D17. We found strong negative correlation between the higher QoL and HAM-D17 (p=0.000).

Conclusions: Results of this study evaluating depressive symptoms in patients with epilepsy demonstrate that our patients mainly experience mild depressive symptoms, with no significant differences on HAM-D17 regarding gender and age. Patients with epilepsy with less pronounced depressive symptoms were found to have higher QoL. We did not find statistically significant differences regarding the type of epilepsy and results on HAM-D17, nor between the AEDs (older vs. newer AEDs, or both types AEDs) and results on HAM-D17.

**Key words:** epilepsy - antiepileptic drugs - depression - quality of life

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## **INTRODUCTION**

Epilepsy is often associated with comorbid psychiatric illnesses and the most frequent of these, in around 40% of patients, is major depressive disorder (Wiglusz et al. 2012, Mijatovic et al. 2019, Conway et al. 2018). Compared to general population epidemiological studies show a consistent increased prevalence of depression in epilepsy (Mula et al. 2019). Different studies have investigated this topic (Mula et al. 2019, Elger et al. 2017, Gill et al. 2017, Mula 2017, Singh et al. 2017, Asadi-Pooya et al. 2018). The main aim of this study was to evaluate the relationship between epilepsy, anti-

epileptic drugs (AEDs) and depression. We also wanted to evaluate possible association between depressive symptoms in patients with epilepsy with the quality of life (QoL).

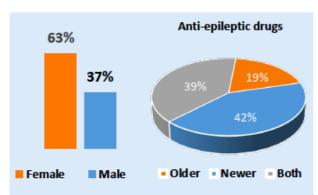
# SUBJECTS AND METHODS

This was a prospective cross-sectional study carried out at the tertiary teaching hospital (University Hospital Centre Zagreb, Croatia) with Ethics committee approval. Questionnaires evaluating depressive symptoms and QoL were administered to consecutive patients treated in the Referral Centre of the Ministry of Health of the

Republic of Croatia for Epilepsy. Depressive symptoms were evaluated using Hamilton Rating Scale for Depression (HAM-D17) (Hamilton 1960). Quality of life was assessed using Quality of life in epilepsy-31 inventory (QOLIE-31) (Cramer et al. 1998, 2003, Lusic et al. 2011). Statistical analysis was done using statistical software IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp, using t-test, one way ANOVA, post hoc Scheffe test, Bonferroni, Tukey test, and Pearson correlation coefficient.

## **RESULTS**

108 patients (63% women, 37% men; mean age 39.54±15.91 years, range 18-80 years) (Figure 1) with epilepsy were included. 14.8% of patients had focal, 35.2% generalised and 40.7% both types of epilepsy (Figure 2). Majority of patients (65.74%) were on two and more AEDs and quarter was on monotherapy (25%); 42% were on newer, 19% on older and 39% on both AEDs (Figure 1). Mean total score on HAM-D17 was 9.94±8.18 (men - mean total score 10.16±8.85, women - mean total score 9.81±7.84). There were no significant



**Figure 1.** Gender distribution and anti-epileptic drugs (AEDs): 42% of patients were on newer AEDs, 19% on older AEDs and 39% on both AEDs (older and newer)

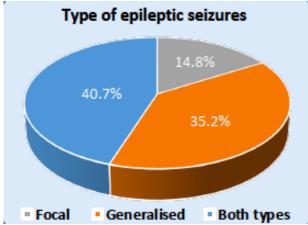


Figure 2. Seizure type distribution

differences on HAM-D17 regarding gender and age. We didn't find statistically significant differences regarding AEDs (older vs. newer AEDs, or both types AEDs) and results on HAM-D17, nor between the type of epilepsy and results on HAM-D17. We found strong negative correlation between the higher QoL and HAM-D17 (p=0.000).

## **DISCUSSION**

The main aim of this study was to evaluate the relationship between epilepsy, AEDs and depression. Analysis of our results showed that there were no statistically significant differences between the type of epilepsy and results on HAM-D17, nor regarding AEDs (older vs. newer AEDs, or both types AEDs) and results on HAM-D17. The relationship between epilepsy and depression is still not elucidated yet. In study by Grabowska-Grzyb et al. (2006) 49.2% with epilepsy suffered from concurrent depression, with majority (37.4%) having severe depression and 11.8% experiencing mild depression (Grabowska-Grzyb et al. 2006). In our study, mean overall HAM-D17 score was 9.94±8.18 (men 10.16±8.85, women 9.81±7.84), which is suggestive of mild depressive symptoms. However, we can see that responses range from 0 up to 33, later suggesting severe depressive symptoms. Although women had less pronounced depressive symptoms, there were no significant differences between the male and female gender. There were no significant differences on HAM-D17 regarding age. Unlike in study by Grabowska-Grzyb A. et al. (2006), where focal onset seizures with impaired awareness and evolution to bilateral tonic - clonic seizures, as well as generalized onset motor and non -motor (absence) seizures were found to be the risk factors for depression, we did not find statistically significant differences between the type of epilepsy and results on HAM-D17 (Grabowska-Grzyb et al. 2006). Regarding the AEDs, we did not find statistically significant differences regarding AEDs (older vs. newer AEDs, or both types AEDs) and results on HAM-D17. Harden CL. et al. (1999) sought to demonstrate a psychoactive effect of gabapentin (GBP) when used as add-on AED therapy. They demonstrated that gabapentin (GBP) treated group had a significant decrease in the Cornell Dysthymia Rating Scale (CDRS) score over time compared with the control group, while there were no significant differences between the control and the treated groups on Beck Depression Inventory (BDI), and Hamilton Depression and Anxiety Scales (Harden et al. 1999). Mazza M. et al. did a prospective study that examined whether continued add-on treatment with oxcarbazepine (OXC) is associated with quantitative improvement in mood and anxiety symptoms in adult patients with focal onset epilepsy. Depressive symptoms and anxiety were

assessed by clinical interview using the Hamilton Depression Rating Scale, CDRS, the BDI, and the Hamilton Anxiety Rating Scale. A significant improvement in affect was demonstrated on CDRS during the course of OXC treatment for 3 months, while Hamilton Depression Rating Scale and BDI scores also declined in the OXC-treated group, but these decreases did not reach statistical significance. The authors hypothesized about a potential use of OXC as an antidepressant in improving mood (Mazza et al. 2007). Possibly, our results regarding type of AEDs and their association with results on HAM-D17 are connected to the fact that our patients predominately experienced mild depressive symptoms. Published literature supports the idea that either depression represents the premorbid phase of some epileptic syndromes or the occurrence of epileptic seizures is part of the natural course of some depressive disorders, with possible neurobiological links in terms of anatomical structures (i.e. mesial temporal lobe structures) and neurotransmitter changes (i.e. GABA, serotonin and glutamate pathways). Among novel AEDs currently under investigation for the treatment of epilepsy, some aim to modulate neurobiological targets which may be relevant in depression (Conway et al. 2018). In this study we also wanted to evaluate possible association between depressive symptoms and quality of life (QoL). Strong negative correlation was found between the higher OoL and HAM-D17. Our results are consistent with the study by Siarava et al. They compared depression and QoL between patients with epilepsy and healthy controls and found that patients with epilepsy in Northwest Greece had higher rates of depression than reported in patients with epilepsy and poorer QoL compared to controls (Siarava et al. 2019). In the study by Erlich et al., authors examined the contribution of depression, verbal memory (VM) and executive functioning (EF) to the QoL in medically refractory temporal lobe epilepsy (TLE) patients, and found that the depression was the strongest predictor of the QoL in TLE patients (Ehrlich et al. 2019). Bala A. et al. found that depression was an important factor affecting QOLIE-31-P in both sexes (Bala et al. 2016).

#### **CONCLUSIONS**

Results of this study evaluating depressive symptoms in patients with epilepsy demonstrate that our patients mainly experience mild depressive symptoms, with no significant differences on HAM-D17 regarding gender and age. Patients with epilepsy with less pronounced depressive symptoms were found to have higher QoL. We did not find statistically significant differences regarding the type of epilepsy and results on HAM-D17, nor between the AEDs (older vs. newer AEDs, or both types AEDs) and results on HAM-D17.

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Informed consent was obtained from all patients included in the study.

#### Conflict of interest: None to declare.

#### Contribution of individual authors:

- Željka Petelin Gadže organised the study and collection of the data, collected the data and contributed data or analysis tools, helped with interpretation of the results, wrote and approved the final version of the manuscript.
- Katarina Ivana Tudor helped design the study and wrote the protocol, helped with collecting the data and contributed data or analysis tools, partially did statistical analyses, interpreted the results and helped wrote the manuscript.
- Maja Živković, Andreja Bujan Kovač, Biljana Đapić Ivančić, Sibila Nanković, Vlatko Šulentić, Ira Brezak, Petra Nimac Kozina, Barbara Sitaš, Borislav Radić, Monika Mudrovčić, Dragana Mijatović & Ana Vukasanović collected the data, contributed data or analysis tools.
- Zdravka Poljaković & Saša Jevtović interpreted the results and approved the final version of the manuscript.
- Sanja Hajnšek conceived and helped design the protocol of this study.

## References

- 1. Asadi-Pooya AA, Kanemoto K et al: Depression in people with epilepsy: How much do Asian colleagues acknowledge it? Seizure 2018; 57:45
- 2. Bala A, Szantroch M, Gleinert et al: Differences in quality of life of women and men with drug-resistant epilepsy in Poland. Epilepsy Behav 2016; 94-8
- 3. Conway CR, Udaiyar A, Schachter SC: Neurostimulation for depression in epilepsy. Epilepsy Behav 2018; 25-32
- 4. Cramer JA, Perrine K, Devinsky O et al: Development and cross-cultural translations of a 31-item quality of life in epilepsy inventory. Epilepsia 1998; 81-8
- Cramer JA, Van Hammee G, Group NS: Maintenance of improvement in health-related quality of life during longterm treatment with levetiracetam. Epilepsy Behav 2003; 118-23
- 6. Ehrlich T, Reyes A, Paul BM, et al: Beyond depression: The impact of executive functioning on quality of life in patients with temporal lobe epilepsy. Epilepsy Res 2019; 30-6
- 7. Elger CE, Johnston SA, Hoppe C: Diagnosing and treating depression in epilepsy. Seizure 2017;184-93.
- 8. Gill SJ, Lukmanji S, Fiest KM et al: Depression screening tools in persons with epilepsy: A systematic review of validated tools. Epilepsia 2017; 695-705
- 9. Grabowska-Grzyb A, Jedrzejczak J, Naganska E et al: Risk factors for depression in patients with epilepsy. Epilepsy Behav 2006; 411-7

- Hamilton M: A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 56-62
- 11. Harden CL, Lazar LM, Pick LH et al: A beneficial effect on mood in partial epilepsy patients treated with gabapentin. Epilepsia 1999; 1129-34
- 12. Lusic I, Dzamonja G, Titlic M, et al: Psychometric validation of the Croatian version of the Quality of Life in Epilepsy Inventory (QOLIE-31). Coll Antropol 2011; 1177-84
- 13. Mazza M, Della Marca G, Di Nicola, et al: Oxcarbazepine improves mood in patients with epi-lepsy. Epilepsy Behav 2007; 397-40
- 14. Mijatovic D, Petelin Gadze Z, Derke F et al.: Impact of Invasive EEG Monitoring and Resective Neurosurgical Treatment on the Quality of Life in Patients with Drug Resistant Epilepsy - Preliminary Results. Psychiatr

- Danub 2019; 31(Suppl. 5):769-73. (Medicina Academica Mostariensia 2019; 7:47-51)
- 15. Mula M, Sander JW: Current and emerging drug therapies for the treatment of depression in adults with epilepsy. Expert Opin Pharmacother 2019; 41-5
- 16. Mula M: Depression in epilepsy. Curr Opin Neurol 2017; 180-6
- 17. Siarava E, Hyphantis T, Katsanos AH et al: Depression and quality of life in patients with epilepsy in Northwest Greece. Seizure 2019; 93-98
- 18. Singh T & Goel RK: Managing epilepsy-associated depression: Serotonin enhancers or seroto-nin producers? Epilepsy Behav 2017; 93-9
- 19. Wiglusz MS, Cubala WJ, Galuszko-Węgielnik M et al: Mood disorders in epilepsy - diagnostic and methodological considerations. Psychiatr Danub 2012; 24:44-50

Biljana Đapić Ivančić, MD Department of Neurology, University Hospital Centre Zagreb Kispaticeva 12, 10 000 Zagreb, Croatia E-mail: biljana.dapic@gmail.com