

Quality of Life and Psychiatric Comorbidities in Patients of Juvenile Myoclonic Epilepsy

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Abstract: *Epilepsy is a stigmatizing disorder. The impact of epilepsy on an individual's life extends beyond direct effects of seizure which lead to reduced quality of life and disability. Assessment of the quality of life is now an important component of clinical care in epilepsy. Psychosocial factors such as low self-esteem, professional difficulties, and social rejection significantly contribute to psychiatric co morbidities as anxiety, depression in people with epilepsy. Juvenile Myoclonic Epilepsy is an age-related idiopathic epilepsy syndrome representing 5-10 % of all epilepsy cases. It is well controlled with appropriate anti-epileptic drugs but requires lifelong treatment due to high relapse rate attributed to psychiatric co morbidities and psychosocial characteristics. It is to be reviewed if there is any association of psychiatric comorbidity with sociodemographic factors, antiepileptic medication and duration of illness in patients with JME. Also, the quality of life in relation to psychiatric co morbidities needs to be evaluated.*

1. Introduction

Epilepsy is one of the commonest chronic neurological conditions with stigmatization even in the modern world [1,2]. Understanding and assessment of its impact on an individual's quality of life is increasingly being recognized as an important aspect of clinical care. Psychosocial factors as "learned despair", restraints to normal daily living activities, low self-esteem, educational and professional difficulties, stigmatization, and social rejection significantly contribute to psychiatric co morbidities as anxiety, depression in people with epilepsy. Juvenile myoclonic epilepsy (JME) or Janz syndrome is exemplary of a well-defined age-related idiopathic epilepsy syndrome [3]. It represents 5-10 % of all epilepsy cases. There is general consensus that JME does not represent a severe progressive epileptic condition and is controlled with Valproic Acid (VPA) or other appropriate drugs in about 76–88% [4]. Treatment response to appropriate antiepileptic drugs (AED) is generally good but there is a widespread though ill-evidenced belief that these patients need lifelong treatment because of a high relapse rate [5, 6]. JME paradoxically results in a confounded perception of its prognosis. This has been attributed to some specific psychiatric, psychological, and psychosocial characteristics. These aspects have generated a significant amount of interest in the last two decades.

2. Historical Perspective

Since the first comprehensive description by Janz and Christian, Juvenile Myoclonic Epilepsy (JME) has appeared as a well-shaped disease entity. Juvenile myoclonic epilepsy (JME) is the most common idiopathic generalized epilepsy syndrome, constituting approximately 3% to 11% of adolescent and adult cases of epilepsy [4]. The hallmark seizure indispensable for the diagnosis, was single or arrhythmic bilateral, predominantly brachial myoclonus mostly on awakening that could be combined with generalized tonic-clonic seizures (GTCS) and absences. Seizures are often triggered by sleep deprivation, alcohol

intake, fatigue, and stress. Interictal EEGs show generalized rapid spike-waves and polyspike waves without close correlation between EEG spikes and jerks [8]. The first citation of JME was made in 1857 when Théodore Herpin described a 13-year-old boy suffering from myoclonic jerks, which progressed to tonic-clonic seizures within the next three months [3]. In 1957, Janz and Christian published a journal article describing several patients with JME. The name Juvenile Myoclonic Epilepsy was proposed in 1975 and adopted by the International League Against Epilepsy [6].

2.1 Epidemiology

The mean age of onset for GTCS in JME is 15.5 years, absence seizures 11.5 years and myoclonic seizures 15.4 years. The gender ratio in JME is generally considered to be equal, but many studies have reported a female preponderance of up to 2.9:1. Long-term studies have shown that JME is a lifelong disorder for the majority as myoclonic seizures subside in the fourth decade in JME and a resistant course is seen in 1/6th of JME patients which is not fully explained. Also, 74% of JME patients have been shown to have at least one major marker of unfavourable social outcome [7]. It has often been stated that epilepsy in general is associated with a high risk for psychiatric comorbidity of approximately 17-80%. Lundet al., in the year 1976 assessed the personality of 33 JME patients retrospectively from their clinical records and subsequently by means of a clinical interview at a follow-up investigation. Twelve patients (36.4%) were diagnosed as "character neurotic," that is, a form of personality disorder.

2.2 Pathophysiology

An abnormal secretion of serotonin (5-HT) in the central nervous system explains the common pathogenic mechanisms shared by depression, anxiety, and epilepsy. Serotonin's anxiolytic effects may be related to an inhibition of noradrenergic activation through raphe nuclei projections to the locus coeruleus [9,10]. A lower binding of 5-HT_{1A} in

the anterior and posterior cingulate gyrus and raphe was manifested in patients with panic disorder as compared with controls. Depression in JME can be explained on the basis of a biopsychosocial model: biological (endocrine related effects of seizure; metabolic effects of seizure; adverse effects of antiepileptic drugs); psychological (personality factors, individual's perception and attitude towards epilepsy and its treatment); social (stigma attached to epilepsy, psychosocial support burden of treatment, employment related issues, compromised quality of life due to epilepsy). Also, abnormalities in a specific thalamo-cortical circuit with reduced structural and task-induced functional connectivity may underlie the functional abnormalities in JME [13].

2.3 Importance of Quality of Life in JME Patients

JME can be projected as an interesting model to understand the Quality of Life in these patients and the various factors affecting it [14]. Fallowfield states that quality of life is a "complex amalgam of satisfactory functioning in terms of physical, social, psychological and vocational well-being. With regard to Juvenile myoclonic epilepsy, mostly starting in adolescence is a phase of emotional instability in any individual's life and a turning point. How a person had been in adolescence has a major impact on his future life pertaining to his career, job, relationships, ability to handle stress, thought process and attitude towards life. JME has been the subject of intensive research over the past 25 years [11]. Its clinical spectrum now incorporates cognitive and psychiatric symptoms as significant comorbidities, and the elaboration of its multiple genetic mechanisms is an ongoing process of research. JME patients exhibit problems with compliance to antiepileptic drugs (AEDs) as well as a tendency to downplay the severity of the disease. This may result in problems with regards to seizure control and psychosocial integration. Keeping this in mind, only two studies so far specifically have addressed the psychosocial long-term outcome of patients with JME.

In a study by Holtkamp M et al in 2013, all JME patients were tested with Quality of Life in Epilepsy Inventory 31 (QOLIE-31; German version), which was shown to have good reliability and validity. The QOLIE-31 is a widely adopted epilepsy-specific questionnaire for assessment of quality of life (QoL). It comprises 30 items divided into seven subscale domains: seizure worry (five items), emotional well-being (five items), energy/fatigue (four items), cognitive functioning (six items), medication effects (three items), overall QoL (two items), and social functioning (five items). Each domain was scored by calculating the mean score of responses within that domain. The raw scores were converted to "0-100," with higher scores reflecting better QOL. Total and subscale scores were calculated according to the QOLIE-31 scoring manual. The results were as follows:

Table 1: QOLIE 31 subscale domains in JME patients [15]

QOLIE-31 subscale domains	Mean Score of all JME patients (n=41) ^a
Seizure worry	89 ± 2.8
Overall QOL	71.1 ± 3
Well-being	70.6 ± 2.6
Energy fatigue	57.9 ± 2.8
Cognitive Functioning	73.7 ± 3.4
Medication effects	83 ± 3.9
Social functioning	86.8 ± 3
Overall score	74.4 ± 2.6

In this study, it was seen that current or previous psychiatric comorbidity (n = 10 patients) was significantly associated with and was thus an indicator for lower total scores in QoL (65.6 ± 3.2 total score QOLIE vs. 79.6 ± 2.4 total score QOLIE in 31 patients without psychiatric comorbidity; p = 0.02). Total QOLIE-31 scores did not differ significantly in all other variables assessed, comprising male/female, AED yes/no, employed/unemployed, university degree/no university degree, married/not married, children/no children, satisfied with social situation/not satisfied with social situation, and satisfied with friendships/not satisfied with friendship [15].

In a study by Schneider et al, the mean QOLIE-31-P score was 68.2 (SD ± 15.89; range 39.42–88.87). Seizure freedom correlated significantly with a higher QoL (>70) (p = 0.001), whereas the lowest scores (<50) were seen in the group of JME patients with the following: (1) higher scores on Beck's depression inventory I-II (mild-moderate [BDI-II 14–19] or moderate-severe [BDI-II 20–28] depression; OR 17; p = 0.02^a), (2) side effects of AED treatment (p = 0.04) (3) sleep disturbances (OR 2.667) and (4) occurrence of all three seizure types.

In a study by Erthem D et al., in 2017, the Quality of Life of JME patients (n=30) was compared to that of patients of Mesial Temporal Lobe Epilepsy (n=30). The scale used was QOLIE-89 which is a self-report inventory that evaluates life satisfaction in four scales and 17 subscales. It was developed in the USA and contains 89 items. The 17 subscales are: Overall QOL, Emotional Well-Being, Role Limitations Due to Emotional Problems, Social Support, Social Isolation, Energy/Fatigue, Worry About Seizure, Medication Effects, Health, Discouragement, Work/Driving/Social Function, Attention/Concentration, Language, Memory, Physical Function, Pain, Role Limitations Due to Physical Problems, and Health Perception. There were no statistically significant differences in terms of QOL subscale scores and comorbid psychiatric disorders, except that patients with mood disorders had statistically significantly worse QOLIE-89 Attention/Concentration subscale scores (P = 0.013). However, comparing the demographic and clinical features of patients with JME and MTLE and their mean QOL scores, we did not detect any statistically significant difference [19].

2.4 Psychiatric Co Morbidities in Patients of JME

Janz and Christian first distinguished JME as a syndrome in 1957, in their classic description of JME narrated the distinctive personality features of these patients as unsteadiness, lack of discipline, hedonism, and an

indifference to their disease [4]. These patients were “attractive but emotionally labile, switching between comradeship and distrust, rather immature, childlike behaviour that can lead to difficulties in social adjustment,” and show a “denying attitude towards the disease,” and “often have character neurotic which often complicated treatment of JME [17]. JME might show certain personality characteristics such as impressionability, unreliability and emotional instability which are similar to those observed in frontal lobe lesions. The treatment of such patients tends to be difficult because of their specific personality traits. Due to their erratic lifestyle, it may be challenging for JME patients to follow a compact daily routine with avoidance of the seizure triggers. This may result in problems with seizure control and psychosocial integration.

Sh. Somayajula et al., in 2000, found the association between clinical factors and the two major psychiatric disorders (anxiety disorders and depressive disorders) in 165 JME patients and the implications for their psychosocial and socio professional integration. 77(46.6%) patients were diagnosed with psychiatric disorders while 50 were categorized as having anxiety disorders and 27 patients had depressive disorders [16].

In a study by Filho et al. in 2010, 170 MTLE and 100 JME patients were compared in terms of psychiatric comorbidity. They detected psychiatric disorders in 50% of MTLE patients and in 49% of JME patients. In JME patients, psychiatric comorbid disorders were as follows: anxiety disorders, 23%; mood disorders, 19%; and psychotic disorders, 8% [20].

Gelisse et al. 2001 investigated a large sample of 170 JME patients from Nice and Marseille (France); psychiatric diagnoses according to *DSM-IV*, 1994 were assigned in retrospect from a thorough analysis of the clinical records, but the patients were not seen face to face. The authors found psychiatric disorders in 26.5% of the patients, with 1.8% depressive disorders, 3.5% anxiety disorders, 2.9% psychotic disorders, 4.1% other Axis I disorder, and 14.1% personality disorders [4].

In a study by O’Muircheartaigh et al., in 2011 provide convincing evidence for abnormalities in a specific thalamo-cortical circuit, with reduced structural and task-induced functional connectivity, which may underlie the functional abnormalities in JME. Dysfunction in these areas results in deficits of concept formation, abstract reasoning, planning and self-regulation of behaviour, and control of impulsivity and emotions [21].

Devinsky et al., in 1997 suggested that the personality dysfunction might be a result of frontal lobe deficits in JME patients after they found impairment on tests of concept formation, abstract reasoning and mental flexibility, cognitive speed, and planning and organization [18].

R. Thomas et al., in 2014 examined 60 patients with drug-refractory JME and concluded that the patients were profoundly impaired across the range of tests evaluating intellectual function, language and naming, executive function, the impact of epilepsy, and AED side effects.

Eighty-three percent of patients exhibited frank executive dysfunction, which was moderate to severe in 66% [22].

3. Conclusion

Reduced Quality of Life and comorbid personality and nonpsychotic psychiatric disorders are a common problem in JME management. The disorders in patients with JME often go undiagnosed and untreated. Therefore, this problem requires further and extensive investigation. A comprehensive psychiatric evaluation should be offered at the time of diagnosis to detect these comorbidities and to treat them. The neurologist should understand that liaising with mental health professionals is beneficial. Along with the professional treatment plan, one should also discuss lifestyle and self-care strategies of patients with JME.

Conflict of interest

Nil

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