Current Trends in Neurology
Vol. 9, 2015

Review

Transitional issues for adolescents with epilepsy

Erika Takle Axeen and Jennifer E. Langer*
University of Virginia, Department of Neurology, PO Box 800394, Charlottesville, VA 22908, USA.

ABSTRACT

Adolescence may be a tumultuous period for most and presents unique challenges for adolescents with epilepsy. Identity formation, independence, sexuality, as well as social pressures may be impacted by epilepsy. Traditionally, late adolescence is a time for 'transfer' of the pediatric patient to adult care. This is a critical period during which support and education for the patients with epilepsy and their caregivers is essential. The 'transition' should address specific topics such as understanding their epilepsy, importance of adherence to medications, reproductive issues, employment and empowerment for navigation of the healthcare system. Models for transition clinics discussed in the literature include referral 'transfer' letters between providers, a joint 'hand-off' clinic with both pediatric and adult neurologist, nurse-led clinics, and diagnosis-independent transition programs. Critical evaluation of efficacy of these programs is limited. Further investigation into what constitutes effective transition is therefore necessary.

KEYWORDS: transition to adult healthcare, transition, models of transition, epilepsy, child, adolescence

1. Introduction

Of those children who are diagnosed with epilepsy, about 1/3 or more continue to have seizures into adulthood [1]. This necessitates the transfer of care from a pediatric neurologist to an adult neurologist. Adult-style care with emphasis on the individual may be markedly different from pediatric-style care with emphasis on the family. Without adequate preparation the adolescent and his/her family may be ill equipped for this change. As a result, the concept of 'transition' was introduced in 1993 as a 'purposeful, planned, multidisciplinary movement of adolescents and young adults from child-versus-adult-oriented health care systems' [2]. This transition involves not just the adolescent with epilepsy but also must take into account the interests and concerns of the parents or caregivers. There is an abundance of literature surrounding the importance of the transitional process in other pediatric chronic diseases such as diabetes and sickle cell disease. Over the past few years the concept of transition in the setting of epilepsy has been explored. Despite the recent exploration of this topic, there remains a paucity of published evidence to guide transition.

2. Implications of epilepsy on adolescent development

Adolescence is a period of great change, physically, emotionally, and socially that includes struggles for independence, autonomy, and identity formation. Issues emerge including driving, alcohol use, changing social relationships, sex, preparation for college or work, and increase in independence. All of these issues are complicated by the presence of chronic neurological disease leading to poorer quality of life in teenagers with epilepsy.

The burden of epilepsy on the quality of life (QOL) of adolescents can be significant. A comparison between teens with epilepsy and asthma suggested that adolescents with epilepsy have a poorer QOL in psychological, social and academic domains,

*Corresponding author: Jl2gw@virginia.edu

particularly in females and those with severe epilepsy [3]. Other risk factors for poor QOL among teens with epilepsy include increased seizure severity, older adolescent age, and symptoms of neurotoxicity [4]. Psychosocial impact of epilepsy is significant with higher rates of depression, anhedonia and social anxiety in patients with epilepsy when compared with healthy controls [5]. Unfortunately, teens continue to have concern for social stigma given that many as 36% of children/ adolescents have kept their epilepsy a secret from their peers for fear of being treated differently [6]. Adolescents with concerns that epilepsy impacts their social interactions are less likely to adhere to their medication regimen [7]. A 2001 survey of 19,441 high school students by the Epilepsy Foundation showed that about 75% of teens believed that their peers with epilepsy would be more likely to be bullied and that only 31% would date someone with epilepsy [8]. Unfortunately, this suggests that concerns about social stigma may be justified. Thus, the impact of epilepsy extends to many domains of life which may have distinct implications on healthy adolescent development [9].

Teens with epilepsy also have poorer social outcomes as they transition to adulthood, making this transitional period a potentially important time for intervention. Young adults with chronic illness have lower rates of high school graduation, decreased employment, and increased reliance on public financial assistance [10]. Specifically in patients with juvenile myoclonic epilepsy evaluated 25 years after seizure onset, 74% had at least one unfavorable social outcome including failure to complete high school, unplanned pregnancy, depression, unemployment, living alone, or never in a romantic relationship for more than three months [11]. In this cohort, 80% of pregnancies were unplanned or outside of a stable relationship.

3. The goals of transition

The goal of the transitional process is to safely and successfully move the teenager from a pediatric model of epilepsy care to an adult model equipped with necessary tools to successfully manage a future living with epilepsy and to do this in an environment that fosters the development of independence, if feasible, but also provides support for family and caregivers. This transition time provides a valuable opportunity to verify the epilepsy diagnosis, consider additional testing, and determine if there is a continued need for treatment. Past treatments should be reviewed to determine best course of action in the future.

The transitional process must be flexible and variable due to the heterogeneity of the epilepsy population. We would suggest that for the development of a transitional program three distinct populations should be considered: (1) patients with normal/relatively normal cognition and epilepsy diagnosed in early childhood, (2) patients with normal/relatively normal cognition diagnosed in adolescence, (3) patients with epileptic encephalopathies and other epilepsy syndromes associated with significant cognitive limitations. In addition, the Camfields suggested another important group of patients with remission of seizures but with persistence of other associated comorbidities such as cognitive deficits, behavioral disorders, and motor impairments in their transitional framework [12].

For group (1) patients with normal/relatively normal cognition and epilepsy diagnosed in childhood, we have often found that these adolescents know very little about their epilepsy as the bulk of education was aimed at their caregivers at the time of diagnosis. For this group, we spend a considerable amount of time reviewing the diagnosis including defining what epilepsy is, why they have it, what their seizure types are, and what are the goals of treatment. For group (2) patients with normal/relatively normal cognition diagnosed in adolescence, a new diagnosis is stressful for both the patient and the caregiver; thus a significant amount of time is required reassuring and educating both the caregiver and the patient. We provide the bulk of the education at the level of the adolescent but always leave a significant amount of time for answering questions from both the adolescent and caregiver.

For groups (1) and (2), the goal for transition is the achievement of independent epilepsy management including the ability to accurately report seizures and side effects of anti-epileptic medications. To track and measure this goal, we use a grading system (Figure 1) which allows us to follow an adolescent's progress over multiple visits. Once he/she has

Transition level 1	
	Know your medications, doses, timing, and importance of compliance
	Know about the side effects of your medications
	Know how to fill out or make a seizure calendar
	Know the key details of your health history
Transition level 2	
	Self-administration of medication and importance of compliance
	Maintain a seizure calendar
	Know key details of your health history
	Know how to describe your seizures
	Know and self-report medication side effects
	Begin to feel comfortable calling the clinic if there is a problem
Transition level 3	
	Self-administration of medications including calling in for refills and new prescriptions
	Maintain a seizure calendar
	Know key details of your health history
	Know your seizure descriptions
	Know and self-report side effects of your medications
	Calling the clinic if there is a problem or to make or change an appointment

Langer JE- used at University of Virginia Transitional Clinic, unpublished

Figure 1. Transitional levels of disease self-management.

achieved the final level, level 3, we consider him/her to be able to independently manage his/her epilepsy and graduate the adolescent from the program. In contrast, for group (3) patients with epileptic encephalopathies and other epilepsy syndromes associated with significant cognitive limitations, independent disease management is often not a realistic goal. Instead, we must focus on continuing education for the caregiver and providing support for future planning.

A transitional process must educate the adolescent patient while providing support to the caregiver. A supportive caregiver can improve the likelihood of a successful transition for the adolescent. The transition process is often tough on a caregiver who has been managing his/her child's epilepsy for years including managing medication schedule, tracking seizure frequency, scheduling appointments, etc. Parents may have many fears about relinquishing the primary responsibility for their child's epilepsy. Education ideally involves both the parent and the adolescent to facilitate the gradual shift in the roles as adolescent autonomy develops. In the clinic setting, this includes a shift to the adolescent being the focus of history-taking which is demonstrative to both the clinician and the parent. Over time, the adolescent should also be provided time alone with the clinician.

4. Educational topics for the transitional period

Adolescents and their caregivers have concerns and questions that are often distinct from other younger pediatric patients or adults. This was recognized in Liverpool, England in the 1990s with the development of a specific clinic for adolescents with epilepsy to provide adolescent-specific education and aid in the transitional process. Through this clinic, they established that the concerns of adolescents were broad and variable including education/career choices, side effects of medication, need for continuing

antiepileptic medications, driving issues, concerns regarding alcohol and other 'leisure activities', contraception, pregnancy, genetic risk of epilepsy and epilepsy surgery [13]. In our transitional clinic population at the University of Virginia, we independently surveyed teens and caregivers asking them to rank educational topics of importance using a Likert scale ranging from least important to most important. Survey questions ranged from gaining information about understanding epilepsy, triggers, medication, driving, birth control options, pregnancy, mood disorders, bone health, epilepsy support groups, internet based resources, or risk of sudden unexpected death in epilepsy (SUDEP). Both teens and caregivers were most interested in learning about epilepsy and seizure triggers and both groups were least interested in internet-based resources and support groups (Langer, J. E., unpublished).

The above data suggests that adolescents and their families have questions about epilepsy and desire answers. There is little evidence suggesting the best way to deliver information. A structured psychoeducational intervention showed a positive impact on some aspects of patient perceived QOL following group educational sessions on selected epilepsy topics [14]. From informal questioning of pediatric and adult neurologists, there is clearly a heterogeneous approach to education including use of internet-based resources, direct provider-based education in clinic, support groups, retreats, or combinations of multiple approaches. Preferred methodology is often related to variations in health care delivery and utilization of resources in specific clinic and hospital settings.

The American Epilepsy Society (AES) developed two practice tools for adolescent epilepsy patients to aid in the development of recommended content during the transitional period [15]. These practice tools are divided into recommendations for adolescents without significant developmental delay with a plan for independence and adolescents with significant developmental delay with independence unlikely. For each group, there are age-specific recommendations starting with age 10-13 years and they can be found on the AES website (https://www.aesnet.org/clinical_resources/practice_tools/transition_tools_adolescents).

Using AES practice tools and our personal experience, we have compiled a list of educational topics that should be included when designing an adolescent transitional clinic remembering that due to the heterogeneity of the epilepsy population, not all topics are applicable to all adolescent epilepsy patients. In addition to these topics, we suggest appropriate screening for co-morbidities associated with epilepsy including mood disorders, attention deficit hyperactivity disorder and cognitive problems.

4.1. Understanding epilepsy

It is of paramount importance that adolescents understand their own epilepsy. Epilepsy knowledge consists of patient-specific seizure types and descriptions, options for treatment, names and doses of anti-epileptic medications, how and when to call the neurologist, seizure first aid, and seizure precautions. This type of knowledge of disease is suggested to lead to improved self-management across chronic diseases of adolescence [15, 16]. Low levels of epilepsy knowledge have been associated with higher levels of depression, low self-esteem and social anxiety [5].

If epilepsy is diagnosed early in childhood, the adolescent may know very little about the diagnosis. We recommend using early transitional visits to review important aspects of diagnosis including specific epilepsy syndrome (if known), seizure types, magnetic resonance imaging and electroencephalogram findings, and specific seizure triggers. Through the transitional process, the adolescent should be able to describe his/her seizures and know details about their workup. General topics including seizure precautions and seizure first aid should be reviewed. As increasing amounts of time are spent in places other than home or school, adolescents should be encouraged to discuss their epilepsy with their friends and co-workers. An emergency care plan for these situations should be reviewed. Additionally, teenagers must learn practical skills for the navigation of the health care system such as 'How do I make an appointment with my doctor?' and 'How do I get refills on my medications?' as they gain increasing levels of independence.

4.2. Triggers for seizure exacerbation

The most common self-reported precipitating factors for seizures amongst adults include stress, sleep deprivation and fatigue [17]. Women may also report a catamenial pattern of seizure frequency related to their menstrual cycle. As many behavioral risk factors for worsening seizures are common

amongst adolescents, education is paramount. A frank discussion of drug and alcohol use in relation to exacerbation of seizures should occur. Stress reducing strategies may be considered.

4.3. Antiepileptic drug (AED) issues

For patients with epilepsy, a medication regimen is generally a daily part of life. Non-adherence is often a problem for adolescents. Amongst 232 adolescent survey responders in Finland, 34% reported poor compliance [18]. Strong predictors of good compliance include support from parents and physicians, self-motivation from the patient and perceived social acceptance of their epilepsy [7]. Improved disease knowledge often leads to improved compliance as well. The clinician should openly acknowledge the challenges of taking a medication two or three times daily and attempt to address barriers to compliance. We often suggest strategies such as using alarms or texting programs in conjunction with pill boxes. Parental reminders may also be very important for some. Consideration of long acting medications may help simplify the regimen and therefore improve compliance.

Side effects of AEDs have been noted in more than a third of children/adolescents including specific complaints of weight change, headaches, dizziness and shaking [6]. The adolescent should understand what the possible side effects of medications may be and what to do if these occur. We have found that asking an open-ended question such as 'Are you having side effects or problems with your medication?' is not usually informative. Instead consider more directed questioning such as 'Does your medication make you feel dizzy, sad, sleepy, etc?' which are more likely to result in reliable self-reporting of side effects.

4.4. Reproductive health

Reproductive health is a critical topic of discussion with adolescents, particularly in young women. Epilepsy and use of AEDs may impact sexual functioning, fertility, options for birth control, safety of pregnancy, and breastfeeding. As both genders may be impacted by fertility and sexual function, the clinician should feel comfortable discussing such topics in relation to epilepsy.

For young women with epilepsy, beginning in the early adolescent time period we discuss implications of epilepsy and AED use both on birth control options and pregnancy. These discussions are important early in adolescence as multiple studies have shown that adolescents with epilepsy are more likely than their peers to have unplanned pregnancies [11, 19]. Specifically, the interactions between oral contraceptives and some AEDs must be discussed. The rate of oral contraceptive pill (OCP) failure is increased in women on enzyme-inducing AEDs such as phenytoin, phenobarbital, or carbamazepine [20]. If oral contraceptive pills are desired in patients using enzyme-inducing AEDs, higher dose estrogen pills should be considered. Additionally, use of oral contraceptives with estrogen has been shown to increase the rate of lamotrigine metabolism thereby reducing blood levels which may affect seizure control [21-23]. Alternative contraceptive methods, such as progesterone and intrauterine hormone-releasing systems, do not interfere with hepatic enzymes and may be considered.

Epilepsy has the potential to significantly impact pregnancy. As increased rates of unintended pregnancy are seen in young women with epilepsy, we recommend discussions of pregnancy-specific issues begin in early adolescence. Seizures may be detrimental to the developing fetus including risks of physical injury, theoretical risks of hemodynamic changes during a seizure, and risks of preterm labor with poorly controlled epilepsy. AEDs may also be associated with major birth defects including neural tube, heart and urinary tract defects, and skeletal abnormalities [24]. The risk of birth defects is known to be elevated with the use of some antiepileptic medication such as valproate, phenytoin, carbamazepine, phenobarbital and topiramate [25-27]. Valproate is associated with a particularly high risk for major congenital malformations [28]. These considerations should be discussed with adolescent females, and high-risk medications should be avoided if possible in women of childbearing age.

Folic acid should be recommended to all female adolescent patients. Unfortunately, this is not uniformly followed, as in one transition referral epilepsy clinic, only 12 of 86 women of childbearing age were already on prophylactic folic acid supplementation [29]. Folic acid supplementation before pregnancy has been shown to reduce the incidence of neural tube defects in high-risk

pregnancies [30]. Although it is unclear whether folic acid supplementation can prevent neural tube defects in all women on AEDs, folic acid should be initiated in all women of childbearing age on AEDs.

4.5. Driving

Driving is a marker for independence in adolescence and can impact the teen's view of their quality of life. Driving is particularly important for teenagers living in rural areas without access to public transportation. Though laws vary state by state and internationally, physicians are involved in the assessment of safety on the road. Considerations for the adolescent with epilepsy's ability to drive include level of seizure control or length of time since last seizure, medication compliance, as well as cognitive abilities [31]. This is made all the more complicated in adolescence, a population where risk taking behavior is inherent [32].

4.6. Employment

Surveys have shown that a high number (73%) of adolescents expect their epilepsy to impact future employment [6]. This expectation may be correct for some as evidenced by a 1993 survey of adults with epilepsy reporting a 33% unemployment rate compared with the then-current rate of 13% unemployment in the general population [33]. Similarly, in a population based study, patients with epilepsy without cognitive impairment followed from childhood had an adult unemployment rate of 20% [34]. Intelligence, age of epilepsy onset, and amount of vocational training are suggested to be factors for employment [35]. While only very few occupations limit employment due to past or current history of epilepsy, specific jobs involving the expectation of climbing ladders or trees, operating heavy machinery or other vehicles, or handling of fire arms may not be appropriate for patients with intractable epilepsy.

4.7. Bone health

AEDs have been implicated for increased risk of osteoporosis. Increased frequency of fractures has been noted in populations on AEDs, with higher risk seen in enzyme-inducing medications [36]. Vitamin D deficiency in adults with epilepsy is prevalent with 54% on enzyme-inducing and 37% on non-enzyme inducing AEDs with levels <20 ng/ml [37]. All patients on antiepileptic medications should receive Vitamin D and calcium supplementation. Adolescents should be screened for vitamin D deficiency and their level optimized with supplementation.

4.8. Sudden unexpected death in epilepsy (SUDEP)

Sudden unexpected death in epilepsy (SUDEP) is defined as sudden, unexpected, witnessed or unwitnessed, non-traumatic, and non-drowning death in a patient with epilepsy [38]. SUDEP incidence within the epilepsy population ranges widely, from 0.09 per 1000 person-years in newly diagnosed patients to 9.3 per 1000 person-years in epilepsy surgery candidates [38]. Most of the available incidence data is based on adults, but a less robust report on children with epilepsy suggests that incidence ranges 0.20-0.43 per 1000 person-years. Identified risk factors have included young age, male sex, poor compliance with AED treatment, and intractable convulsive seizures.

A debate exists in the literature regarding how to discuss SUDEP with patients and with which patients to do so. Unfortunately, patient understanding about risk of SUDEP is limited as a recent survey of adults showed that only a few knew about SUDEP (14.3%) [39]. The majority of patients wished to discuss SUDEP (89.5%) suggesting that this should be broached during childhood and adolescence. Though some of the suggested risk factors for SUDEP are not modifiable (young age, male gender) other modifiable factors such as optimizing control of epilepsy, encouraging medication compliance, and avoiding alcohol use may decrease risk of SUDEP [40].

5. Models for transition

At this time, there is no best practice measure for providing transitional care for adolescents with chronic disease. Much of the literature consists of policy statements [2] and descriptions of transition clinics. Common components of transition in other pediatric chronic diseases include educational materials (sometimes computer-based), a transition-specific clinic and a coordinator for the transition process [41]. The 2013 American Epilepsy Society transitional practice tools address some important aspects of transitional care specific to epilepsy.

A key component of transition is the accurate transfer of information. At a minimum, if an adolescent is changing care to an adult neurologist a written summary of medical history, diagnosis, testing, and treatment history is necessary [42]. This could be a referral accompanied by a standardized form or a written discourse prior to transfer as well as inclusion of the patient's records [43].

Most commonly, transitional clinics described in the literature involve a joint approach between pediatric and adult providers. A nurse-driven model is described in Alberta, Canada consisting of a one-time visit with both pediatric and epilepsy nurses and a pediatric neurologist [43]. A questionnaire of patient and caregiver perspectives suggested that all parties agreed that the clinic was beneficial and lessened fears of transitions. A physician-led transition clinic for adolescents with epilepsy was initiated in Liverpool in 1991 [13]. This referral clinic consisted of joint visits with both a pediatric and adult neurologist with special interest in epilepsy as well as an epilepsy nurse. The patients were 'graduated' to an adult neurologist when deemed appropriate by the group. A similar clinic was started in Wales in 1997 consisting of a joint visit with a pediatric and adult neurologist [29]. Patients were most often seen at this clinic for one visit. The emphasis of this clinic was to 'smoothen the transition' as well as review of diagnosis, medications and education as appropriate. Neither the Liverpool nor the Wales clinic include any data regarding efficacy. Interestingly, both clinics reported a revision of diagnosis from epilepsy to non-epileptogenic etiology (such as vasovagal syncope, panic attacks, migraine, etc.) in 10% and 14%, respectively [13, 29]. A referral transition clinic may thus provide an opportunity for independent review of the diagnosis during this important period. Our transitional clinic at the University of Virginia has been developed by an adult epileptologist with interest in adolescents (JEL), pediatric nurse practitioner, and nurse coordinator. This multi-visit clinic has 2 components, the office visit with the adult epileptologist followed by an educational session with the pediatric nurse practitioner. Once the adolescent has 'graduated' our transitional program, they are followed exclusively by the same adult epileptologist to reduce the number of physician transitions.

Several other international models are mentioned by Carrizosa [44]. In France, patients with severe epilepsy may be referred to a single, dedicated adult epileptologist, ideally at an early age. In Germany, there has been a recent push to institute a diagnosis-independent transition program with a standardized educational program. Given the lack of formal transitional programs in Latin America there is the consideration of a checklist of essential topics to be reviewed at physician visits during years of transition [44].

In additional to office visits, peer group education of adolescents may be beneficial for addressing common adolescent concerns regarding epilepsy [13, 44]. The adolescent may benefit from a sense of community. Educational groups have been employed in other chronic diseases with success. A peer-led educational group in teens with asthma resulted in decreased morbidity and increased quality of life as compared to the control group [45].

6. Successful transition

Data is limited on how transition in epilepsy should best be accomplished. Issues that remain unsettled include when transition should be initiated, which healthcare providers best facilitate this transition, what setting is most appropriate, and how long should transition last. Further research regarding how best to support adolescents with epilepsy as they move through this challenging time of life is needed.

CONFLICT OF INTEREST STATEMENT

Neither author has any conflicts of interest.

REFERENCES

1. Beghi, E., Camfield, P. R. and Camfield, C. S. 2014, Epilepsia, 55(Suppl. 3), 3-7.
2. Blum, R. W., Garell, D., Hodgman, C. H., Jorissen, T. W., Okinow, N. A., Orr, D. P. and Slap, G. B. 1993, J. Adolesc. Heal., 14(7), 570-76.
3. Austin, J. K., Huster, G. A., Dunn, D. W. and Risinger, M. W. 1996, Epilepsia, 37(12), 1228-38.

4. Devinsky, O., Westbrook, L., Cramer, J., Glassman, M., Perrine, K. and Camfield, C. 1999, Epilepsia, 40(12), 1715-20.
5. Baker, G. A., Spector, S., McGrath, Y. and Soteriou, H. 2005, Epilepsy Behav., 6(4), 556-62.
6. Baker, G. A., Hargis, E., Hsih, M. M., Mounfield, H., Arzimanoglou, A., Glauser, T., Pellock, J. and Lung, S. 2008, Epilepsy Behav., 12(3), 395-401.
7. Kyngäs, H. 2001, Seizure, 10(8), 549-53.
8. Austin, J. K., Shafer, P. O. and Deering, J. B. 2002, Epilepsy Behav., 3(4), 368-75.
9. Thomson, L., Fayed, N., Sedarous, F. and Ronen, G. M. 2014, Dev. Med. Child Neurol., 56(5), 421-33.
10. Maslow, G. R., Haydon, A. A., Ford, C. A. and Halpern, C. T. 2011, Arch. Pediatr. Adolesc. Med., 165(3), 256-61.
11. Camfield, C. S. and Camfield, P. R. 2009, Neurology, 73(13), 1041-45.
12. Camfield, P., Camfield, C. and Pohlmann-Eden, B. 2012, Epilepsy Curr., 12(4s), 13-21.
13. Appleton, R. E., Chadwick, D. and Sweeney, A. 1997, Seizure, 6(1), 27-30.
14. Snead, K., Ackerson, J., Bailey, K., Schmitt, M. M., Madan-Swain, A. and Martin, R. C. 2004, Epilepsy Behav., 5(4), 547-56.
15. Rakshit, R. C. and Mayberry, J. F. 2008, Inflamm. Bowel Dis., 14, S66-67.
16. McDonagh, J. E., Southwood, T. R. and Shaw, K. L. 2007, Rheumatology (Oxford), 46(1), 161-68.
17. Ferlisi, M. and Shorvon, S. 2014, Epilepsy Behav., 33, 101-5.
18. Kyngäs, H. 2000, Seizure, 9(8), 598-604.
19. Wirrell, E. C., Camfield, C. S., Camfield, P. R., Dooley, J. M., Gordon, K. E. and Smith, B. 1997, Arch. Pediatr. Adolesc. Med., 151(2), 152-58.
20. Zupanc, M. L. 2006, Neurology, 66(6 Suppl. 3), S37-45.
21. O'Brien, M. D. and Guillebaud, J. 2006, Epilepsia, 47(9), 1419-22.
22. Reimers, A., Helde, G. and Brodtkorb, E. 2005, Epilepsia, 46(9), 1414-17.
23. Christensen, J., Petrenaite, V., Atterman, J., Sidenius, P., Ohman, I., Tomson, T. and Sabers, A. 2007, Epilepsia, 48(3), 484-89.
24. Holmes, L. B., Harvey, E. A., Coull, B. A., Huntington, K. B., Khoshbin, S., Hayes, A. M. and Ryan, L. M. 2001, N. Engl. J. Med., 344(15), 1132-38.
25. Hunt, S., Russell, A., Smithson, W. H., Parsons, L., Robertson, I., Waddell, R., Irwin, B., Morrison, P. J., Morrow, J. and Craig, J. 2008, Neurology, 71(4), 272-76.
26. Diav-Citrin, O., Shechtman, S., Arnon, J. and Ornoy, A. 2001, Neurology, 57(2), 321-24.
27. Harden, C. L., Meador, K. J., Pennell, P. B., Hauser, W. A., Gronseth, G. S., French, J. A., Wibe, S., Thurman, D., Koppel, B. S., Kaplan, P. W., Robinson, J. N., Hopp, J., Ting, T. Y., Gidal, B., Hovinga, C. A., Wilner, A. N., Vazquez, B., Holmes, L., Krumholz, A., Finnell, R., Hirtz, D., Le Guen, C., American Academy of Neurology. and American Epilepsy Society. 2009, Neurology, 73(2), 133-41.
28. Hernández-Díaz, S., Smith, C. R., Shen, A., Mittendorf, R., Hauser, W. A., Yerby, M., Holmes, L. B. and AED Pregnancy Registry North American. 2012, Neurology, 78(21), 1692-99.
29. Smith, P. E. M., Myson, V. and Gibbon, F. 2002, Eur. J. Neurol., 9(4), 373-76.
30. 1991, Lancet, 338(8760), 131-37.
31. Nashef, L., Capovilla, G., Camfield, C., Camfield, P. and Nabbout, R. 2014, Epilepsia, 55(Suppl. 3), 41-45.
32. Olsen, E. O., Shults, R. A. and Eaton, D. K. 2013, Pediatrics, 131(6), e1708-15.
33. Theodore, W. H., Spencer, S. S., Wiebe, S., Langfitt, J. T., Ali, A., Shafer, P. O., Berg, A. T. and Vickrey, B. G. 2006, Epilepsia, 47(10), 1700-1722.
34. Camfield, C., Camfield, P., Smith, B., Gordon, K. and Dooley, J. 1993, J. Pediatr., 122(6), 869-73.
35. Sillanpää, M. and Schmidt, D. 2010, Epilepsia, 51(6), 1053-60.
36. Vestergaard, P., Rejnmark, L. and Mosekilde, L. 2004, Epilepsia, 45(11), 1330-37.
37. Teagarden, D. L., Meador, K. J. and Loring, D. W. 2014, Epilepsy Res., 108(8), 1352-56.
38. Tomson, T., Nashef, L. and Ryvlin, P. 2008, Lancet. Neurol., 7(11), 1021-31.

39. Xu, Z., Ayyappan, S. and Seneviratne, U. 2014, Epilepsy Behav., 42C, 29-34.
40. Shankar, R., Cox, D., Jalihal, V., Brown, S., Hanna, J. and McLean, B. 2013, Seizure, 22(10), 812-17.
41. Davis, A. M., Brown, R. F., Taylor, J. L., Epstein, R. A. and McPheeters, M. L. 2014, Pediatrics, 134(5), 900-908.
42. Sommelet, D. 2013, Handb. Clin. Neurol., 111, 101-5.
43. Jurasek, L., Ray, L. and Quigley, D. 2010, J. Neurosci. Nurs., 42(4), 181-89.
44. Carrizosa, J., An, I., Appleton, R., Camfield, P. and Von Moers, A. 2014, Epilepsia, 55(Suppl. 3), 46-51.
45. Shah, S. 2001, BMJ, 322(7286), 583-583.