Consequences of Epilepsy: Why do We Treat Seizures?

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ABSTRACT: Improving health-related quality of life in epileptic patients, rather than simply reducing seizures, has become the principal goal in epilepsy management. Reducing seizure frequency is one of the main factors contributing to improved quality of life. Evidence for and risk of the following potential adverse effects of seizures is reviewed: brain damage from seizures, sudden unexpected death, status epilepticus, kindling, falls or injury and psychosocial consequences. Although the evidence for seizure frequency influencing some of these factors is not clear-cut, as a whole, they offer a strong impetus toward an aggressive approach to controlling recurrent seizures in most cases.

RÉSUMÉ: Les conséquences de l'épilepsie: pourquoi contrôler les crises? L'amélioration de la qualité de vie en relation avec la santé chez les épileptiques plutôt que le simple contrôle des crises est devenue le but principal du traitement de l'épilepsie. La diminution de la fréquence des crises est un des facteurs principaux contribuant à l'amélioration de la qualité de vie. Nous revoyons les données sur les effets secondaires possibles des crises et les risques qui y sont associés: dommage cérébral causé par les crises, mort subite, état de mal épileptique, aggravation des crises, chutes ou blessures et conséquences psychosociales. Bien que les données en faveur de l'influence de la fréquence des crises sur certains de ces facteurs ne soient pas claires, en général elles incitent, dans la plupart des cas, à une approche agressive dans le contrôle des crises récurrentes.

Can. J. Neurol. Sci. 1998; 25: S24-S26

Evaluation of quality of life looks at relationships, level of independence, employment and transportation issues, as perceived by or experienced by the patient. These concerns are dynamic and may change over time changing from the impact of the initial diagnosis and adaptations of the disorder and then through years of poor and good seizure control. In addition to the traditional "history and physical" there are now tools that are being developed to help assess selected aspects of quality of life such as seizure severity, neurotoxic effects, etc.[1]

The balance of this paper is framed around the question "Why should we treat a patient with seizures or epilepsy?" The answer has to be because of the consequences of having seizures and how they negatively impact on one's quality of life.

It is not "because they are there" nor is it because "we know that they are bad and progressive". In fact, with modern treatment, over 70% of patients will be controlled and ultimately most of those patients will stop their anti-epileptic medications.[2] In considering who to treat, when to treat and with what to treat, one needs to look at the "risk-benefit ratio". Some of the following concerns regarding consequences also come into that decision process.

Potential Consequences of Seizures

Potential For Neurological Damage

Somewhat contrary to experimental animal data, there is really no evidence that a single brief tonic clonic seizure, or even a small number of tonic clonic seizures, produces neurological damage unless the seizures last longer than 30 minutes (status epilepticus) when damage could possibly ensue. There is, nevertheless, considerable evidence that cognitive and emotional problems occur to a greater extent in individuals with epilepsy than the normal population.[3]

There are problems trying to relate recurrent seizures to brain damage and cognitive decline. Both seizures and decreased cognition share similar pathology. For example, the genetic syndrome, tuberous sclerosis, gives rise to both the mental retardation and epilepsy, or the diffuse brain injury from encephalitis or a hypoxic injury give rise to both cognitive decline and seizures.

A concern regarding anti-epileptic drugs effects on cognition is appropriate although recent studies have shown that effects are relatively minor in the non-toxic patient.[4] There is a perception on the part of parents, teachers and society that people with epilepsy, especially children, have increased learning difficulties and have lesser intellectual capacity and potential. This often leads to over protection, restriction of activities, and lack of encouragement in academic endeavours that results in emotional and social regression and educational under achievement independent of seizure frequency or anti-epileptic medications.[4]

Many studies over the years have shown that the early onset of seizures is associated with mental retardation or lowered IQ. A pioneering study by Keith[5] in 1955 looked at 288 patients referred to his academic centre and showed that in those with

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RECEIVED JULY 10, 1998.
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epilepsy onsetting at less than age 6 months, 65% were retarded. In those beginning between 6 months and 2 years, and 2 to 4 years respectively, figures for mental retardation were 49% and 34%. Patients whose epilepsy began between age 4 and 7 years, or 7 and 15 years, had even lower rates of retardation: 22% and 12%. The association of mental retardation is likely with the etiology of the seizures/epilepsy and not with seizures as the following important work would suggest. The collaborative perinatal project (NCPP)[6] in the mid-80's prospectively looked at over 50,000 children followed to age 7. In the 5% of this cohort who developed seizures, IQ was the same at age 7 as it was at age 4 and also the same as age match controls. Other similarly designed prospective studies have failed to demonstrate a decline in mental function over time in epileptic patients using a test/re-test paradigm. The conclusion from these studies is that mental retardation, when present, antedated the seizures or shared a common etiological link rather than being caused by the seizures.

It is difficult to do controlled experiments in humans, but there is one situation that also sheds light on the relationship between seizures and cognitive decline. Electroconvulsive therapy (ECT) is well known to cause both short term retrograde and antegrade memory impairment. The effects are transient, lasting in the order of a few months. Investigators have looked at the larger issue of whether ECT has long term accumulative effects. Goldman et al. (1972)[7] found "some" accumulative damage in a group of schizophrenics receiving ECT but only in those having more than 50 treatments. More recent studies from Lawson et al. (1990)[8] and Sackheim et al. (1993)[9] applying a variety of cognitive tests to patient groups and controls, showed no residual changes three months after ECT. Calev (1991),[10] in a group of depressed patients, again applying psychometric testing, showed no deterioration and, in fact, found both verbal and performance IQs improved. Devanand (1991)[11] addressed the criticism that perhaps "a few ECTs" doesn't mimic the experience of a patient with chronic epilepsy. He was able to find 8 patients who had more than 100 ECTs who showed no accumulative or long term cognitive or memory defect when compared to psychiatric control patients.

Risk of Sudden Unexpected Death

Sudden, unexpected death occurs in approximately one of one thousand patients with epilepsy. Coroners' studies, however, have shown that approximately 20% of these patients have therapeutic anti-epileptic drug levels, suggesting that treatment with anti-seizure medications would not necessarily be expected to prevent this tragedy. Males outnumber females by a factor of three. The age range is variable, but the average age is about 30. The predominant seizure type is generalized tonic clonic seizures. Epilepsy is usually of many years duration, and seizures are frequent with approximately 40% of patients averaging at least one a week and 50% having at least 3-10 a year. Sixty percent of the patients are found dead at home, usually in bed or on the floor, and usually there are no signs that they strangled or suffocated. The mechanism of death isn't known, although a cardiac arrhythmia or neurogenic pulmonary edema is often hypothesized. The syndrome of sudden unexpected death in epilepsy (SUDEP) has many parallels with the sudden infant death syndrome (SIDS).

Risk of Status Epilepticus

The chance of someone with one or two seizures going into status is unknown, but presumably small. The influence of treatment with anti-epileptic on the risk of developing status is also unknown but most patients who have had seizures and then developed status epilepticus had previously been prescribed anti-epileptic drugs. Anti-epileptic drugs, if abruptly discontinued, paradoxically can lead to status. In animal models, prolonged status can produce selective cell damage in regions of susceptibility such as the CA1 and the CA3 areas of the hippocampus.[12] In humans, however, it may be difficult to distinguish the sequelae of status from pre-existing neurological pathology. Also, an illness that precipitates status, such as meningitis or hypoxic brain injury from cardiac arrest, is usually a more important factor than the status itself in producing morbidity. In any large series looking at the etiology of status epilepticus, poorly compliant epileptic patients with epilepsy comprise approximately 20%; the rest have non-epileptic etiologies such as encephalitis, etc.[13] Dodrill[14] examined a group of patients with serial psychometric testing five years apart. The group that had a bout of status epilepticus in the interval was at higher risk of cognitive deterioration. Their baseline IQ was already 14 points lower than the control group of epileptic patients who didn't have status, suggesting that their brains were already significantly compromised. Nevertheless, the IQ scores, both in the control group of epileptic patients not having status and in those having status were not significantly changed, suggesting that status did not provoke a decline in cognitive function. There were, however, some trends that did not achieve statistical significance for the status group.

In general, it appears that status epilepticus can have some adverse effect on mental function and mental abilities which emphasizes the importance of timely aggressive treatment. It is basically only older studies[15] that report any significant IQ loss or significant morbidity in the cohort with status epilepticus, likely reflecting less effective treatment before the era of intensive care units and a variety of IV medications, and imprecise etiological diagnosis.[15]

Possibility of Kindling

Clinical data also suggest that "seizures **do not** beget seizures".[15] Feksi et al.[17] looked at a group of untreated epilepsy patients from Kenya where anti-epileptic drug treatment initiation is often delayed, and showed that seizure remission rates were comparable to those in developed countries. Fifty percent of their patients had experienced grand mal seizures for greater than five years and 38% had experienced more than one hundred grand mal seizures before treatment was instituted. Camfield[18] also demonstrated in children that response to medication was not influenced by having up to ten seizures. Specifically, there was no less chance of seizure control or early remission if anti-epileptic drugs were delayed until after the tenth seizure. Treatment is to stop seizures, it doesn't "cure" or stop the disorder epilepsy, therefore if treatment is delayed the outcome is still favourable.

Risk of Falls/Injuries

Clearly, the risk of death or injury may be greater for individuals with epilepsy, but it also varies with the degree of

independence. In other words, adults with epilepsy would be expected to undergo more injuries than young children who live in a relatively protected environment. Kirby and Sadler,[19] who were interested in the morbidity of seizures did a study looking at all patients who presented with seizures to the emergency departments of the Halifax County Hospitals. In total 0.38% of all emergency room visits were precipitated by patients having seizures. Of those, death or injury occurred in 15%. The injuries were head contusions, head lacerations, fractures, dislocations and burns. Although the risk of serious injury and death was low (15%), Kirby pointed out that this study only surveyed a one year period. In a life time, patients who continue to have seizures incur substantial risk of serious injury or premature death.

Ryan[20] looked at the coroner's data on Alberta patients who drowned in a ten year period. Five percent of all drowning deaths in the province occurred in patients with epilepsy. In 60%, the drowning occurred in patients' homes during a bath which was unsupervised. Although 5% of all drownings is a small number, it nevertheless represents a potentially preventable cause of death in patients with epilepsy.

The risk of injuries-falls is clearly one of the two major reasons to treat patients and prevent seizures because of the significant risk of morbidity and a small risk of mortality.

Psychosocial Consequences

The psychosocial consequences of seizures are potentially great and are a major reason for attempting to prevent seizure recurrence. Seizures involve a loss of self-control, are embarrassing, anxiety provoking and frightening. They may also lead to lifestyle restriction such as over protection, loss of job, loss of driving and independence. Repeated seizures worsen all of the above. These consequences are somewhat age-dependent becoming more relevant as one develops increasing degrees of freedom going from childhood to adolescence to adult life.[21] The negative features of continuing seizures may lead to a life of isolation, passivity, dependence, poor self-esteem and development of poor social skills. This leads to both academic and vocational under achievement.

In conclusion, the potential complications of status epilepticus, IQ decline, sudden death, and kindling, although important, are relatively rare. The major problems of falls and injuries and the negative psychosocial consequences that develop from repeated seizures are the reasons "Why We Treat Seizures".

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