REVIEW

Alternative approaches to conventional antiepileptic drugs in the management of paediatric epilepsy

R Kneen, R E Appleton

Arch Dis Child 2006;**91**:936–941. doi: 10.1136/adc.2005.080002

Over the last two decades, there has been a rapid expansion in the number and types of available antiepileptic drugs (AEDs), but there is increasing concern amongst parents and carers about their unwanted side effects. Seizure control is achieved in approximately 75% of children treated with conventional AEDs, but non-conventional (or non-standard) medical treatments, surgical procedures, dietary approaches, and other non-pharmacological treatment approaches may have a role to play in those with intractable seizures or AED toxicity. Many of the approaches are largely common sense and are already incorporated into our current practice, including, for example, avoidance techniques and lifestyle advice, while others require further investigation or appear to be impractical in children.

Effective pharmacological treatments for epilepsy were identified with the bromides in the mid-1850s and phenobarbital in 1912. Over the last two decades, there has been a rapid expansion in the number and types of available antiepileptic drugs (AEDs) and it may be easy to overlook and be sceptical about non-pharmacological treatments. In addition, there is increasing concern amongst parents and carers about the unwanted side effects of conventional AEDs, often fuelled by the media and internet chat rooms. Historically, more holistic approaches were taken in epilepsy management, ranging from herbal remedies and dietary manipulation (including fasting) to spiritual rituals. For example, in the New Testament (Mark 9: 14–29) Jesus cast out a demon in a young man with what many have speculatively considered (but not proven) to have been epilepsy, and later told his disciples that the cure was in prayer and fasting.

This brief review will focus on the non-conventional (or non-standard) medical treatments, surgical procedures, dietary approaches, and other non-pharmacological treatment approaches that may have a role in the current management of the epilepsies (tables 1 and 2). It must be emphasised that, apart from steroid usage in treating infantile spasms (West syndrome) and some epilepsy surgery procedures, the evidence base for the majority of these treatment options is generally very limited and usually restricted to non-randomised and uncontrolled, and often retrospective, studies. Readers who would like further information on the quality of evidence available are directed towards the cited references for these alternative treatments.

See end of article for authors' affiliations

Correspondence to: Dr Richard Appleton, Roald Dahl EEG Unit, Department of Neurology, Alder Hey Children's Hospital, Liverpool, L12 2AP, UK; richard.appleton@rlc.nhs.uk

Accepted 22 June 2006

NON-CONVENTIONAL MEDICAL TREATMENTS OF EPILEPSY

Although steroids, immunoglobulins, vitamins, and melatonin are drugs, a brief overview of their use in epilepsy is included because they provide another approach in addition to AEDs.

Corticosteroids

Corticosteroids have been used in the treatment of paediatric epilepsy for over 50 years. The first report described the use of intramuscular adrenocorticotrophic hormone (ACTH) in children with West syndrome (infantile spasms) in 1958, but since then corticosteroids have been used for many other drug resistant epilepsy syndromes.[1] Their mechanism of action in epilepsy is unclear. Currently, ACTH is unavailable and has been replaced by tetracosactide in the UK and by hydrocortisone in France. A recent multicentre randomised controlled trial (RCT) suggested that corticosteroids (prednisolone or tetracosactide) may be more effective than vigabatrin in the short term management of infantile spasms and they are therefore considered by many to be the first line treatment for this syndrome.[2] Corticosteroids may also be useful for exacerbations of seizures or episodes of non-convulsive status epilepticus (NCSE) in other epileptic encephalopathies, including severe myoclonic epilepsy in infancy (also known as Dravet's syndrome), Lennox-Gastaut syndrome, cryptogenic epilepsy syndromes, or Rasmussen's encephalitis (more appropriately termed Rasmussen's syndrome, RS). Corticosteroids have also been reported to be successful (as monotherapy or in combination with sodium valproate) in Landau-Kleffner syndrome (LKS)[1] and also in the related syndrome of electrical status epilepticus during slow wave sleep (ESES). The main disadvantages of all corticosteroid preparations are their serious side effects, including possible death. There is no consensus of opinion on the corticosteroid doses, preparations, and treatment regimes that are

Abbreviations: ACTH, adrenocorticotrophic hormone; AED, antiepileptic drug; CBT, cognitive behaviour therapy; ESES, electrical status epilepticus during slow wave sleep; GABA, gamma butyric acid; IVIG, intravenous immunoglobulin; KD, ketogenic diet; LKS, Landau-Kleffner syndrome; MCT, medium chain triglyceride; NCSE, non-convulsive status epilepticus; OD, oligoantigenic diet; RCT, randomised controlled trial; RS, Rasmussen's syndrome

Table 1 Non-conventional antiepileptic drug (AED) treatment of epilepsy

Non-AED medical treatment
Steroids (for example, ACTH [tetracosactide], prednisolone)
Intravenous immunoglobulins
Vitamins (for example, pyridoxine, pyridoxal phosphate, biotin, folinic acid)
Melatonin
Dietary manipulation
Ketogenic diet
Classical ketogenic diet
MCT diet
Atkins diet
Oligoantigenic diet
Epilepsy surgery techniques
Lesional surgery (for example, tumour, amygdalo-hippocampectomy, temporal lobectomy, extra-temporal resections, anatomical hemispherectomy or functional hemispherotomy, removal of cortical seizure foci)
Specific surgical techniques (for example, sub-pial transection for Landau-Kleffner syndrome)
Palliative surgery (for example, callosotomy or vagus nerve stimulator implantation)

ACTH, adrenocorticotrophic hormone; MCT, medium chain triglyceride.

Table 2 Non-pharmacological treatment of epilepsy

Lifestyle changes
Exercise
Avoidance of sleep deprivation
Avoidance of excessive alcohol consumption
Psychological approaches
Techniques to abort seizures or reduce seizure frequency (for example, avoidance, relaxation, biofeedback, aversive therapy)
Promotion of emotional wellbeing (for example, yoga)
Reduction of psychiatric co-morbidity (for example, anxiety or depression)
Coping strategies for living with epilepsy (for example, CBT , counselling, psychotherapy, educational interventions)
Alternative therapy
Herbal medicine
Homeopathy
Others
Aromatherapy
Hypnosis
Acupuncture
Seizure alert dogs

CBT, cognitive behaviour therapy.

most effective. In our practice, we tend to use prednisolone in a dose of 2–3 mg/kg/day for a minimum of 2 weeks and then a taper over 1–2 weeks for West syndrome (depending on the initial response) and an exacerbation of seizures or NCSE in the epileptic encephalopathies. We would use a longer course (usually up to 3–4 months) of alternate day prednisolone in LKS and RS. There is a need for more robust (including RCT) evidence to determine whether early treatment with corticosteroids may improve the long term developmental and cognitive outcome in the epileptic encephalopathies. Such controlled trials would have to be undertaken in as ''pure'' and as homogeneous a population of children with a specific epileptic encephalopathy (and its cause) as possible.

Immunoglobulins

In the 1970s it was observed that seizure control appeared to improve in children with epilepsy who were given human pooled immunoglobulin therapy for allergic rhinitis.[3] Intravenous immunoglobulin (IVIG) has subsequently been used for the treatment of RS and seizure exacerbations in West syndrome and Lennox-Gastaut syndrome. Several regimens have been used with varying doses and duration, ranging from 100 to 1000 mg/kg given for 1, 2, or 3 consecutive days and then repeated after 1, 2, or 3 weeks. As with corticosteroids, there is no clear mechanism of action. Potential side effects include fever and allergic type reactions acutely (especially in children with IgA subclass deficiency) and the risk of blood borne infections. It is a very expensive option, particularly if treatment is maintained with repeated courses, and is therefore a relatively uncommon treatment choice. Limited evidence would suggest that it may be of some benefit in treating RS in adults.[4] It is unclear whether more robust RCT of IVIG would be of any clinical benefit, given the relatively high cost of repeated doses and its required route of administration.

Melatonin

Melatonin is a chronobiotic hormone secreted by the pineal gland which regulates circadian rhythm and is intimately involved in circadian rhythm sleep disorders. It is frequently prescribed for sleep disorders in children with a range of developmental disorders and neurodisabilities, despite very limited RCT evidence of its efficacy.[5] As a group, these children also frequently have epilepsy and some anecdotal reports have suggested that melatonin may improve seizure control, particularly in myoclonic and nocturnal seizures,[6] although it is unclear whether this is through improved sleep quality or by a specific neuroprotective role. A single report has suggested that supplemental melatonin may exacerbate seizures in some children.[7] A proposal for an RCT to evaluate the use of melatonin in children with epilepsy and neurodisability has recently been approved and will be funded by the NHS Health Technology Assessment Unit (R Appleton, personal communication). This should provide clinicians with more scientific information on which to base their use of melatonin in patients with epilepsy in the future.

Vitamins in epilepsy

There are two general indications for vitamin supplementation in epilepsy. The first is for replacement therapy in inherited metabolic defects, including pyridoxine dependent seizures, biotinidase deficiency, and folinic acid responsive neonatal seizures. The second is where a vitamin may reduce seizure frequency through a presumed anticonvulsant role, possibly by ''resetting'' the inhibitory gamma butyric acid (GABA) and excitatory (glutaminergic) systems. Vitamin E, folic acid, and pyridoxal phosphate may have a role in both of these potential mechanisms.

Pyridoxine (vitamin B6)

This is the treatment of choice in the rare recessive pyridoxine dependant seizure syndrome. The diagnosis is clinical and should be considered in all babies with intractable seizures under the age of 18 months, even if seizures are presumed to be due to hypoxic ischaemic encephalopathy.[8] Patients can either be tested by giving 100 mg of pyridoxine intravenously while undergoing EEG monitoring or given a 3 week course of oral pyridoxine (100–200 mg daily), ideally while no other changes to any other AED therapy are made. Administering pyridoxine intravenously has two potential problems: the drug may precipitate a respiratory arrest and normalisation of the EEG may actually take place after monitoring has stopped.

Pyridoxal phosphate

Pyridoxal phosphate is the major activated form of vitamin B6. There has been recent interest in an open trial of pyridoxal phosphate for children with intractable cryptogenic epilepsy with an improvement reported in up to 11% of cases.[9] It appeared to be most effective in children with intractable infantile spasms. However, the medication is expensive, difficult to administer and source (capsule form only) in the UK, and may be poorly tolerated due to vomiting

and other side effects. The recommended oral dose is 50 mg/kg/day for a minimum of 2 weeks, but some children may respond to lower doses. There is some evidence that rather than treating a metabolic disorder, it may act as an anticonvulsant, particularly in neonatal seizures and early infantile epileptic encephalopathy (Ohtahara's syndrome).

Biotin

Biotinidase deficiency is a very rare, autosomal recessively inherited defect in the recycling of the essential B vitamin, biotin. Biotinidase deficiency causes slowing of the function of biotin dependent multiple carboxylase enzymes which have important roles in fatty acid oxidation, amino acid catabolism, and gluconeogenesis. It causes a treatable leucoencephalopathy which may present with intractable seizures in infants and young children.[10] Plasma levels can be measured and, if low, treatment is with daily biotin supplementation (5–20 mg/day).

Folinic acid

Folinic acid responsive seizures appears to be a rare inherited syndrome which presents typically in the neonatal period with intractable seizures that do not respond to pyridoxine, biotin, or other AEDs.[11] Neonates with the condition usually respond to folinic acid (5 or 10 mg daily) within 24–48 h.

Other vitamins

The use of other vitamin supplementation for seizure control in children and adults with epilepsy has been the subject of a recent Cochrane review.[12] The rationale for trials of other vitamins follows studies suggesting that AEDs may lower plasma levels of several different vitamins, and specifically vitamin D. The review concluded that the few RCT looking at both vitamins D and E and folic acid supplementation to reduce seizure frequency were of poor methodological quality and that further trials were needed to address the role of vitamins in treating the epilepsies.

DIETARY CHANGES FOR THE TREATMENT OF EPILEPSY

Ketogenic diet

The ketogenic diet (KD) mimics fasting by having a high fat and low carbohydrate content which promotes prolonged ketone production. It is not really understood why this diet is effective for some children with epilepsy. The KD was devised and became popular in the 1920s before AEDs became widely available.[3] Interest in the KD was reawakened in the 1990s following media reports and prospective observational studies, although as yet no RCT has been published.[13] There are broadly two types of KD, the first or ''classical diet'' and a modified version, the medium chain triglyceride (MCT) diet. A detailed description of the KD is beyond the remit of this paper; however, compared to the classical diet, the MCT diet begins with either no or a shorter fast and allows more dietary choices, but it probably causes more unacceptable gastrointestinal side effects. More detail can be found in recent reviews of the KD.[14] Indications for the KD in children include intractable epilepsy or unacceptable AED toxicity, or both. It is most practical and effective in younger children (age 1–10 years) due to better compliance and also appears to be more effective in the generalised rather than the focal epilepsies. It is also the treatment of choice in the rare, though probably under-diagnosed, metabolic disorder, glucose transport protein (GLUT1) deficiency.[15] There are several disadvantages and risks associated with the KD including frequent blood/urine monitoring, parental commitment, patient compliance, gastrointestinal upset and weight loss, risk of dehydration and hypernatraemia, kidney stones, and vitamin and trace element deficiencies. In addition, the diet frequently loses its effect after many months or, less commonly, a number of years, and for reasons that are not always clear. The long term effects of continuing the diet are unknown but potentially could include atherosclerosis and hypertension. If effective, children often have improved cognition and behaviour through a direct effect of reducing clinical and electroencephalographic seizure frequency but also sometimes indirectly through a reduction in maintenance AEDs.

Atkins diet

The Atkins diet has become very popular in the UK for weight control in obese adults.[16] The diet is similar to the KD, but differences include a lower fat and higher protein content, no fluid or calorie restriction, and no fast at the beginning of the diet. These differences may make it easier to implement and sustain in children. A single open study of six patients (three children) with refractory epilepsy has been reported. All three children had a more than 90% reduction in seizure frequency including a reduction in their AED.[17] This study raises the possibility that the Atkins diet may have a role in drug resistant epilepsy, although further data are required and it would need to be determined whether this diet is more effective and easier to administer than the KD.

Oligoantigenic diet

The oligoantigenic diet (OD) is essentially a diet containing very few foods, for example one meat, one starch, one fruit, one vegetable, one oil, multivitamins, calcium, and mineral water. There are very limited data on the possible role of an OD. In a study of children with both migraine and epilepsy,[18] headache and seizure frequency were reported to improve, but it was difficult to identify the potentially allergic foodstuffs and the diet was expensive and hard to maintain. The mechanism of action is unclear but might relate to neurotransmitter-like substances present either in food or derived from an intestinal reaction to certain foods, possibly similar to the postulated mechanism in coeliac disease and epilepsy.[19] Unfortunately, skin prick testing or IgE antibody levels are usually unhelpful in identifying foods likely to provoke seizures. The authors have received anecdotal comments from some families who found that excluding specific types of food and drinks led to an improvement in their child's seizure control or behaviour, or both; clearly, this may simply represent a non-specific response or reflect the avoidance of specific preservatives or food colourings. It is most unlikely that the OD will become as recognised as the KD in the management of epilepsy in children.

EPILEPSY SURGERY

For a discussion of paediatric epilepsy surgery (pre-operative assessment, predictors of outcome, and seizure outcomes), including vagus nerve stimulation, neither of which are covered in detail in this review, the reader is referred to recent comprehensive reviews.[20–22] However important issues include:

- epilepsy surgery (whether the procedure is resective or disconnective) offers a realistic and potentially very effective and even curative therapeutic option for a significant number of children with drug resistant temporal and extra-temporal lobe epilepsy,
- any surgical procedure should be considered sooner rather than later, and
- children undergoing a surgical option require detailed pre, intra and post-operative assessments, expertise, and care and this must be in place before any surgical procedure can and should be undertaken.

NON-PHARMACOLOGICAL TREATMENTS OF EPILEPSY

Lifestyle changes

Exercise

Participation in exercise should be recommended for children with epilepsy, providing they are adequately supervised. This is intended to have an impact on quality of life and social inclusion rather than seizure control. There is no RCT assessing the effect of exercise on patients with epilepsy. One prospective study of 21 adults (acting as their own controls) reported no difference in seizure control during a 4 week aerobic exercise programme.[23] There are also case reports of seizures induced by exercise in children.[24] Exercise is difficult for many children with epilepsy due to their motor problems and learning disabilities, but this should not preclude their attempts to participate in games and sports activities whenever possible.

Sleep hygiene

Sleep deprivation is well recognised as a precipitant for seizures (and most epilepsies), particularly in the idiopathic generalised epilepsy syndromes and temporal lobe epilepsy. Interictal EEG discharges are promoted by sleep deprivation, possibly by increasing neuronal excitability.[25] Patients with epilepsy should therefore be advised to have good sleep hygiene. They should try to ensure regular and consistent sleep and if they go to bed later than usual, they should try to get up later the next morning. Similar advice should also concern air travel when crossing time zones; it is relatively common for an older child's or teenager's first tonic-clonic seizure to occur when on holiday, and often within 12–24 h of arriving at their holiday destination. Teenage patients are most at risk of seizures arising either de novo or exacerbated by sleep deprivation and when control has previously been good, it is worth enquiring about missed sleep and late nights (and maybe the occasional alcoholic drink) before increasing an AED for breakthrough seizures.

Alcohol

Excessive alcohol consumption is a potential problem for any patient with epilepsy, and particularly teenagers. Seizures characteristically occur within 48 h of excessive and, often, binge drinking. Alcohol may also increase seizure frequency through disturbed sleep and interaction with AEDs. All teenage epilepsy patients should be given this factual information and not simply told or advised what not do.

PSYCHOLOGICAL APPROACHES

Techniques to abort seizures or reduce seizure frequency

Avoidance

In reflex epilepsies, patients describe specific triggers that can precipitate seizures. The most common reflex epilepsy is that triggered by visual stimuli (flickering lights or specific visual patterns or both). Other triggers include thinking, listening to specific types or pieces of music, eating, reading, immersion in hot water, chess playing, or brushing hair.[24] Some patients may actually induce seizures; some children with mild learning difficulties and photosensitive epilepsy wave their hands in front of their eyes to induce seizures or have a tendency to be drawn towards a television screen (this may be less of a problem with plasma television screens). As stated above, the most common reflex seizures are in patients who are photosensitive as part of their epilepsy syndrome (particularly in juvenile myoclonic epilepsy) or who have pure photosensitive epilepsy. If photosensitivity is documented following intermittent photic stimulation on an EEG recording, measures to try to avoid seizures should be advised including sitting more than 2.5 m away from the television in a well lit room, using the remote control, and approaching the television with one eye covered. Children should also avoid playing video games in a darkened room or when they are excessively tired. Covering one eye can also be used when a patient is exposed to other visual stimuli, such as flashing lights. These techniques are called avoidance techniques. However, it is often difficult, if not impossible, to avoid some of the other triggers described above, including those provoked by eating or higher mental functions. In these situations there may be a clear justification for an AED, although, as in all epilepsies, this cannot guarantee seizure freedom.

Relaxation techniques

The role of relaxation techniques in adults and children with intractable epilepsy has been discussed in a recent Cochrane review.[26] Four RCTs were examined and outcome measures included seizure frequency and improvement in quality of life scores. Only one study included children.[27] Children were randomised to a control group or to a 6 week treatment phase during which they were taught to recognise pre-seizure signs and then apply relaxation techniques. The treatment group experienced fewer seizures both at 10 weeks and at 1 year follow up. Unfortunately, as there were only 18 children in this study it is difficult to make any firm conclusions or recommendations concerning the role of relaxation techniques in seizure control in children. Nevertheless, successfully taught relaxation techniques might indirectly improve seizure control in a number of children with epilepsy (for example, through improved sleep).

Biofeedback

In the 1970s biofeedback became a popular psychological treatment for a variety of disorders including epilepsy. The theory behind this technique is that patients can be trained to increase certain frequencies (12–14 Hz) on the EEG recordings from the sensorimotor regions of the cortex (termed the sensorimotor rhythm) that are known to inhibit seizures in animal studies.[28] Patients are trained to do this by obtaining positive visual feedback with coloured lights and images on a screen after producing the 12–14 Hz activity. Three biofeedback studies were also included in the recent Cochrane review which concluded that the these studies were of limited value due to small patient numbers and wide confidence intervals.[26] The technique is very time consuming (30 min training sessions several times a week for at least 3 months) and involves high levels of co-operation and concentration, making it impractical for young or cognitively impaired children.

Aversive therapy

According to the principles of operant conditioning, a seizure may be a behaviour that is learned to avoid something unpleasant or to gain a reward. Therefore, the chain of events which occurs during a seizure could be altered by presenting a noxious stimulus at the time of or following a seizure. The technique became popular in the 1960s and 1970s. Case reports and small series in the literature document studies where noxious smells or skin shocks were administered; shaking children's shoulders and shouting ''no'' at seizure onset and painful dorsiflexion of the palm have also been described.[29] These techniques have no obvious scientific basis and are clearly inappropriate and unethical in current practice.

Promotion of emotional well being

Yoga

Stress is considered to be a precipitant for seizures and yoga is believed to induce relaxation and therefore stress

reduction. Yoga involves breathing exercises, postures, and meditation techniques. The role of Sahaja yoga in intractable adult epilepsy has been investigated in a Cochrane review.[30] During Sahaja yoga, meditation is believed to awaken dormant divine energy in the body which can heal disorders. The review found only one RCT with 10 patients undertaking Sahaja yoga, another 10 undertaking ''sham'' yoga, and 12 controls. All patients continued their usual AEDs. The review concluded that the study was too small to allow any useful conclusions. It is difficult to see how yoga could have a role in the paediatric age group.

Reduction in psychiatric co-morbidity

Anxiety, depression, and psychosis may complicate epilepsy, both before certain seizures and also between seizures in individuals with epilepsy. These symptoms may be part of the epilepsy syndrome or iatrogenic arising as a consequence of surgery or the use (or withdrawal) of AEDs. The incidence of these problems in children is unknown. Paediatricians should seek help from the local child and adolescent psychiatry teams if severe symptoms of depression or psychosis develop, as occasionally neuroleptic and antidepressant medication may be indicated to control these often very disabling symptoms.[31]

Coping strategies for living with epilepsy

Epilepsy can have a profound effect on patient's lives. Psychological treatments that focus on the emotional impact of seizures are now considered as standard management practice in adult patients.[26] Techniques include both individual and group/family counselling and psychotherapy. Cognitive behaviour therapy (CBT) is another useful approach. Patients are taught coping skills to try to recognise and control their symptoms. There is some evidence that this technique may have a beneficial role in depression but not in seizure control in adults with epilepsy.[26] In the UK, these methods are not commonly offered to young children with epilepsy, but may be to the older child or teenager and their families. Patient support groups and occasionally group meetings organised by nurse specialists may be helpful, and may even obviate (but never substitute) the need for formal psychological support, including CBT.

Educational interventions

There have been several RCTs that have evaluated whether residential educational programmes for adults and children with epilepsy can improve their quality of life. Results suggest a significant improvement in the knowledge and understanding of epilepsy, coping with epilepsy, and concordance (adherence) with medication.[26] The school achievements, behaviour, and social skills of children were also perceived to have improved. The majority of these studies have been undertaken in the USA but there is no reason why the principle and the approach could not be adopted within the UK.

ALTERNATIVE (COMPLEMENTARY) THERAPIES

Herbal medicine and homeopathy

Herbal remedies are used as first line treatments for all illnesses in an estimated 80% of the world's population. These methods are becoming increasingly popular in Western countries, but clinics are currently poorly or unregulated. No RCT has examined whether herbal remedies may have a role in epilepsy. Two open label studies published in the Chinese medical literature reported benefits of two remedies in intractable epilepsy. In one, a remedy containing 13 herbs was reported to have a similar efficacy when compared to phenobarbitone (3–6 mg/kg/day) in an open study of 100 children treated for 8 months. In the other study, a different herb (zhenxianling) was given to 239 adult patients in an open study for 6 months to 2 years. Seizure reduction was reported to be more than 75% in two thirds of the patients. The main constituents of the herbal remedy were thought to be human placenta and peach flower buds.[32] The lack of scientific studies militates against herbal remedies being recommended by doctors practicing conventional medicine in Western countries, particularly in children.

OTHER NON-PHARMACOLOGICAL TREATMENTS FOR EPILEPSY

Aromatherapy and hypnosis

Hypnosis has been used with and without aromatherapy in an open study of 100 adults with intractable epilepsy.[33] The most promising results were seen when both techniques were used together, with over one third of patients becoming seizure free for more than 12 months. However, treatments were very time consuming. Hypnosis has also been reported to be effective in small numbers of children and adults to induce non-epileptic seizures.[34]

Acupuncture

There have been two RCTs of an 8 week course of acupuncture versus sham acupuncture in adult patients with intractable epilepsy. Both studies were performed by the same research team. All the patients had drug resistant epilepsy and the treatments were given in addition to their usual AEDs. Outcome measures included seizure control[35] and data derived from quality of life questionnaires.[36] No significant differences were found between the two groups in either study. Two children under the authors' care have undergone acupuncture without success. It is unlikely that acupuncture will ever have a role in the management of paediatric epilepsy, if only because of children's aversion to needles.

Seizure alert dogs

A recent prospective open study evaluated whether seizure alert dogs could reduce seizure frequency in 10 adults with intractable epilepsy. Seizure frequency was reported to be improved by nine patients after 48 weeks.[37] While these statistics look promising, there are no RCTs on how effective seizure alert dogs are at predicting seizures.

CONCLUSIONS

Seizure control is achieved in approximately 75% of children treated with conventional AEDs. Non-conventional AED treatments and non-pharmacological approaches may have a role in those with intractable seizures or AED toxicity; this is often the perception of many families, particularly if their child's epilepsy has not responded to, or their child has developed toxicity on, anticonvulsants. Unfortunately, however, evidence for most of these other treatment approaches is very limited. Some treatments are currently being investigated in a controlled manner, but national or even international collaboration will be needed to address many of the unanswered questions concerning their effectiveness and role. Until more trial data are available, the non-conventional AED medications, dietary manipulations, and surgical techniques outlined in this paper will continue to be prescribed or undertaken in an unscientific way based on anecdotal evidence, personal practice, and also prejudice. Many of the psychological approaches are largely common sense and are already incorporated into our current practice, including, for example, avoidance techniques and lifestyle advice, while others require further investigation or appear to be impractical in children.

In recent years, alternative or complimentary medicine has become popular for many chronic illnesses especially where Western medical treatments have a frustrating lack of

efficacy. Doctors involved in the management of children with intractable epilepsy understand why parents may seek other non-medical and non-surgical approaches, but with our current level of understanding, more time should be spent in educating families about their child's condition and its often poor prognosis, rather than advocating the use of the many unproven, and potentially dangerous, remedies or alternative approaches.

Authors' affiliations

R Kneen, Child Development Centre, Department of Neurology, Alder Hey Children's Hospital, Liverpool, L12 2AP, UK
R E Appleton, Roald Dahl EEG Unit, Department of Neurology, Alder Hey Children's Hospital, Liverpool, L12 2AP, UK

Competing interests: None declared.

REFERENCES

1 **Gupta R**, Appleton R. Corticosteroids in the management of the paediatric epilepsies. *Arch Dis Child* 2005;**90**:379–84.
2 **Lux AL**, Edwards SW, Hancock E, *et al*. The United Kingdom Infantile Spasms Study comparing vigabatrin with prednisolone or tetracosactide at 14 days: a multicentre, randomised controlled trial. *Lancet* 2004;**364**:1773–8.
3 **Prasad AN**, Stafstrom CF, Holmes GL. Alternative epilepsy therapies: the ketogenic diet, immunoglobulins, and steroids. *Epilepsia* 1996;**37**(Suppl 1):S81–95.
4 **Leach JP**, Chadwick DW, Miles JB, *et al*. Improvement in adult-onset Rasmussen's encephalitis with long-term immunomodulatory therapy. *Neurology* 1999;**52**:738–42.
5 **Phillips L**, Appleton RE. Systematic review of melatonin treatment in children with neurodevelopmental disabilities and sleep impairment. *Dev Med Child Neurol* 2004;**46**:771–5.
6 **Sweis D**. The uses of melatonin. *Arch Dis Child Ed Pract* 2005;**90**:ep74–7.
7 **Sheldon SH**. Pro-convulsant effects of oral melatonin in neurologically disabled children. *Lancet* 1998;**351**:1254.
8 **Gordon N**. Pyridoxine dependency: an update. *Dev Med Child Neurol* 1997;**39**:63–5.
9 **Baxter P**. Pyridoxine or pyridoxal phosphate for intractable seizures? *Arch Dis Child* 2005;**90**:441–2.
10 **Grunewald S**, Champion MP, Leonard JV, *et al*. Biotinidase deficiency: a treatable leukoencephalopathy. *Neuropediatrics* 2004;**35**:211–16.
11 **Torres OA**, Miller VS, Buist NM, *et al*. Folinic acid-responsive neonatal seizures. *J Child Neurol* 1999;**14**:529–32.
12 **Ranganathan L**, Ramaratnam S. Vitamins for epilepsy. *Cochrane Database Syst Rev* 2005;(2):CD004304.
13 **Levy R**, Cooper P. Ketogenic diet for epilepsy. *Cochrane Database Syst Rev* 2003;(3):CD001903.
14 **Sinha SR**, Kossoff EH. The ketogenic diet. *Neurologist* 2005;**11**:161–70.
15 **Gordon N**, Newton RW. Glucose transporter type 1 (GLUT-1) deficiency. *Brain Dev* 2003;**25**:477–80.
16 **Atkins RC**. *Dr Atkins' new diet revolution*. New York: Avon, 2002.
17 **Kossoff EH**, Krauss GL, McGrogan JR. Efficacy of the Atkins diet as a therapy for intractable seizures. *Neurology* 2003;**61**:1789–91.
18 **Egger J**, Carter CM, Soothill JF, *et al*. Oligoantigenic diet treatment of children with epilepsy and migraine. *J Pediatr* 1989;**114**:51–8.
19 **Mavroudi A**, Karatza E, Papastavrou T, *et al*. Successful treatment of epilepsy and celiac disease with a gluten-free diet. *Pediatr Neurol* 2005;**33**:292–5.
20 **Lachhwani DK**. Pediatric epilepsy surgery: lessons and challenges. *Semin Pediatr Neurol* 2005;**12**:114–18.
21 **Tonini C**, Beghi E, Berg AT, *et al*. Predictors of epilepsy surgery outcome: a meta-analysis. *Epilepsy Res* 2004;**62**:75–87.
22 **Wheless JW**, Baumgartner J. Vagus nerve stimulation therapy. *Drugs Today* 2004;**40**:501–15.
23 **Nakken KO**, Bjorholt PG, Johannessen SI, *et al*. Effect of physical training on aerobic capacity, seizure occurrence, and serum level of antiepileptic drugs in adults with epilepsy. *Epilepsia* 1990;**31**:88–94.
24 **Schmitt B**, Thun-Hohenstein L, Vontobel H, *et al*. Seizures induced by physical exercise: report of two cases. *Neuropediatrics* 1994;**25**:51–3.
25 **Malow BA**. Sleep deprivation and epilepsy. *Epilesy Curr* 2004;**4**:193–5.
26 **Ramaratnam S**, Baker G, Goldstein L, *et al*. Psychological treatments for epilepsy. *Cochrane Database Syst Rev* 2005;(4):CD002029.
27 **Dahl J**, Melin L, Brorson L, *et al*. Effects of a broad-spectrum behavior modification treatment program on children with refractory epileptic seizures. *Epilepsia* 1985;**26**:303–9.
28 **Walker JE**, Kozlowski GP. Neurofeedback treatment of epilepsy. *Child Adolesc Psychiatr Clin N Am* 2005;**14**:163–76.
29 **Thompson PJ**, Baxendale SA. Non-pharmacological treatment. In: Shorvon SD, eds. *The treatment of epilepsy*. Oxford: Blackwell Scientific, 1996:345–55.
30 **Ramaratnam S**, Sridharan K. Yoga for epilepsy. *Cochrane Database Syst Rev* 2000;(3):CD001524.
31 **Kanner AM**, Dunn DW. Diagnosis and management of depression and psychosis in children and adolescents with epilepsy. *J Child Neurol* 2004;**19**(Suppl 1):S65–72.
32 **Tyagi A**, Delanty N. Herbal remedies, dietary supplements, and seizures. *Epilepsia* 2003;**44**:228–35.
33 **Betts T**. Use of aromatherapy (with or without hypnosis) in the treatment of intractable epilepsy - a two-year follow-up study. *Seizure* 2003;**12**:534–8.
34 **Barry JJ**, Atzman O, Morrell MJ. Discriminating between epileptic and nonepileptic events: the utility of hypnotic seizure induction. *Epilepsia* 2000;**41**:81–4.
35 **Kloster R**, Larsson PG, Lossius R, *et al*. The effect of acupuncture in chronic intractable epilepsy. *Seizure* 1999;**8**:170–4.
36 **Stavem K**, Kloster R, Rossberg E, *et al*. Acupuncture in intractable epilepsy: lack of effect on health-related quality of life. *Seizure* 2000;**9**:422–6.
37 **Strong V**, Brown S, Huyton M, *et al*. Effect of trained seizure alert dogs on frequency of tonic-clonic seizures. *Seizure* 2002;**11**:402–5.