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Vagus nerve stimulation in patients with catastrophic childhood epilepsy, a 2-year follow-up study

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KEYWORDS
Vagus nerve stimulation (VNS);
Neuropsychological functioning;
Side effects;
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Summary *Purpose*: To establish the long-term efficacy and tolerability of vagus nerve stimulation (VNS) in children with a Lennox-like syndrome. *Method*: This study was a longitudinal observational prospective cohort analysis. Baseline: 6 months. Follow-up: 24 months. Screening (baseline and every 6 months): MRI (baseline only), EEG, neuropsychological evaluation, ECG and blood sampling for antiepileptic drug levels. Nineteen children are included. *Results*: A seizure frequency reduction of 20.6% was found at the end of the follow-up period. No relationship was detected between the length of the stimulation period and the reduction in the seizure frequency. 21% of the patients showed a reduction in seizure frequency of 50% or more. The seizure severity showed improvement in the first 12 months of treatment. The largest seizure reduction was found in the patients with highest frequency of background activity at the baseline EEG. Neuropsychological findings: no negative impact on behaviour, moderate improvement in function, behaviour and mood. Largest seizure reduction was found in the group with the highest baseline mental function. The scores for mental age improved independently of the seizure control. Twelve patients (63%) experienced minor side effects, which subsided after 1 month. *Conclusion*: (1) There was a *significant* reduction in seizure frequency and severity. (2) No serious side effects were recorded. (3) No negative effects on cognition or quality of life were apparent. (4) Patients with highest baseline mental functioning showed the highest seizure reduction. (5) Those patients with less disturbed EEG (high background activity and less interictal epileptic activity) showed the highest seizure reduction.

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Introduction

Epilepsy has a prevalence of 0.7—0.8%. Adequate seizure control is achieved in only 75—80% of these patients while 20—25% suffer from intractable epilepsy.[1] Vagal nerve stimulation (VNS) might be an alternative treatment option as randomised studies show a success rate of 12% in intractable epilepsy. The success rate is defined as the measured treatment response rate corrected for placebo, measuring bias and natural course, while the response rate is defined as a seizure frequency reduction of 50% or more. This success rate is small but it is in line with the success rates of new antiepileptic drugs in pharmacotherapy resistant patients, which range from 12 to 29%.[2]

Clinical trials in children

The effectiveness of VNS is positively correlated to the duration of treatment, both in adults and children.[3,4—8]

Hornig studied the effect of VNS in 19 children, 6 of them being diagnosed as having Lennox—Gastaut syndrome.[5] The preoperative baseline period was 1 month and the postoperative follow-up 21—29 months. He reported that five of the six children showed a seizure frequency reduction of 90% or more.

Parker presented the results of VNS in 16 children with encephalopathic epilepsy.[8] Ten of these children were diagnosed as Lennox—Gastaut syndrome, four suffered from myoclonic epilepsy and two from myoclonic astatic epilepsy. The situation 1 year after surgery was compared with a 2-month preoperative baseline period. There was one drop out. Two children showed an increase in seizure frequency of more than 50% and four a decrease of more than 50%. The mean reduction was 17%. A similar study was conducted by Lundgren et al.[6] In this case, 16 children aged between 4 and 19 years were evaluated during a baseline period of 6 months and the results were compared with those from a treatment period of 12—24 months. Eight children suffered from partial seizures and eight from generalised seizures; four of these were diagnosed as Lennox—Gastaut syndrome. Six children (37%) showed a reduction in seizure frequency of 50% or more; one of them was diagnosed as Lennox—Gastaut syndrome.

Ben Menachem reported the results of a prospective long-term open study with a follow-up of 3—64 months.[4] The last 3 months of treatment with VNS were compared with a preoperative baseline of 3 months. The subgroup of patients with Lennox—Gastaut syndrome showed a mean reduction in seizure frequency of 24%.

Nagarajan et al. studied the efficacy of VNS in children with refractory epilepsy.[9] The children showed multiple seizure characteristics and the majority suffered from a moderate to severe mental handicap. 62.5% achieved a seizure frequency reduction of 50% or more; 25% of this prognostically unfavourable group achieved a seizure reduction of more than 90%. Similar results were found by Zamponi et al. in a group of 13 children with intractable epilepsy, multiple seizure characteristics, mixed aetiology, and moderate to severe mental handicap:[10] 66% of the children showed a seizure frequency reduction of 50% or more.

In these studies the reported side effects were minor and most patients showed habituation. It should be stressed that the reason for discontinuing VNS was primarily due to insufficient clinical results and rarely due to side effects or complications of treatment.[2,3,11—14]

In 1998, the Epilepsy Centre Kempenhaeghe and the Neurosurgical Department of the University Hospital Maastricht initiated a prospective study in children with refractory epilepsy, diagnosed as Lennox—Gastaut syndrome or Lennox-like types of epilepsy.

The issues to be studied were the efficacy and tolerability of VNS in children with a Lennox—Gastaut syndrome or Lennox-like type of epilepsy in long-term follow-up.

Methods

VNS surgery and VNS stimulator

Bipolar stimulation of the vagus nerve was undertaken by placing the electrodes around the left vagus nerve, while the pulse generator (Neurocybernetic prothesis NCP®, Cyberonics Inc., Webster, TX, USA) is normally implanted below the clavicle.[15] Because the group of children involved in this study were mentally retarded and may show behavioural problems, we chose to implant the device below the pectoralis major to prevent them manipulating the device and to give a more acceptable cosmetic effect. All surgical procedures were performed by the same neurosurgeon in the Maastricht University Hospital (M.W.B.). The device was programmed telemetrically the day after the implantation (H.J.M.M.) using the following parameters: stimulation for 30 s followed by a stimulation-free period of 3 min, pulse width 500 μs, output current 0.25 mA. Over a period of 10—20 days, the