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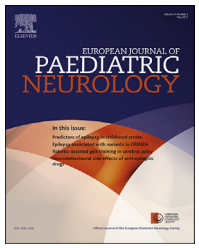

Review article

Vagus Nerve Stimulation in children: A focus on intellectual disability

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ABSTRACT

Introduction: Vagus Nerve Stimulation (VNS) can be an efficacious add-on treatment in patients with drug-resistant epilepsy, who are not eligible for surgery. Evidence of VNS efficacy in children with intellectual disability (ID) is scarce.
Objectives: The purpose of this study was to review all available VNS data in the pediatric population (≤18 years old) and focus on the subpopulation with ID since appropriate treatment of these children is often challenging and complex.
Methods: Cochrane, EMBASE, PubMed and MEDLINE were used to collect all research associated to VNS and ID (or synonyms) leading to a total of 37 studies. Seven studies showed the results of patients with ID and those without separately; thereby only these studies were included in the VNS meta-analysis.
Results: Our meta-analysis showed that VNS was less effective in pediatric epilepsy patients with ID compared to those without ID (Mantel-Haenszel meta-analysis; $p = 0.028$, OR 0.18 (CI 95% 0.039 −0.84)). However, there were no prospective controlled studies. Numerous studies reported quality of life (QoL) improvements in this subpopulation. The most common adverse events were transient and well tolerated. Side effects on cognition and behavior were not reported.
Discussion: These results might be a reason to consider VNS early on in the treatment of this subgroup. The significantly greater amount of retrospective studies, differences in follow-up (FU), lack of control data, heterogeneous series and limited number of patients could have biased the outcome measurements. Hence, current data do not exclude VNS for children with drug-resistant epilepsy and ID but should be interpreted with caution.

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Contents

1. Introduction

Epilepsy is characterized by recurrent, unpredictable and unprovoked epileptic seizures that interfere with normal brain function.[1] Around one out of three children with epilepsy shows cognitive and/or behavioral impairments[2] and treatment of seizures in these patients is often challenging and complex.[3–6] Since 30% including a considerable amount of children with ID does not respond to current anti-epileptic drugs (AEDs), other treatment options like ketogenic diet and VNS can be promising.[7] VNS is indicated in patients with drug-resistant epilepsy for whom epilepsy surgery is not possible.[8–13] For the adult population it has been proven to be efficacious and well tolerated.[14] Moreover, QoL improvements have been reported[15] and VNS can improve mood significantly which highlights the clinical application of VNS for the treatment of severe, drug-resistant depression.[16] Less is known about the pediatric population. In 1996 the first randomized controlled trials (RCTs) (E01-E05) were conducted but only one included some children ≥12 years of age, suffering from drug-resistant localized epilepsy.[17] The first RCT with solely children with drug-resistant epilepsy, also below the age of 12, was 16 years later.[12] Hence, the minority of the herein reviewed studies was large and most evidence of VNS efficacy in children is retrieved from case series, either retro- or prospective. Children, with drug-resistant epilepsy, have a significantly higher chance for intellectual and mental deterioration, and therefore might benefit from VNS' potential contribution to cognition and behavior.[2]

In conclusion, data are scarce regarding the efficacy of VNS and related QoL improvements in children. Our aim was to review all available data about VNS efficacy and safety in children with ID.

2. Methods

2.1. *Search strategy*

Cochrane, EMBASE, PubMed and MEDLINE served to obtain all available literature until May 2015. The subsequent terms were used: "VNS", "Vagus Nerve Stimulation" or "nervous vagus stimulation" in combination with "mental retardation", "mental retarded", "low IQ", "developmental disabled", "developmental disabilities", "intellectual disabled", "intellectual disabilities", "quality of life", "QoL" (*Species*: *humans*).

2.2. *Selection criteria*

A review of the full text of the obtained articles was performed to exclude articles: (1) without notion of intellectual or developmental status, (2) with insufficient