

# Canadian Experience with Vagus Nerve Stimulation for Epilepsy in Adults

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Vagus nerve stimulation (VNS) was approved in Canada in 1997 as adjunctive therapy for partial onset seizures with or without secondary generalization, as well as for patients with generalized seizures refractory to antiepileptic drugs. There have only been a few Canadian studies of VNS in adult patients with epilepsy reflecting the limited use here compared to other countries.

The initial study in Canada exploring the effects of VNS on adult patients with epilepsy by Clark et al included ten patients in a small randomized clinical trial<sup>1</sup>. The study showed there were more consecutive seizure free days with VNS suggesting that this should be the outcome measure for future studies. The same group showed that VNS improved cognitive motor performance in small ON and OFF trials<sup>2</sup>.

McLachlan et al published findings from six different Canadian centers in 2003<sup>3</sup>. This study included 23 adults and 4 children with intractable epilepsy who were followed prospectively for one year. In contrast to previous industry funded trials showing >50% seizure reduction in 50-60% of patients, this study showed that seizures were reduced by more than 50% in only 19% of patients, by less than 50% in 46%, and unchanged in 35%. Antiepileptic drugs were reduced in 43% of the patients and there was a significant improvement in the mean overall QOLIE-89 score and other measures of quality of life. However, quality of life did not correlate with changes in seizure frequency. The authors concluded that the effect of VNS was modest and further studies were required. Minor adverse events occurred in 24 patients including hoarseness, cough, shortness of breath, minor pain, and heartburn while eight subjects had severe adverse events (transient vocal cord paralysis lasting up to six weeks in three patients, stimulation associated swallowing difficulties, intractable vomiting, severe neck or throat pain).

In 2008, McGlone et al<sup>4</sup> published the Halifax experience with VNS in 16 adult patients with refractory partial seizures followed prospectively over one year. A 50% or more reduction in seizures was seen in four (25%) patients. Similar to the McLachlan et al<sup>3</sup> study, there was improvement in quality of life but this was not associated with seizure control and did not differ from similar changes seen in a control group treated with standard medical management.

The study of Qiabi et al<sup>5</sup> is another single center Canadian experience with VNS.<sup>4</sup> This retrospective study included 34 patients. The main outcome was the seizure frequency assessed after 6, 12, 24 and 36 months. After six months of follow-up 41% of patients had a >50% reduction in seizure frequency compared to baseline, 47% at 12 months, 57% at 24 months and 60% at 36 months. Compared with the study of McLachlan, the complications related with the implantation were less severe including eight cases with limited cervical hypoesthesia, two minor scar infections and one Horner syndrome. Some patients experienced voice hoarseness, throat paresthesia, and coughing

related to stimulation that improved over time. Despite improved seizure control, only 9% of patients had less anti-seizure medication at the last follow-up. The authors conclude that VNS is an efficacious, safe treatment for refractory epilepsy and suggest that more patients should be receiving this form of therapy.

The results of Qiabi et al<sup>5</sup> clearly differ from the findings in the two previous Canadian studies. One potential explanation for this difference is the longer two year follow-up period. It has previously been shown that the effects of VNS improve over time and this study appears to support that with 41% responders at six months compared to 60% at two years. Although all three studies included similar patients with intractable epilepsy, those in the previous studies may have had more severe seizure disorders which would be less likely to respond to treatment. Otherwise, surgical techniques, programming of the device and the implanted technology are all similar. However there were fewer complications in this study possibly reflecting the greater surgical experience now with this treatment compared to more than ten years ago when the McLachlan et al study was done<sup>3</sup>. As Qiabi et al<sup>5</sup> point out, the use of VNS in Canada at 3.5 units per million inhabitants is considerably less than the 25 units per million population implanted in the United States (data from Cyberonics). One reason for this difference includes limitations in funding for VNS devices (current \$29000) in every provincial jurisdiction. Further, there is little or no reimbursement for the extra time involved for regular follow-up and reprogramming visits after the device is implanted. Finally, there continues to be confusion and skepticism among Canadian neurologists regarding efficacy, cost effectiveness and the type of patients who should be considered for VNS.

This study supports the potential use of VNS in more patients across Canadian centers. It is clearly a consideration in a subset of those patients with intractable epilepsy. However, we have to agree with Dr. Bill Murphy who summarized his views on the paper by McGlone et al<sup>4</sup> in this journal in 2008: "At this moment in time VNS therapy remains expensive, with limited availability and modest effect."<sup>5</sup> Time has not altered the reality of that statement.

*JF Tellez-Zenteno*  
*University of Saskatchewan*  
*Saskatoon, Saskatchewan, Canada*

*RS McLachlan*  
*University of Western Ontario*  
*London, Ontario, Canada*

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