Pilot Study of Stimulation of the Cholinergic Anti-inflammatory Pathway with an Implantable Vagus Nerve Stimulation Device in Patients with Rheumatoid Arthritis

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Abstract

Background

The inflammatory reflex is a neural mechanism that maintains the inflammatory state in chronic inflammatory diseases. Vagus nerve stimulation (VNS) reduces systemic inflammation (Andersson U, Tracey K, Annu. Rev. Immunol. 2012; 30:313). Activation of the cholinergic anti-inflammatory pathway (CAP), which involves the vagus nerve, is sufficient to normalize systemic inflammation in several animal models of inflammation and in the Guillain–Barre syndrome, a human disorder associated with immune-mediated inflammation in the peripheral nervous system.

Methods

In this pilot study VNS was generally well tolerated, with an Adverse Event (AE) reported in 5 patients (4 female, 7/8 RF+, 6/8 CRP+: 17.5 (9.02)). A total of 11 AEs occurred in 7 patients: 4 were mild or moderate, 6 severe, and 1 life-threatening. The most frequent AEs were nausea (4/7), headache (4/7), and dizziness (4/7). A total of 8 patients (4 female, 7/8 RF+) were treated with active stimulation and 4 with single-stimulation (28 joint scoring).

Results

Overall, VNS efficacy was not sufficient to achieve clinical remission or control of disease activity in this small patient population. EULAR Response Rates were achieved in 4/8 patients, with 2 patients meeting the American College of Rheumatology (ACR) 20 criteria for improvement in joint counts, and 2 meeting the European League Against Rheumatism (EULAR) remission criteria. A total of 2 patients achieved a Composite Measures of Arthritis Improvement 40 (CMAI-40) score of 20 or greater.

Summary & Conclusions

The inflammatory reflex integrates local inflammation into a systemic inflammatory state and generates an inflammatory response that is sufficient to modify systemic inflammation in chronic inflammatory diseases. VNS reduces systemic inflammation and improves clinical outcomes in RA patients.

References

5. M Boric (Neurosurgeon), K Rotim (Neurosurgeon), M Mlinar (Coordinator), S Grazio (PI), A Kogler (Neurosurgeon), A Bogut (Sub-I), D Miller (Site Device Specialist), Y Levine (Biomarker Assay Design and Analysis), S Sturlic (Data Management), C Wilson (Senior Director, Regulatory Affairs), S Sokolovic (PI), P Krstic (Orthopedics/Synovial Biopsies).