VAGUS NERVE STIMULATION REDUCES INFLAMMATION OF THE SMALL INTESTINAL MUCOSA IN THE INDOMETACIN-INDUCED ENTEROPATHY MODEL

Y.A. Levine, A. Caravaca, M. Faltyš, A. Arnold, R. Zitnik
SetPoint Medical Corporation, Valencia, CA, USA

Introduction
The vagus nerve provides tonic inhibition of inflammation in the gut through the cholinergic anti-inflammatory pathway (CAP) (Olofsson, 2012) and in a variety of animal models of acute and subacute inflammation. Vagus nerve stimulation (VNS) is effective in the treatment of clinical rheumatoid arthritis (Rosas-Ballina, 2008) and in the indomethacin-induced enteropathy model. There are no experimental evidence linking vagus nerve stimulation to disease therapy in diseases including Crohn’s disease and ulcerative colitis. To date, there is no experimental evidence linking vagus nerve stimulation to disease therapy in inflammatory bowel disease.

Methods

Results

As expected, the majority of the lesions were localized to the distal jejunum and the proximal ileum. VNS significantly inhibited disease severity in the small intestinal mucosa as determined by gross pathology assessment as well as tissue-specific and systemic markers of inflammation and damage:

- The total lesion area in the intestine was reduced by 50% (Figure 5a).
- An example of VNS-induced improvement in gross pathology is shown in Figure 5b.
- Intestinal IL-23, an important mediator of inflammation in both Crohn’s disease and ulcerative colitis, was reduced by 50% (Figure 7).
- Serum levels of HMGB1, a marker and promoter of intestinal inflammation, were reduced by 52% (Figure 5a).
- Hepatic inflammation coincident with enteropathy (Sham, 1999) was reduced (Figure 5b), as indicated by TNF levels.

Summary & Conclusions
Activation of the Cholinergic Anti-inflammatory Pathway by electrical stimulation of the vagus nerve in rats alleviates structural damage and reduces production of tissue-specific and systemic inflammatory mediators in a model of intestinal injury induced by systemic indomethacin administration.

Implications
These observations represent the first demonstration of electrical vagus nerve stimulation ameliorating enteropathy observed in the small intestinal mucosa. These findings provide supportive preclinical evidence for clinical study on the efficacy of implantable neurostimulation devices in the treatment of Crohn’s disease, ulcerative colitis, and other diseases of inflammation.

REFERENCES

DISCLOSURE OF INTEREST
SL, AG, MF, AA and RZ are employees of SetPoint Medical Corporation.

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