NEUROSTIMULATION OF THE CHOLINERGIC ANTI-INFLAMMATORY PATHWAY (NCAP) AMELIORATES CIA IN RATS

Y. Levine¹, M. Faltys¹, K. Black¹, A. Caravaca¹, A. Bendele², R. Zilnik¹

¹ SetPoint Medical Corporation, Boston, MA; ² Boulder BioPATH, Boulder, CO, United States

Introduction

Objectives: To assess NCAP effects on clinical signs, joint histology, and systemic cytokine levels after induction of CIA in rats.

Criteria: Rats with CIA were randomized to receive NCAP or sham treatment for 14 days, followed by further observation for 8 days.

Methods

Experimental Groups:

- Disease induced/implanted (-) VNS (n = 12)
- Disease induced/implanted (+) VNS (n = 12)
- Disease induced/implanted (-) VNS (n = 12)
- Disease induced/implanted (+) VNS (n = 12)

Results

NCAP significantly inhibited CIA progression with regard to the physical signs as assessed by ankle-caliper measurement. Mean ankle diameter of the NCAP group (n=12) was significantly lower than that of the unstimulated group (n=12) from D13-16, and mean ankle swelling was reduced by 47% over this time period (Figure 6).

The summed histopathological scores were significantly reduced at the ankle and knee, by 47% and 52%, respectively (Figures 7 and 8).

Bone resorption resulted in significant improvements in joint inflammation (Figures 9 and 10).

Histopathological evidence of structural damage, as assessed by pannus formation, cartilage destruction and bone erosion, was all significantly reduced at the ankle (Figure 9 and 10).

An example of NCAP-induced improvement in histopathology is shown in Figure 11.

Three positive effects of NCAP at the joint level were associated with reductions in several systemic inflammatory mediators including serum IL1-beta, IL6, TNF, Interferon-gamma, and l-arginine (Figure 12).

Summary & Conclusions

Neurostimulation of the Cholinergic Anti-inflammatory Pathway by electrical stimulation of the vagus nerve in rats improved physical signs, histological evidence of joint inflammation and structural damage, and production of systemic inflammatory mediators in the CIA model.

Implications

These data represent the first demonstration of amelioration of arthritis using electrical vagal NCAP and provide supportive preclinical evidence for clinical study of a novel approach to treatment of RA and other diseases of inflammatory nature using implantable medical devices.

REFERENCES


DISCLOSURE OF INTEREST

Y. Levine, R. Zilnik, R. Zilnik for employment by SetPoint Medical Corporation.