

BACKGROUND

- RA is a debilitating disease affecting approximately 1% of the population, which leads to marked disability, considerable pain and fatigue, and early mortality.¹
- Although many pharmacologic treatment options are available for RA, three major problems complicate the use of these drugs: many are only marginally successful, have potentially serious side effects, or have exorbitant costs.¹
- Previous studies have shown that activation of the vagal nerve results in a marked improvement in RA disease activity. Placement of a vagal nerve stimulator had a measurable and significant reduction in RA disease activity in 70% of patients.²
- Vagal nerve stimulation likely has a therapeutic effect in systemic inflammatory disease through two potential mechanisms: activation of the cholinergic anti-inflammatory pathway and enhanced parasympathetic activity.³
- The Valsalva maneuver is often employed to stimulate the vagal nerve and slow the heart rate down, such as with supraventricular tachyarrhythmias.⁴

OBJECTIVES

We hypothesize that vagal nerve stimulation through non-invasive methods can lower systemic inflammation and improve RA disease. This pilot study will test this hypothesis through the following two specific aims:

- We will determine if the Valsalva maneuver, which we call non-invasive vagal nerve stimulation (NIVaNS) breathing, is effective in lowering disease activity in RA patients who are on stable but inadequate pharmacologic therapy.
- We will determine if NIVaNS breathing in RA patients results in measurable declines in inflammatory cytokines found in the serum.

METHODS

- Double-blind randomized control trial, randomized 1:1 to either NIVaNS breathing (5 min, twice daily) or a placebo intervention (relaxation breathing).
- RA patients must be on stable DMARDs for 3 months.
- 4 week intervention (visits at week 0, 2, 4); At week 4, placebo patients invited to open 4 week NIVaNS breathing extension.
- Data objectively measured using ESR and number of tender/swollen joints on exam. DAS28-ESR, RAPID3, and CDAI scores also measured at each visit.
- Plasma collected and preserved for cytokine analysis.

RESULTS

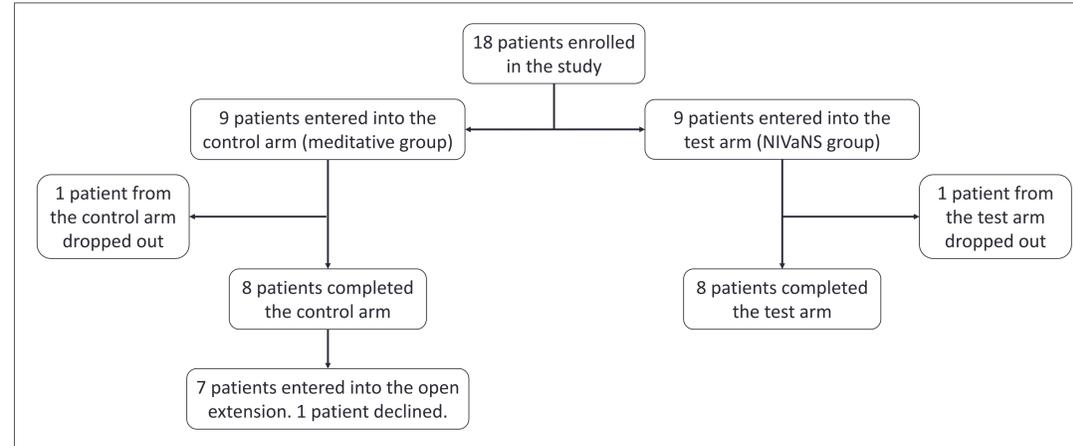


Figure 1. Patient enrollment and treatment arms.

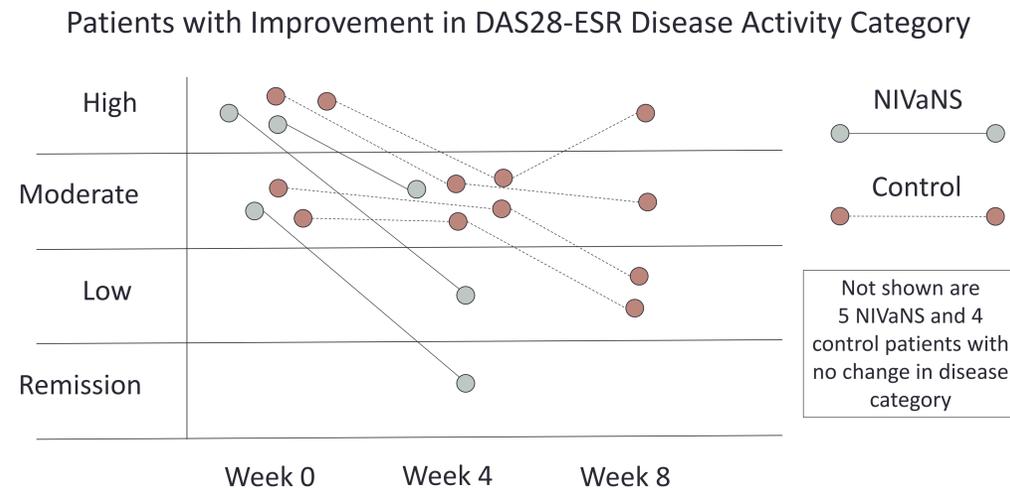


Figure 2. DAS28-ESR is a disease activity measure that allows for 4 categories of disease activity. NIVaNS breathing led to a drop in disease activity category in 5 patients (3 NIVaNS patients and 2 who started NIVaNS breathing at week 4), compared to 2 patients randomized to meditative breathing.

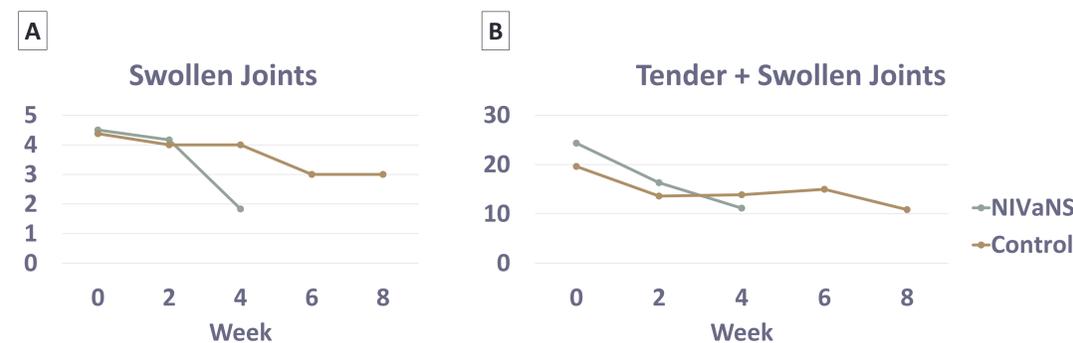


Figure 3. Change in swollen joint count (A) and combined tender and swollen joint count (B).

CONCLUSIONS

- Of 8 patients originally randomized to NIVaNS breathing, 3 had a significant decrease in RA disease activity, including 1 who went into remission and 1 into low disease activity.
- Of 8 patients originally randomized to control meditative breathing, 2 had a drop in RA disease activity. Seven switched to 4 more weeks of NIVaNS breathing, with 2 having a drop in RA disease activity.
- Thus, 5 patients doing NIVaNS breathing compared to 2 patients doing control breathing had improvement in RA disease activity.
- Several patients expressed some difficulty in understanding instructions in how to do the Valsalva breathing maneuver. This may have been a major limitation in the study.

FUTURE IMPLICATIONS

- Vagal nerve stimulation via the Valsalva maneuver (NIVaNS breathing) requires further study to assess potential symptomatic and anti-inflammatory benefits for the treatment of RA.
- Better clarity with instruction on NIVaNS breathing may improve outcomes.
- We intend to do additional studies to confirm that NIVaNS breathing actually activates vagal nerve activity.
- We intend to perform further studies at this and other institutions with a larger patient population, followed for 8 weeks, and with additional testing to better assess potential impact on vagal nerve activity.

REFERENCES

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