Clinical improvement of gastroesophageal reflux disease (GERD) patients with warm ear stimulation, initial exploratory study on the anterior branch of the vagal nerve (Jacobson’s nerve)

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INTRODUCTION

In recent years, researchers have been very enthusiastic in researching autonomic nerve stimulation, especially trans-auricular vagal stimulation. The inner earlobe has a branch of the vagal nerve known as Jacobson’s. Trans-auricular vagal nerve stimulation has been carried out in animals and humans regarding immunity, epilepsy, decreased consciousness, cognition, and pain. All of these studies show clinical improvement. In many studies, researchers use electrical stimulation. Electrical stimulation will stimulate pain fibers, namely type C.¹⁻¹⁰

To our knowledge, only our research has stimulated the vagal nerve in the ear using warm stimulation. Stimulation using warm temperatures will go through the same pathway as pain stimulation through type C nerve fibers.¹¹ Even though they both stimulate type C fibers, there will be differences in comfort for the patient. We assume that stimulation using warm temperatures will be felt more comfortable by patients compared to electrical stimulation in the form of painful stimuli. In this study, we want to prove the effect of warm stimulation on the trans-auricular vagal nerve for treating gastroesophageal reflux disease (GERD). This disease is known to have a large population in society, and there is no satisfactory therapy. Based on research, it has been proven that stimulation of the trans auricular vagal nerve can have an effect on the movement of the digestive organs and can also affect the subject’s psychology. This is appropriate when applied to GERD patients, considering that this disease is based on many things that influence people's digestive movements, including psychological factors.¹²,¹³

As far as we know, no research has been conducted on trans-auricular vagal nerve stimulation for treating GERD. As a first step, we will conduct a preliminary study in the form of a clinical trial of a device used in Europe and America to warm the ears in winter. Still, this device has not been tested to see whether it has a clinical effect on GERD or gastroesophageal reflux disease.

ABSTRACT

Introduction: Jacobson’s nerve, also known as the auricular branch of the vagus nerve, is situated on the medial part of the earlobe. Research has demonstrated that electrical stimulation of this nerve can influence various aspects of gastrointestinal motility and function. This study investigated how warm stimulation affects Jacobson’s nerves as an adjuvant therapy in patients with gastroesophageal reflux disease (GERD).

Methods: The investigation was carried out using a single-blind design, wherein the participants were unaware of their assigned group and the nature of the ear-warming therapy they were getting, whether genuine or placebo. The present study involved a sample of 15 individuals who were diagnosed with gastroesophageal reflux and had undergone medical treatment. The participants were allocated into three distinct groups for the study. Group 1 was administered anti-gastritis medication and instructed to utilize ear warmers. Group 2 was given a placebo medication and required a device resembling an ear warmer. Lastly, Group 3 was solely administered anti-gastritis medication without additional ear warmers instructions.

Results: This study showed a significant difference between the three groups after the intervention (p = 0.03). Post-intervention comparison between groups 1 and 3 revealed a significant difference (9 ± 3 vs 15 ± 14, p = 0.008).

Conclusions: Warm stimulation can serve as a viable and secure supplementary therapeutic approach for individuals diagnosed with gastroesophageal reflux disease (GERD).
**METHODS**

**Study Design**

The research subjects consisted of 15 people suffering from gastroesophageal reflux who had received therapy from a doctor to treat gastroesophageal reflux attacks. Subjects were randomized into three groups consisted of 5 subjects: test, sham, and control group. The test group used routine medication and ear warmers, the sham group used regular and fake ear warmers made to look like real ones, while the control group used regular medication without treatment in the form of natural or phony ear warmers.

Group 1, the test group received anti-gastritis medication and ear warmers. Group 2, the sham group, received commonly consumed anti-gastritis medication and a device similar to an ear warmer. Group 3, the control group, with widely consumed anti-gastritis drugs.

**Data Collection**

We used the gastroesophageal reflux disease questionnaire (GERD-Q) to monitor the clinical response of research subjects during attacks, drink channel blockers, anti-emetics, and antispasmodics with absolute ear heaters. Subjects were asked to complete a questionnaire regarding clinical symptoms of gastroesophageal reflux before and after intervention in the clinical trial and shams groups. The study was single-blind; the subjects did not know which group they belonged to and did not know whether they were getting real or fake ear-warming therapy devices. The researcher know which group the subject belongs to and what type but what is given.

We assume the patient will feel more comfortable with stimulation in the form of temperature. We plan to use warm stimulation on the vagus nerve in the ear using a tool that has not been used as therapy so far but only used as a warmer when winter comes (Figure 1). The tool depicted in Figure 1.

**Data Analysis**

Statistical test for data consisting of three paired groups in numerical data. The Kruskal-Wallis test was used to analyze the different results among groups. Results were considered significant if p-value $\leq 0.05$.

**RESULTS**

The result presented in Table 1. Figure 2 describe post-intervention comparison between groups using Kruskal Wallis Test. The analysis showed that there was a significant difference between the three groups after the intervention ($p = 0.03$). This means anti-gastritis drugs and ear warmers affect the sham and control groups differently. Post-intervention comparison between group 1 and group 2 revealed no significant difference [9 (3-11) vs 16 (9-17), $p = 0.055$]. This means that anti-gastritis drugs and ear warmers did not have a significantly different effect on the sham group. Post-intervention comparison between groups 1 and 3 revealed a significant difference [9 (3-11) vs 15 (14-16), $p = 0.008$]. This means that anti-gastritis drugs and ear warmers had a better effect on the control group. However, post-intervention comparison between groups 2 and 3 showed no significant difference [16 (9-17) vs 15 (14-16), $p = 0.914$).

The comparison between pre and post-intervention in each group depicted in Figure 3.

There were significant difference in group 1 and group 3 between pre and post-intervention ($p = 0.039$ and $p =$...
Figure 2. Comparison of post-intervention between groups.

Figure 3. Comparison between pre and post-intervention in each group.

0.041, respectively). This indicated that anti-gastritis drugs and ear warmers provide improvement in group 1. Based on these results, we assume that adding ear heating devices to GERD therapy produces clinical changes in the form of significant improvement.

**DISCUSSION**

Butt et al. examined the mechanism and anatomy of the auditory nerve, which is a tributary of the ear. The visual depiction is a schematic diagram illustrating the complex interconnections of the facial, glossopharyngeal, and vagal nerves. The Auricular Branch of the Vagal Nerve (ABVN) originates from the glossopharyngeal nerve’s petrous ganglion and the vagal nerve’s jugular ganglion. It then proceeds to ascend through the mastoid canaliculus. The facial nerve traverses the fallopian canal within the mastoid region, precisely positioned approximately 3-4 mm superior to the stylomastoid foramen. Following this, it then bifurcates into two discrete branches.

The chorda tympani is connected to the initial division of the ABVN, which innervates the sensory component of the dura mater located in the posterior cerebral fossa. The posterior epidermis of the external auditory meatus and the opposite tympanic membrane get innervation from the vagal nerve’s second branch of the ABVN. Upon its emergence from the stylomastoid foramen, a connection arises between the second branch’s inferior division and the facial nerve’s posterior auricular branch. This image encompasses the facial nerve (FN), the chorda tympani nerve (CT), the tympanic branch of the glossopharyngeal nerve (TBGN), and the ABVN. The primary aim of this research is to investigate the effects of various environmental factors on the growth of plants. The user’s text is already written in an academic style.

Furthermore, Butt et al. conducted a study examining the relationship between the afferent projections of the external auricle and the upper cervical spinal cord and medulla. The auricular nerve, which is more extensive, exhibits projections towards the trigeminal tract, cuneate nucleus, and, to a lesser extent, the solitary tract nucleus within the brainstem. The auriculotemporal nerve terminates at the cuneate nucleus, caudal trigeminal nucleus, and trigeminal tract. The auricular branch of the vagal nerve supplies innervation to the nucleus of the solitary tract, cuneate nucleus, and caudal trigeminal nucleus. The more significant auricular nerve exhibits a wide-ranging distribution inside the upper cervical cord, from lamina I to lamina V. In contrast, the auriculotemporal nerve demonstrates a more limited dispersion pattern, primarily localized within laminae III-IV. The termination site of the ABVN is located within laminae III-IV. To enhance clarity, the discussion has excluded the hierarchical layers of the central nervous system.

The auriculotemporal nerve is commonly referred to as ATN, the auricular branch of the vagal nerve is abbreviated as ABVN, and the tremendous auditory nerve is denoted as GAN. There exists a potential approach to rephrase the user’s text in a more scholarly manner. Depicts a schematic representation of a possible pathway that elucidates the process.
underlying the stimulation of the auricular branch of the vagal nerve. The potential impact of the ABVN on the cardiovascular system deserves attention. Stimulation of the ABVN results in an augmentation of sensory input to the nucleus of the solitary tract (NTS) located in the medulla. As a result, this phenomenon affects the functioning of NTS neurons, which are responsible for transmitting signals to cardioinhibitory vagal efferent neurons situated in the dorsal vagal nucleus (DVN) and nucleus ambiguous (NA). Vagal efferent neurons communicate vagal tone to the sinoatrial (SA) node for communication. There is a potential for the stimulation of the ABVN to induce neuronal excitement within the Nucleus Tractus Solitarius (NTS), which can then result in the transmission of excitatory signals to the caudal ventrolateral medulla (CVLM). The research has demonstrated the inhibitory impact of the CVLM on the rostral ventrolateral medulla (RVLM). The RVLM is essential for delivering excitatory stimulation to sympathetic preganglionic neurons in the spinal cord’s intermediolateral cell column (IML). The process of inhibition will decrease sympathetic activity.\textsuperscript{2}

Gastroesophageal reflux disease is a disease that involves many body functions, especially the autonomic nerves. This condition is commonly found in various countries, such as Indonesia. In Indonesia, the prevalence of GERD is 27.4%. This disease is characterized by an increased stomach acid so high that reflux occurs, namely flow towards the esophagus and even the pharynx. Symptoms of this disease are characterized by heartburn, nausea, vomiting, and burning sensation in the throat and pharynx due to irritation of stomach acid, and often post nasal drip, namely the flow of fluid from the nose to the pharynx and esophagus, which causes discomfort.\textsuperscript{13} Medical therapy in various groups, including different gastric acid channel blockers, bacofen, and gabapentin, has not shown satisfactory results. Meanwhile, operative treatment on the sphincter between the stomach and esophagus, which is suspected to be loose, has not produced a good effect.\textsuperscript{15} Based on literature studies, it appears that the autonomic nerves control the motility of the digestive organs. Many studies that stimulate the autonomic nerves have shown results in slowing or accelerating the motility of the digestive organs. Acupuncture practitioners often perform stimulation of the ear to treat various complaints, including digestive disorders. Western medicine suggests stimulation of the Jacobson’s nerve, a branch of the vagal nerve.\textsuperscript{16}

Theoretically and in research on experimental animals, it appears that not only can the digestive organs be affected by stimulation of the vagal nerve, but it can also affect memory and the limbic area of the system to influence neurobehavior. Direct stimulation of the vagal nerve via acupuncture on Jacobson’s nerve can cause uncomfortable side effects for the patient, although it is rare. We observed empirically that in GERD patients who stimulated the ear with a warm feeling using a warming bag filled with warm water, a clinical improvement effect could occur in the form of reflux symptoms that increasingly subsided, followed by the cessation of post-nasal drip and a feeling of comfort. In this regard, we tried to test a tool similar to the description above, which is very popular in four-season countries, namely an ear warmer used when winter arrives. This tool does not cause any side effects, but whether it will reduce the clinical symptoms of reflux gastroenteritis is unknown.\textsuperscript{17} For comparison, we will discuss ear vagal nerve stimulation research in cardiology. Here is electrical stimulation of the vagal nerve for cardioprotective purposes. The vagal nerve will enter the medulla oblongata from this ear branch, influencing the heart and nerve modulation.\textsuperscript{8} Cardiology research employs a technique known as Low-Level Tragus Stimulation (LLTS). This technique involves applying anode and cathode to deliver tragus stimulation to the afferent fibers of the vagal nerve, with a specific focus on the auricular branch. The subsequent penetration of the excitatory electrical charge occurs within the medulla oblongata, a brain stem region. As a result, it evokes a reaction from the efferent fibers of the vagal nerve, initiating the desired cardiac neuromodulation. Numerous investigations have been conducted about the vagal nerve stimulation in the auditory domain within the realm of cardiology, with favorable outcomes in diverse pathological conditions. The user’s text needs to be longer to be rewritten academically.\textsuperscript{4} The study conducted by Choi et al. investigated the effects of transcutaneous auricular vagal nerve stimulation on cerebrospinal fluid circulation and cognitive function in a rodent model of vascular cognitive impairment. The researchers employed electrodes and applied vagal stimulation to the ears of mice as part of their experimental procedure. Empirical evidence has substantiated the efficacy of this testing methodology in augmenting cognitive functioning.\textsuperscript{18} Corrêa et al. have undertaken a study, The present study investigates the effects of transcutaneous auricular vagal nerve stimulation on inflammation, cardiac modulation, and clinical symptoms in individuals diagnosed with COVID-19. A randomized clinical trial design was employed to examine the potential benefits of this intervention. The objective of this research endeavor is to investigate the impact of transcutaneous auricular vagus nerve stimulation (taVNS) on pre- and post-treatment concentrations of cortisol (D), interleukin 10 (IL-10), C-reactive protein (CRP) (A), interleukin 6 (IL-6) (B), and interleukin 10 (C) after 14 taVNS sessions. Both the a-taVNS group (n = 26) and the s-taVNS group (n = 26) comprised the two distinct groups for this study. A statistically significant level was observed in a sample size of 17, with a p-value less than 0.05.\textsuperscript{19} Regarding improving the olfactory system, the research conducted by Maharjan et al. investigated the effects of auditory nerve stimulation. In a study conducted by Zhang et al., the researchers aimed to examine the efficacy of auricular vagal nerve stimulation as a potential therapeutic approach for individuals with chronic depression. The researchers utilized functional magnetic resonance imaging (fMRI) to assess the observed effects of this intervention.\textsuperscript{20} Gagliardi et al., (2019) did a study on acupuncture, focusing on the impacts
of stimulating the complex nerves in the auricular region. Their inquiry mainly aimed to examine the effect of this stimulation on the microcirculation beneath the stimulated area. Wu et al. conducted a study to investigate the utilization of transcutaneous electrical nerve stimulation (TENS) as a therapeutic intervention for stimulating the nerves in the inner ear of individuals who have insomnia in their study. Krusche-Mandl et al. have presented findings that support the potential use of nerve stimulation in the ear as a therapeutic strategy for treating osteoarthritis. A study was undertaken by Go et al. to examine the impact of ear vagal nerve stimulation on inflammation in mice. The investigation conducted by Go et al., (2021) revealed that applying this stimulus exhibited anti-inflammatory effects. Karemaker et al. has investigated the role of vagal nerves in the modulation of blood pressure. Hou et al. conducted a study to examine the impact of vagal nerve stimulation in the auricular region on the functioning of gastrointestinal organs. Their findings suggest that such stimulation can enhance motility and alleviate depressive-like behavior. A study conducted by Yakunina et al. presents the investigation of electrodes utilized to stimulate the anterior branch of the vagal nerve in tinnitus therapy. The survey by Evensen et al. aimed to assess the safety and feasibility of taVNS in a sample of 15 individuals diagnosed with severe depression. The participants were recruited from both an inpatient psychiatric institution and an outpatient psychiatric clinic. The researchers found instances of anxiety attacks that resulted in hospitalization among participants in the active ta-VNS group. These observations were made based on the temporal relationship between ta-VNS and the occurrence of anxiety attacks and, to a certain extent, the plausibility of the nine criteria suggested by Bradford Hill. Bauer et al. reported one additional significant adverse event. The researchers evaluated the effectiveness and safety of taVNS in individuals diagnosed with drug-resistant epilepsy. During the period of stimulation, a skin lesion presumed to be basal cell carcinoma was discovered in one patient. Based on the authors’ statement that histology was not confirmed and the event adhered solely to the temporal criteria of the nine criteria, we conclude that despite their severity, the two adverse events mentioned cannot be attributed to the intervention. It is worth noting that there have been no documented instances of severe cardiac adverse events associated with ta-VNS. The findings of our study validate prior research indicating that there were no significant alterations in instantaneous heart rate (HR), as well as systolic, diastolic, and mean blood pressure, as a result of the taVNS. Consequently, it can be concluded that taVNS is a safe and well-tolerated intervention. The user's text is missing, so it cannot be rewritten academically.

Drawing from the literature review, we conducted a comparable clinical examination utilizing temperature as a stimulus instead of electrical stimulation. This choice was motivated by the established theoretical framework positing that temperature and pain (induced by electrical stimulation) traverse the identical afferent nerve pathway, specifically the minor variant of nerve fibers known as type C.

The acquired results are based on meta-analysis research. Out of the 167 studies that were examined, it was found that only two instances of adverse events were categorized as severe, as reported in two distinct research. The survey conducted by Evensen et al. aimed to assess the safety and feasibility of taVNS in a sample of 15 individuals diagnosed with severe depression. The participants were recruited from both an inpatient psychiatric institution and an outpatient psychiatric clinic. The researchers found instances of anxiety attacks that resulted in hospitalization among participants in the active ta-VNS group. These observations were made based on the temporal relationship between ta-VNS and the occurrence of anxiety attacks and, to a certain extent, the plausibility of the nine criteria suggested by Bradford Hill. Bauer et al. reported one additional significant adverse event. The researchers evaluated the effectiveness and safety of taVNS in individuals diagnosed with drug-resistant epilepsy. During the period of stimulation, a skin lesion presumed to be basal cell carcinoma was discovered in one patient. Based on the authors’ statement that histology was not confirmed and the event adhered solely to the temporal criteria of the nine criteria, we conclude that despite their severity, the two adverse events mentioned cannot be attributed to the intervention. It is worth noting that there have been no documented instances of severe cardiac adverse events associated with ta-VNS. The findings of our study validate prior research indicating that there were no significant alterations in instantaneous heart rate (HR), as well as systolic, diastolic, and mean blood pressure, as a result of the taVNS. Consequently, it can be concluded that taVNS is a safe and well-tolerated intervention. The user's text is missing, so it cannot be rewritten academically.

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CONCLUSION

Based on preliminary research findings, it is evident that ear warmers, typically employed in regions experiencing four distinct seasons initially intended for non-therapeutic applications, had potential therapeutic utility. Using Jacobson's nerve stimulation to facilitate the clinical manifestations of GERD presents a promising avenue for developing a specialized therapeutic device. Therefore, further studies are needed to validate these findings.

ACKNOWLEDGMENTS

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CONFLICT OF INTEREST

There is nothing to declare.
ETHICAL CONSIDERATION

The research has obtained ethical approval from the Ethics Committee of the Faculty of Medicine, UPN Veterans Jakarta. The ethical clearance number 343/ VIII/2023/KEPK indicates the approval of the relevant ethical committee for the specified research project.

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AUTHOR CONTRIBUTION

AYS collects the data, then processes and analyzes it. A manuscript is prepared as a result. T.F.K., H.Z., and A.P.K. are responsible for processing and analyzing the data, while R.Y. and I.P. edit the text.

REFERENCES