Tumor necrosis factor-α (TNFα) is a cytokine produced during infections and has been determined to significantly increase at the site of sinusitis. This cytokine has various functions including stimulating chemokine release to attract neutrophils and macrophages, increasing vascular permeability, and recruiting leukocytes. Based on these functions, TNFα levels should increase in the blood after facial effleurage because increasing amounts of this cytokine have the ability to leave the site of infection.

Acute rhinosinusitis is an inflammatory condition that millions of Americans face every year. Approximately 12% of adults in the United States face this illness. Acute rhinosinusitis is most commonly caused by a bacterial or allergic condition causing mucosa inflammation of the paranasal sinuses and the nasal sinuses. Symptoms last less than four weeks, and more typically resolve within two weeks. The symptoms commonly reported include nasal congestion and drainage, sinus pressure, fever, or facial pain. Because this infection is extremely common, it also places a substantial economic burden on the American people and healthcare system. Some estimates report over 5.8 billion dollars of annual health care expenditure in the United States due to acute rhinosinusitis.

The general clinical consensus is that viral acute rhinosinusitis presents with symptoms that will not persist beyond 7 days, while a bacterial source of infection will last longer and cause more severe symptomology. Physicians may only prescribe antibiotics in severe cases when symptoms last beyond 10 days and a non-viral cause is suspected. Unfortunately, over-the-counter medications such as antihistamines and decongestants have not been found to be effective treatment options for those not receiving antibiotics. This leaves many patients without adequate treatment options.

A potential alternative treatment for patients suffering from acute rhinosinusitis is an osteopathic manipulative treatment called facial effleurage (FE). This technique involves the physician applying pressure along various regions of the face to increase lymphatic drainage. This treatment is indicated for upper respiratory infections and can be used on patients with suspected viral infection, or in conjunction with antibiotics in bacterial infections. FE performed on acute rhinosinusitis patients may help relieve symptoms and expedite recovery time.

One method that can be used to better understand the benefits of the facial effleurage treatment is analyzing the blood contents of patients before and after the procedure for the presence of inflammation markers or immune cells.

Hypothesis: TNFα levels should increase in the blood after facial effleurage because increasing amounts of this cytokine have the ability to leave the site of infection.

METHODS

In a parallel-arm, randomized, placebo-controlled clinical trial, patients that presented to two outpatient, direct primary care clinics in a mid-sized manufacturing town are asked to participate. Informed consent and enrollment eligibility is confirmed. Participants are then randomly assigned to one of the eight treatment groups: healthy control (HC), HC with physical touch (PT), HC with Facial Effleurage (FE), rhinosinusitis (RS) with antibiotics (Abs), RS with PT, RS with FE, RS with Abs and PT, and RS with Abs and FE. Physical touch is the sham/placebo treatment. Peripheral blood samples are then collected. The treatment is performed and 1 hour after the initiation of facial effleurage serum samples are collected again. Peripheral blood is also collected at a follow-up appointment 7 days after treatment. Serum TNFα levels are then measured via ELISA.
Facial effleurage treatment increases serum TNFα levels in patients with acute rhinosinusitis

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The difference between sick patients and healthy controls prior to treatment was not statistically significant, but sick patients tend to have higher levels. Patients who received facial effleurage had significantly increased TNF$\alpha$ levels one hour after treatment compared to healthy patients, patients that received only antibiotics, and patients that received the sham treatment. On follow-up 7 days after facial effleurage, TNF$\alpha$ is increased in sick patients, although not significantly.

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Figure 1. Serum concentration of TNF$\alpha$ is not statistically up-regulated in patients with acute rhinosinusitis. Blood was drawn from patients with and without acute rhinosinusitis prior to treatment. The serum concentration of TNF$\alpha$ was measured via ELISA. Student's t-test was utilized and * indicates a p-value of 0.05

Figure 2. Serum concentration of TNF$\alpha$ decreased after FE treatment by 15 minutes and lasted up to 75 minutes after the start of FE treatment. Blood was drawn from a patient with acute rhinosinusitis prior to treatment (Pre-Tx). Facial Effleurage began and every 15 minutes, additional blood was drawn. The serum concentration of TNF$\alpha$ was measured via ELISA. Student's t-test was utilized and * indicates a p-value of 0.05.

RESULTS

A total of 90 patients were enrolled. None of these patients met the exclusion criteria. Out of the 90 patients, seven were lost to follow-up.

Descriptive statistics were used to determine the mean and standard deviation between groups. ANOVA analyses were used to determine if there are statistical differences in serum TNF$\alpha$ levels between treatment groups. A p-value of 0.05 was used to determine statistical significance. All analyses were performed using GraphPad Prism Software.
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**CONCLUSIONS**

TNFα is significantly upregulated in the blood one hour after facial effleurage treatment, and this increase might persist at least a week after one treatment session. Since pre-treatment values of serum TNFα did not statistically differ from healthy patients, the increase in TNFα after FE may be indicative of the technique causing substantial change to lymphatic or vascular circulation.

One possible explanation for this significant increase in serum TNFα levels is that increasing amounts of this cytokine have the ability to escape the site of infection. TNFα exodus could potentially decrease the swelling and pain the patients experience, as well as ushering in the healing response rather than prolonging the state of inflammation. This would be particularly valuable when the proinflammatory response is no longer warranted.

If occurring, patients may clear the infection at a faster rate than those without treatment or those only receiving antibiotics.

Through this research there is potential for an improved standard of care for acute rhinosinusitis involving facial effleurage, as well as a decreased reliance on antibiotics. At this time, more research is necessary to fully understand the complex relationship between FE, serum TNFα, and acute rhinosinusitis infections.

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