# LOW LEVEL LASER VERSUS ERYTHROMYCIN PHONOPHORESIS IN THE TREATMENT OF CHRONIC RHINOSINUSITIS: A RANDOMIZED CLINICAL TRIAL

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## Abstract

**Aim:** The current study was conducted to investigate the efficacy of low-level laser therapy (LLLT) versus erythromycin phonophoresis in treatment of chronic rhinosinusitis. **Design:** Randomized controlled trial. **Patients and Methods:** The present work was conducted on sixty patients with chronic rhinosinusitis who participated in this study, their ages ranged from 30 to 60 years. The participants were selected from El-Monira general hospital, and randomly divided into two groups; each group consisted of 30 patients. **Group (A) (LLLT group):** received low level laser on maxillary sinuses (wavelength 830-nm in continuous-wave mode at a power output of 30 mW and energy dose of 1 J for 6 minutes), 3 times per week for one month, in addition to traditional medication (topical intranasal steroid), once per day for a month. **Group (B) (Erythromycin Phonophoresis group):** received ultrasound (US) with use of 2% erythromycin topical gel. The US parameters were (Intensity 1 W/ $cm^2$ for maxillary sinuses, pulsed mode for 4 – 5 minutes), 3 days per week for one month in addition to traditional medication. Sinusitis Symptom Scores (SSS) based on a visual analogue scale (VAS) is well established. In this method, the six symptoms are assessed using a scale of 0±10, where zero represents no symptom and 10 represents the most severe symptom imaginable. CT Scan for maxillary sinuses based on 0-3 system: 0 = clear, 1= mild or moderate mucosal thickening, 2 = severe mucosal thickening, 3 = total opacification. This assessment was done pre-treatment and post treatment after one month. **Results.** Comparison between groups post treatment revealed a significant decrease in SSS and CT scan of group A compared with that of group B post treatment ($p < 0.001$). **Conclusion.** Erythromycin phonophoresis has a significantly better impact on chronic rhinosinusitis as compared with low level laser.

**Keywords.** Low Level Laser, Erythromycin Phonophoresis, Sinusitis Symptoms Score, Computerized Tomography Scan, Chronic Rhinosinusitis.

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## INTRODUCTION

Chronic rhinosinusitis (CRS) is a term that has been used to describe a number of entities characterized by chronic symptoms of nasal and sinus inflammation or infection. There has been a lack of consensus regarding definitions and treatments because CRS may be a spectrum of diseases with a range of appropriate treatments. The absence of widely accepted definitions for CRS has resulted in a paucity of research directed at understanding its pathophysiology and has hampered efforts to improve treatment **(1).**

Sinusitis is inflammation that causes pain, pressure, and swelling in the sinuses. Chronic sinusitis is sinusitis that lasts for a long time, usually longer than 12 weeks, and is one of the more prevalent chronic illnesses in the United States, affecting persons of all age groups. **(2).**

Ultrasound (US) is a form of mechanical energy (not electrical), and therefore, strictly speaking, not really electrotherapy at all, but does fall into the Electro Physical Agents grouping. The ultrasound waves penetrate the tissue on the way to the target organ and have two mechanisms of action (thermal and non-thermal), which may potentially work synergistically to reduce nasal symptoms (nasal blockage and secretions)**.** The thermal effects may work by enhancing metabolic activity and circulation within the nasal tissue. The vibration created by the non-thermal mechanism may alter the consistency of nasal secretions. **(3).**

The intensity of the ultrasound treatment may also influence its impact, with potential beneficial effects at low intensities but with high intensities having the potential to damage exposed cells and tissues **(3).** Bacterial biofilms have been implicated in many chronic infective diseases, including chronic rhinosinusitis (CRS). Therapeutic ultrasound enhances the breakdown of bacterial biofilms and is clinically effective in CRS treatment, while phonophoresis has also been utilized for antibiotic delivery through the skin **(4)**.

Erythromycin is an antibiotic used for the treatment of a number of bacterial infections. This includes respiratory tract infections, skin infections, chlamydia infections, pelvic inflammatory disease, and syphilis **(5).**

Laser irradiation has bio-simulative, anti-inflammatory, and analgesic effects. Laser irradiation especially affects cellular membranes, membrane canaliculi and pumps, mitochondria, cytoskeleton, nociceptors, fibroblasts, lymphocytes, polymorphonuclears and Langerhans cells **(6).** Lasers with different wavelengths, varying from 632 to 904 nm, are used in the treatment of musculoskeletal disorders. Wavelengths between 660 nm and 905 nm have the ability to penetrate skin, and soft/hard tissues. This light has a good effect on pain, inflammation and tissue repair **(7)**

The photo biomodulation effect of LLLT is attributed non-thermal events. It involves the absorption of photon radiation by chromophores such as cytochrome C oxidase within the mitochondria leading to release of nitric oxide (NO), and increase in ATP levels. These events can lead modulation of cell metabolism, normalization of cell function, inflammation reduction, pain relief, and tissue repair **(4).** Laser therapy has a direct impact on microcirculation and decreases the potential of relapses. Low-energy helium-neon laser modulates vessel permeability, decreases perivascular edema and blood rheology (red blood cell aggregation), and leads to the significant decrease of the mucosal membrane thickness in the adults with chronic rhinosinusitis **(8).**

The need for this study was designed from the lack of the primary related studies and researches about the role of physical therapy for treatment of chronic rhinosinusitis for reduction of pain and inflammation. It is believed that the value of the present study doesn't lie in describing a new phenomenon but in providing a quantitative information to assess the most affective physical therapy modalities in management of chronic rhinosinusitis.

## SUBJECTS AND METHODS

**Subjects:**

Sixty patients both sex who had chronic rhinosinusitis had participated in this study, with age ranged from 30-60 years and recruited from El-Monira Hospital. The patients were classified randomly into two groups of equal number, 30 patients for each group. Patients were enrolled in the trial if they met the following criteria: (1) both sexes with range 30 and 60 years. (2) All patients who had inflammation in maxillary area. (3) All patients with pain and inflammation in the nose due to chronic rhinosinusitis. Patients who had met one of the following criteria were excluded from the study :( 1) Patients who suffered from mental or psychological disorders. (2) Patients with any systemic diseases that may interfere with the objectives of the study. (3) Pregnant women. (4) Patients with heart pacemaker devices. (5) Patients who had plates and screws. (6) Patients who had inflammations in frontal, ethmoid and sphenoid area.

**Sample size determination**

Unpaired t-test was conducted for comparison of subjects characteristics between groups. Chi- squared test was carried out for comparison of sex distribution between groups. Mann–Whitney U test was conducted for comparison of Sinusitis Symptom Scores and CT-Scan between groups and Wilcoxon signed ranks test was conducted for comparison between pre and post treatment. The level of significance was set at $p < 0.05$. All statistical analysis was conducted through the statistical package for social sciences (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA).

**Design:**

This trial No.P.T.REC/012/003006 was assented by the Ethical Committee of the Faculty of Physical Therapy, Cairo University. All aspects of the study were disclosed and informed consent was obtained. The patients were randomly assigned into two equal groups via the envelope mode. After patients' agreement to participate in the study, cards with either 'LLLT' or 'Erythromycin Phonophoresis' recorded on them were closed in envelopes; then a blinded physical therapist was asked to select one envelope according to the selected card, patients were assigned to their corresponding group. Group A comprised 30 patients who received Low Level Laser therapy and group B comprised 30 patients who received Erythromycin phonophoresis. The examiner physical therapist was not included in randomization procedures and was unaware of the therapy allocation. Patients were asked not to disclose their therapy allocation to the physical therapist during assessment. The participants were informed to report any harmful effects throughout the treatment period.

**Assessment:**

**Sinusitis Symptoms score (SSS)**: Sinusitis Symptom Scores based on a visual analogue scale (VAS) is well established. In this method, the six symptoms were assessed using a scale of 0±10, where zero represents no symptom and 10 represents the most severe symptom imaginable. **(9).**

**Computerized Tomography Scan:** CT scan (TOSHIBA, MODEL TSX-035A, INPUT POWER 50kVA) was used for assessment of mucosal thickening of maxillary sinuses, which is based on 0-3 system: 0 = clear, 1= mild or moderate mucosal thickening, 2 = severe mucosal thickening, 3 = total

opacification. **(10)** This assessment was done pre-treatment and post treatment after one month**.**

**Treatment:**

**Low level laser**

Each participant in group A received low level laser, (ASTAR, POLSKA-POLAND, Ga-Al-As infrared diode laser) with wavelength 830 nm, power output of 30mW, and energy dose of 1 J for 6 minutes on maxillary sinuses, the laser was applied 3 days per week for one month, **(4)** in addition to the traditional medication (topical intranasal steroid) once per day for a month**.**

**Erythromycin phonophoresis**

Each participant in group B received erythromycin phonophoresis, US with use of 2% erythromycin topical gel. The US parameters were (Intensity 1 W/ $cm^2$ for maxillary sinuses pulsed mode for 4 – 5 minutes) for 3 days per week for one month, **(11)** in addition to the traditional medication**.**

## RESULTS

**Subject characteristics:**

Sixty patients with chronic rhinosinusitis participated in this study. Table (1) showed the subject characteristics of group A and B. There was no significant difference between groups in age, weight, height, BMI and sex distribution ($p > 0.05$).

**Table 1. Comparison of subject characteristics between group A and B:**

| | Group A | Group B | p-value |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | |
| **Age (years)** | 32.43 ± 10.53 | 31.67 ± 10.29 | 0.77 |
| **Weight (kg)** | 75.86 ± 16.22 | 79.23 ± 14.87 | 0.41 |
| **Height (cm)** | 168.20 ± 5.64 | 166.96 ± 7.79 | 0.48 |
| **BMI (kg/m²)** | 26.86 ± 5.89 | 28.27 ± 5.09 | 0.32 |
| **Sex** | | | |
| Females | 14 (47%) | 16 (53%) | 0.61 |
| Males | 16 (53%) | 14 (47%) | |

**SD, standard deviation; p value, probability value**

**Effect of treatment on Sinusitis Symptom Scores and CT-Scan:**

- **Within group comparison**

There was a significant decrease in Sinusitis Symptom Scores and CT-Scan post treatment compared with that pretreatment in both groups ($p < 0.001$).

- **Between group comparison**

There was no significant difference between groups pre-treatment ($p > 0.05$). Comparison between groups post treatment revealed a significant decrease Sinusitis Symptom Scores and CT-Scan of group B compared with that of group A ($p < 0.05$). (Table 2).

**Table 2. Median values of Sinusitis Symptom Scores and CT-Scan pre and post treatment of group A and B:**

| | Group A | Group B | U- value | p value |
|---|---|---|---|---|
| | Median (IQR) | Median (IQR) | | |
| **Sinusitis Symptom Scores** | | | | |
| **Pre treatment** | 26.5 (47.25-16.25) | 28 (44.25-14) | 428.5 | 0.75 |
| **Post treatment** | 14 (25.25-8) | 9.5 (14.25-3) | 298.5 | 0.02 |
| **Z- value** | -4.79 | -4.78 | | |
| | ***p = 0.001*** | ***p = 0.001*** | | |
| **CT-scan** | | | | |
| **Pre treatment** | 2 (3-1.75) | 2 (3-1) | 409 | 0.51 |
| **Post treatment** | 1 (1.25-0.75) | 0.5 (1-0) | 277.5 | 0.005 |
| **Z- value** | -4.92 | -4.86 | | |
| | ***p = 0.001*** | ***p = 0.001*** | | |

**IQR: Interquartile range; U value: Mann-Whitney test value; Z- value: Wilcoxon signed ranks test value; p-value, probability value.**

## DISCUSSION:

All patients in this trial achieved improvement in symptoms of chronic rhinosinusitis and mucosal thickness of maxillary sinuses, the low-level laser was effective in treatment of CRS, the possible explanation for this improvement is the deeper penetration and the anti-inflammatory effect of LLLT that increases the phagocyte efficiency and lymphatic vessel amount and thickness thus results in a decrease in blood vessel permeability and restoration of microcapillary circulation, which reduces edema by restoring normal vascular wall permeability. These effects may be responsible for the improvement in mucosal membrane thickness. In cells and soft tissue, it is thought that LLLT generates local anti-inflammatory effects and modifies biochemical inflammatory markers **(9).**

Result of this study showed efficacy of Low-level laser in treatment of chronic rhinosinusitis that was consistent with several studies **(12,13,4).**

In a study applied by **Elkalla et al., 2020. (12),** thirty-four patients with chronic maxillary sinusitis were assigned into two groups. All were assessed before and after treatment. Group A received laser radiation plus standard medical treatment and group B received medical treatment only. The treatment plan was performed in 12 sessions using a Diode laser with a wavelength of 810 nm and 980nm. The result demonstrates high intensity intra-oral laser therapy is more effective than using medical treatment only for treatment of chronic maxillary sinusitis.

Fifteen adult patients with CRS participated in a pilot pretest–posttest clinical study. Patients were treated with a 830-nm Ga-Al-As laser in continuous-wave mode at a power output of 30 mW and energy dose of 1 J. Laser irradiation was delivered on six points over each maxillary or frontal sinus with 33 sec irradiation for each point and a total treatment duration of 198 sec for each sinus LLLT was applied three times a week for ten treatment sessions. Patients were given LLLT three times per week for ten treatment sessions. The results demonstrated the application of LLLT on Chronic Rhinosinusitis after 10 sessions has beneficial effect in treatment of CRS (**4).**

Concerning the efficacy of Erythromycin Phonophoresis in treatment of chronic rhinosinusitis, the results of this study come in line with many studies **(14-17, 10).**

Twenty-six patients with CRS partook in a study, and were randomly allocated to either pulsed ultrasound or phonophoresis groups. Treatment protocol for pulsed ultrasound group: Treatment duration: 5 min for each maxillary sinus; Frequency: 1 MHz; Intensity: 1 W/Cm2 for maxillary sinuses; Ultrasound type: Pulsed (ratio: 1:5). Patients in the phonophoresis group were received erythromycin phonophoresis with the same pulsed ultrasound parameters. Treatment sessions: 10 sessions, 3 days per week, every other day. The results EP, compared to the PUS, illustrated significantly higher percent improvement and larger effect size after 10 treatment sessions over 4 weeks. **(14).**

Forty patients with CRS participated in the study ($n$ = 20/group), was treated with erythromycin phonophoresis to both maxillary sinuses. The US parameters described by the authors were ultrasound while using a topical gel containing erythromycin with intensity 1 W/ cm2 for maxillary sinuses, pulsed mode for 4 to 5 minutes, in the placebo group, taken a conventional medical management. The US was applied 3 days per week for one month. The results demonstrated the efficacy of erythromycin phonophoresis on Chronic Rhinosinusitis at 3 days per week for one month compared to placebo group, so Erythromycin phonophoresis has beneficial effects in treatment of CRS. **(15).**

Finally, from the previous discussion of the results and according to the reports of other investigators in similar studies which claimed that low level laser and erythromycin phonophoresis are important in treatment of CRS, however, this study confirmed that Erythromycin phonophoresis is more effective than low level laser in treatment of chronic rhinosinusitis.

The Scientific explanation about the higher efficiency of Erythromycin Phonophoresis in treatment of Chronic Rhinosinusitis may be illustrated as follow, that both ultrasound and Erythromycin have powerful anti-inflammatory and anti-bacterial effects, as ultrasound has beneficial effects in treating inflammation and related signs of inflammation such as pain, moreover, ultrasound is effectively able to kill the bacteria by cavitation in or on the bacterial cells and peroxide generation and improving antibiotic treatment efficacy. Additionally, Erythromycin phonophoresis enhances the breakdown of bacterial biofilms and is clinically effective in CRS treatment, also increases Macrolides that possess anti-inflammatory and immunomodulatory effects, and prevent many different types of infections caused by killing the bacteria through waves, also Erythromycin has a powerful antibiotic effect that slows the growth of or sometimes kill sensitive bacteria by reducing the production of important proteins needed by the bacteria to survive. **(5).**

The study confirmed the importance of LLLT and erythromycin phonophoresis in treatment

of chronic rhinosinusitis without reporting any adverse effects and presents the preliminary evidences for introducing LLLT and erythromycin phonophoresis as an essential part in treatment of chronic rhinosinusitis, however, some limitations must be considered when explaining these results; the most significant drawback of this experiment was absence of long-term effect of the treatment due to the difficulty of following up after the trial, so future trials with patients' follow up are recommended, And also small sample size is one of the study' limitations so further studies with larger sample are recommended, moreover future studies using different modern and diverse modalities should be conducted on chronic rhinosinusitis.

## CONCLUSION:

Low level laser and Erythromycin phonophoresis are important in treatment of chronic rhinosinusitis, however, erythromycin phonophoresis is more effective than low level laser in management of chronic rhinosinusitis.

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