Effect of Combined Neuromuscular Electrical Stimulation and Disease-Modifying Antirheumatic Drug Therapy Versus Disease-Modifying Antirheumatic Drug Therapy Alone on Enhancing Gait and Reducing Fall Risks in Patients with Rheumatoid Arthritis and Peripheral Neuropathy

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ABSTRACT

Background: Rheumatoid Arthritis (RA) with Peripheral Neuropathy (PN) significantly impacts gait and balance, posing challenges in patient management. While Disease-Modifying Antirheumatic Drug (DMARD) therapy is effective for RA, it may not fully address these functional impairments. Neuromuscular Electrical Stimulation (NMES) has been proposed as a complementary therapy to improve these outcomes.

Objective: This study aimed to assess the effectiveness of combining NMES with DMARD therapy versus DMARD therapy alone in enhancing gait and reducing fall risks among RA patients with PN.

Methods: In a randomized controlled trial, 66 RA patients with PN were allocated to either Group A (NMES + DMARD, n=33) or Group B (DMARD only, n=33). Baseline demographics (age, gender, BMI, RA duration) and clinical outcomes (stride length, gait speed, cadence, etc.) were measured. Assessments were conducted at the study’s onset and after an 8-week intervention period, with data analyzed using independent t-tests.

Results: Baseline data revealed no significant differences between the groups. Post-intervention, Group A exhibited marked improvements: stride length reduced to 58.26 cm (± 5.0) compared to Group B’s 69.1 cm (± 5.2, p=0.036), gait speed decreased to 0.77 m/s (± 5.1) against Group B’s 0.94 m/s (± 5.2, p=0.020), and cadence lowered to 81.43 steps/min (± 4.5) versus Group B’s 97.06 steps/min (± 4.7, p=0.029). Significant improvements were also seen in step width, double support time, and balance scales in Group A. However, biochemical markers did not show significant differences post-intervention.

Conclusion: The integration of NMES with DMARD therapy resulted in significant improvements in gait and balance parameters compared to DMARD therapy alone in RA patients with PN. These findings suggest that NMES could be an effective adjunct to DMARDs in managing functional impairments in this population.

Keywords: Rheumatoid Arthritis, Peripheral Neuropathy, Neuromuscular Electrical Stimulation, Disease-Modifying Antirheumatic Drugs, Gait Improvement, Fall Risk Reduction.

INTRODUCTION

The study of the effects of combined Neuromuscular Electrical Stimulation (NMES) and Disease-Modifying Antirheumatic Drug Therapy (DMARD) versus DMARD therapy alone on gait enhancement and fall risk reduction in patients with Rheumatoid Arthritis (RA) and Peripheral Neuropathy (PN) is a significant area of research. This topic intersects various aspects of chronic disease management, rehabilitation, and pharmacotherapy. Rheumatoid arthritis is a chronic inflammatory disorder that primarily affects joints but can also have systemic manifestations. It is characterized by synovial inflammation and hyperplasia, autoantibody production, cartilage and bone destruction, and, ultimately, joint deformity. The disease varies greatly in its progression and
Peripheral Neuropathy in RA patients is a significant complication, typically presenting as a mixed sensorimotor neuropathy. It can result from a variety of mechanisms, including direct nerve compression due to joint deformities, vasculitis, or medication side effects. The presence of PN in RA patients exacerbates disability by impairing sensory and motor function, which can lead to altered gait and an increased risk of falls. Management of RA revolves around the use of DMARDs, including both traditional agents like methotrexate and newer biologic agents. These drugs work by modifying the underlying disease process to reduce inflammation and prevent joint damage. Symptomatic treatment includes the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids.

Management of PN, on the other hand, involves addressing the underlying cause, if known, and symptomatic relief. This may include the use of pain relievers, anti-seizure medications, and capsaicin cream. Additionally, physical therapy plays a crucial role in managing PN, helping to maintain muscle strength and joint function. The novel approach of combining NMES with DMARD therapy for RA patients with PN is based on the premise that electrical stimulation can enhance muscle strength and improve nerve function. NMES involves the use of electrical impulses to stimulate muscle contractions, potentially improving gait and balance, thus reducing the risk of falls. This can be particularly beneficial in RA patients who have muscle weakness or atrophy due to joint inflammation and pain.

A thorough literature review reveals that while there is extensive research on the individual effects of DMARD therapy and physical rehabilitation techniques like NMES, there is a paucity of studies examining the combined effect of these interventions specifically in RA patients with PN. Most studies focus on either pharmacological management or physical therapy independently. The existing literature underscores the importance of comprehensive treatment approaches in RA, emphasizing the need for interventions that not only control disease activity but also address functional impairments and quality of life. However, there is a gap in understanding how combined therapeutic modalities can optimize these outcomes, particularly in the context of RA with concurrent PN.

This research aims to fill the identified gap by comparing the effectiveness of combined NMES and DMARD therapy versus DMARD therapy alone in enhancing gait and reducing fall risks in RA patients with PN. The rationale behind this study is to explore synergistic effects of these interventions, hypothesizing that the combination may yield greater improvements in mobility and safety compared to pharmacotherapy alone. The potential benefits of this research are significant. Improved gait and reduced fall risks can lead to enhanced mobility, independence, and quality of life for RA patients with PN. Additionally, understanding the efficacy of combined treatment approaches can inform clinical practice, leading to more holistic and effective management strategies for this patient population.

MATERIAL AND METHODS

This clinical trial was conducted as a randomized controlled study. Its primary objective was to scrutinize the differential impacts of a combined Neuromuscular Electrical Stimulation (NMES) and Disease-Modifying Antirheumatic Drug (DMARD) therapy against the sole application of DMARD therapy. This investigation specifically targeted patients with Rheumatoid Arthritis (RA) who were also experiencing Peripheral Neuropathy (PN). The study sought to determine if the addition of NMES could significantly enhance gait dynamics and reduce fall risk compared to conventional DMARD treatment alone. Based on a preliminary power analysis, a sample size of 66 (33 in each group) was determined to be sufficient to detect significant differences between the two treatment approaches. A purposive sampling strategy was employed, selecting participants who met the inclusion criteria: adults aged 18-65 years, diagnosed with RA and concurrent PN. This methodological choice was driven by the need to create a participant pool that accurately represented the specific patient demographic under study.

The study enrolled 66 participants, each diagnosed with RA and experiencing symptoms of PN. Exclusion criteria were strictly adhered to, ruling out individuals with conditions like severe cardiovascular diseases, those with pacemakers, or those who had undergone recent surgical procedures. The allocation of participants into two groups – Group A (NMES + DMARD therapy) and Group B (DMARD therapy alone) – was executed using a computer-generated randomization sequence. To maintain the study's integrity, a single-blind design was implemented, where the participants were not informed about their specific group assignments.

Group A (NMES + DMARD): Participants in this group received NMES sessions, each lasting for 30 minutes, thrice a week over an 8-week period. This regimen was in addition to their ongoing standard DMARD therapy. Group B (DMARD Only): This control group continued with their prescribed DMARD therapy, without the addition of NMES.

Data collection was bifurcated into two phases: at baseline and upon completion of the 8-week intervention period. This timeline was meticulously designed to capture the immediate effects of the interventions. The clinical trial meticulously recorded a range of outcome measures to assess the impact of treatments on participants. Demographic data such as age, gender, and the duration of...
Rheumatoid Arthritis (RA) were collected to establish baseline characteristics of the study population. In terms of gait analysis, several key parameters were evaluated: Stride Length, measured in centimeters, to gauge the length of participants’ steps; Gait Speed, recorded in meters per second, to determine walking speed; Cadence, quantified as steps per minute, to understand the rhythm of walking; Step Width, the lateral distance between feet during walking, indicating balance and gait stability; and Double Support Time, represented as a percentage, reflecting the time during which both feet are in contact with the ground, an important aspect of balance. Additionally, to assess balance and fall risk, the study utilized the Berg Balance Scale, ranging from 0 to 56, to evaluate various balance-related tasks, and the Falls Efficacy Scale, scored from 10 to 40, to measure participants’ fear of falling. The Vibration Perception Threshold, measured in Hertz, was also used to assess sensory feedback relevant to balance. Furthermore, the study included an analysis of several biochemical markers indicative of RA activity: C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR) measured in milligrams per liter and millimeters per hour respectively, to evaluate inflammation levels; Rheumatoid Factor (RF) in International Units per milliliter, a specific marker for RA; and Serum Creatine Kinase (CK) in Units per liter, to detect muscle damage or inflammation. These comprehensive outcome measures were integral in evaluating the efficacy of the interventions on both physical function and RA-related biochemical changes. The collected data were analyzed using SPSS software (Version 25). Given the parametric nature of the data, independent t-tests were employed to compare the post-intervention outcomes between the two groups. The level of significance was set at p < 0.05 (18, 19).

Ethical Compliance: The study was conducted in strict adherence to the ethical guidelines outlined in the Declaration of Helsinki. Approval was obtained from the relevant institutional ethics committee, and informed consent was secured from all participants before their inclusion in the study. This comprehensive approach ensured a robust and reliable investigation into the comparative effectiveness of NMES in conjunction with DMARD therapy versus DMARD therapy alone in RA patients with PN. The study’s focus was not only on clinical efficacy but also on the practical implications of these therapies in managing RA and PN symptoms.

RESULTS

The bar graphs provide a succinct comparison of the demographic data between the two groups in the clinical trial. Group A (NMES + DMARD) had an average age of 45 years (± 10), slightly younger than Group B (DMARD Only) at 47 years (± 11). In Group A, 50% of participants were male, compared to 45% in Group B. The Body Mass Index was similar for both groups, with Group A averaging 27.5 (± 3.5) and Group B at 28 (± 4). The average duration of Rheumatoid Arthritis was 7 years (± 2) for Group A and 6.5 years (± 2.5) for Group B, indicating a comparable disease duration between the groups. These numerical values clearly depict the baseline demographics of each group.

![Figure 1 Baseline Demographic Comparison](image-url)
At the outset of the study, baseline measurements were taken for both Group A (NMES + DMARD) and Group B (DMARD Only), revealing no significant differences between the groups across all outcome measures. The stride length in Group A was 72.82 cm (± 3.0) compared to 65.81 cm (± 3.2) in Group B, with a p-value of 0.134, suggesting similarity at the start of the trial. Gait speed also showed no significant difference, with Group A averaging 0.96 m/s (± 0.2) and Group B at 0.89 m/s (± 0.2), p=0.229. Similarly, cadence, measured at 101.79 steps/min (± 2.5) for Group A and 92.44 steps/min (± 2.7) for Group B, resulted in a p-value of 0.525. Other parameters such as Step Width, Double Support Time, and various scales including Berg Balance Scale, Falls Efficacy Scale, and Vibration Perception Threshold, all demonstrated non-significant differences (p-values ranging from 0.078 to 0.833). Even the biochemical markers, including CRP, ESR, RF, and CK levels, were comparable between the two groups, with p-values all exceeding 0.1, indicating a uniform baseline status across the study cohort.

Following the 8-week intervention, notable differences emerged between the two groups. Group A showed a significant reduction in stride length to 58.26 cm (± 5.0), contrasting with Group B’s increase to 69.1 cm (± 5.2), resulting in a p-value of 0.036. Gait speed in Group A decreased to 0.77 m/s (± 5.1), while Group B saw an increase to 0.94 m/s (± 5.2), yielding a significant p-value of 0.020. Cadence in Group A decreased to 81.43 steps/min (± 4.5) compared to an increase in Group B to 97.06 steps/min (± 4.7), with a p-value of 0.029. Step Width also showed significant changes, with Group A reporting 10.79 cm (± 5.1) and Group B 12.25 cm (± 4.6), p=0.020. Double Support Time, Berg Balance Scale, Falls Efficacy Scale, and Vibration Perception Threshold all followed similar patterns, showing significant improvements in Group A compared to Group B (p-values ranging from 0.014 to 0.036). However, the
post-intervention biochemical markers, including CRP, ESR, RF, and CK, displayed less pronounced differences, with only ESR showing a significant change (p=0.018), underscoring the more pronounced effect of the combined NMES and DMARD therapy on physical functional measures rather than biochemical markers in RA patients with PN.

DISCUSSION

The results of this clinical trial provide insightful contributions to the existing body of knowledge regarding the management of Rheumatoid Arthritis (RA) with concurrent Peripheral Neuropathy (PN), particularly focusing on the efficacy of Neuromuscular Electrical Stimulation (NMES) in conjunction with Disease-Modifying Antirheumatic Drug (DMARD) therapy(20).

The trial commenced with no significant baseline differences between the two groups across all measured outcomes, ensuring a level ground for comparative analysis. Post-intervention, Group A (NMES + DMARD) demonstrated notable improvements in gait and balance-related parameters compared to Group B (DMARD only). Specifically, the significant reduction in stride length, gait speed, and cadence in Group A suggests a potential for NMES to enhance controlled and stable movement in RA patients with PN. This finding aligns with previous studies suggesting the benefits of NMES in improving muscular strength and coordination, thereby influencing gait dynamics. The improvements in gait and balance, as evidenced by the changes in the Berg Balance Scale and Falls Efficacy Scale, are particularly noteworthy. These improvements are in line with research indicating that NMES can positively impact muscle activation patterns, which is crucial for maintaining balance and reducing fall risk in patients with RA and PN. The significant changes in the Vibration Perception Threshold also point towards enhanced sensory feedback in patients undergoing NMES therapy, further contributing to improved balance and gait stability(20, 21).

Interestingly, while physical functional measures showed significant improvements in Group A, the biochemical markers (CRP, ESR, RF, CK) did not exhibit a similar pattern. This observation suggests that while NMES combined with DMARD therapy can enhance physical function and reduce fall risks, it may not significantly alter the inflammatory or immunological aspects of RA, as indicated by these markers. This finding is consistent with prior research that has often shown a disconnect between symptomatic improvement and changes in inflammatory markers in RA treatment. The results of this trial have significant implications for clinical practice. The addition of NMES to standard DMARD therapy could be considered a viable strategy to improve gait and reduce fall risk in RA patients with PN. This approach might be particularly beneficial for patients who have limited options due to the severity of their condition or those who have not responded optimally to conventional therapy alone(22, 23).

CONCLUSION

In conclusion, the integration of NMES with standard DMARD therapy presents a promising approach to managing gait instability and fall risks in RA patients with PN. While the physical functional improvements are evident, the lack of significant changes in inflammatory markers highlights the need for a multifaceted treatment approach. This trial contributes to a growing body of evidence that supports the use of combined therapeutic strategies in RA management, emphasizing the importance of personalized and comprehensive care plans for patients.

While the study provides valuable insights, it also presents limitations that should be addressed in future research. The sample size, though adequate for statistical power, could be expanded in subsequent studies for greater generalizability. Furthermore, long-term follow-up would be necessary to understand the sustainability of the observed benefits. Future research should also explore the impact of NMES on the inflammatory markers in a more diverse RA population.

REFERENCES


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