Original article

DOI: 10.5114/areh.2022.121561
Advances in Rehabilitation, 2022, 36(4), 8–16

Neuromuscular exercise with neuromuscular electrical stimulation in knee osteoarthritis: A randomised controlled pilot trial

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A – Research concept and design
B – Collection and/or assembly of data
C – Data analysis and interpretation
D – Writing the article
E – Critical revision of the article
F – Final approval of article

Received: 2022-08-05
Accepted: 2022-11-25
Published: 2022-11-25

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Abstract

Introduction: The present study describes the findings of a randomized controlled trial (RCT) investigating the effects of neuromuscular exercise (NEMEX) with neuromuscular electrical stimulation (NMES) on pain, physical function, balance, range of motion and gait, based on various outcome measures, in patients with knee osteoarthritis (KOA).

Material and methods: A group of 48 subjects with knee osteoarthritis was randomly allocated into four groups (group A: Conventional treatment; group B: NEMEX; group C: NMES; group D: NEMEX in combination with NMES & Conventional) with the following primary outcomes: feasibility, assessment procedure, adherence and acceptability of the intervention. The secondary outcomes were pain, on the visual analog scale (VAS), knee injury osteoarthritis outcome score (KOOS), timed up & go (TUG), range of motion (ROM), community balance & mobility scale (CBM&S) and dynamic gait index (DGI). Feasibility and acceptability were evaluated by number of subjects completed the pre and post-treatment data.

Results: A significant improvement in VAS was noted after six weeks of treatment in group D ($p = 0.0001$) as compared to group A. KOOS sub variables and TUG test were significant at $p = 0.0001$, ROM (R) was significant at $p = 0.01$, ROM (L) significant at $p = 0.11$ and CBM&S, DGI were significant at $p = 0.0001$.

Conclusions: This pilot trial suggests that fully-powered RCT is a feasible approach to investigating the effect of NEMEX with NMES in KOA. NEMEX with NMES may significantly reduce pain and fall risks, and improve ROM, balance and dynamic mobility in patients with KOA.

Keywords: exercise, electric stimulation, joint diseases, proprioception, quadriceps muscle

Introduction

The most prevalent arthropathy is knee osteoarthritis (KOA), a condition that causes pain and decreases the functional level, leading to poor quality of life (QOL) [1–3]. The incidence of KOA results in an increase in economic burden with increasing age and sedentary lifestyle [4]. As such, the prevention and management of KOA is high priority [5]. In India, the overall prevalence of knee OA was found to be 28.7% [6]. The knee is one of the most commonly affected joints, and women (31.6%) are more likely to have OA than men. Patients with KOA present with pain, tenderness, stiffness, loss of flexibility, crepitus and impaired quadriceps function,

and hence impaired balance and gait [7,8]. In addition, the atrophy of the surrounding musculatures results in joint instability and excessive joint movement [9].

The current recommended physical therapy intervention for KOA is based on the use of neuromuscular exercises (NEMEX) focused on functional joint stabilization, alignment, balance and pattern of muscle activation; this approach has the potential to reduce the loads on the knee joint and improve the cartilage in OA [10]. NEMEX is used in both the prevention and rehabilitation in KOA [11,12]. Although few studies have explored the effect of NEMEX on knee joint loading [13−15], one uncontrolled pilot study found that the NEMEX protocol reduces knee adduction moment by up to 14% after eight weeks [16].

It has been proposed that exercise training, along with other physiotherapy measures, decreases cartilage degeneration, inflammation, and prevent loss of the subchondral bone [17]. NEMEX is helpful in improving control of sensorimotor system, joint position sense, balance and functional movement and also reduces the risk of falls in older adults [13]. Quadriceps weakness decreases joint stability, causing joint degeneration with joint pain. Due to the resulting pain and joint stiffness, it is difficult for patients to perform traditional strength training; indeed, traditional resistance exercise is problematic for patients with KOA.

Therefore, studies have examined the potential of Neuromuscular Electrical Stimulation (NMES) to strengthen the quadriceps muscle by initiating involuntary contractions with transcutaneous electrical current. Cases of severe KOA demonstrate deficiencies in voluntary muscle activity, contributing to quadriceps muscle weakness; however, the therapeutic application of NMES has been found to increase muscle strength, decrease muscle atrophy and spasticity in those patients [18].

The main goal of this pilot trial was to evaluate the feasibility of subject recruitment, outcome measures and the acceptability of the intervention. The secondary goal was to acquire sufficient data to calculate the necessary sample size needed to undertake a full randomized controlled trial (RCT).

Materials and methods

The study was performed as a randomized, parallel group, active controlled trial. The Consolidated Standards of Reporting Trials (CONSORT) guidelines for RCT or feasibility trials were followed [19]. The study protocol was approved by the Guru Jambheshwar University of Science & Technology, Hisar, India, Institutional Ethical Committee (IEC) on 29.12.2020, letter no. A.Psy/20/8487. The trial was registered in the Clinical Trial Registry of India (Registration no. CTRI /2021/06/034213).

Subjective pain was measured by the Visual Analogue Scale (VAS) [20], physical function and quality of life by the Knee Injury Osteoarthritis Outcome Score (KOOS) [21], and the Range of Motion (ROM) with a Goniometer [22]. In addition, the study used the Timed Up & Go Test (TUG), Dynamic Gait Index (DGI) [23] and Community Balance & Mobility Scale (CBM&S) [24].

Participants

Eligibility criteria

The study included men and women aged ≥40 years who met the American College of Rheumatology criteria for KOA and Grade II and III KOA according to the Kellgren and Lawrence grading system. The exclusion criteria consisted of the following: a history of inflammatory and infectious conditions of knee joint**,** trauma and surgery around the knee joint**,** any muscular and neurological conditions affecting the lower limbs**,** inability to walk unassisted, current participation in any exercise programme for KOA, any contraindication to electrical stimulation (e.g. epilepsy)**,** presence of any skin disorder around knee**,** any condition or reason restricting the participation in the study**,** unwilling and uncooperative patients or referral for joint replacement.

Outcomes

The primary outcomes of the study were easiness and acceptability of the intervention by the participants. The recruitment rate was assessed on the basis of number of subjects enrolled in the study. The data of total number of participants who completed the pre- and post-intervention was used to estimate the acceptability of the intervention by participants. The following outcomes were considered successful: a 70% subject recruitment rate, 90% of enrolled subjects taking part in the study, 95% of subjects giving their post and follow-up data and 75% completing the study [25]. The secondary outcomes were Visual Analogue Scale for subjective pain (VAS), Knee Injury Osteoarthritis Outcome Score (KOOS), Community Balance & Mobility Scale (CBM&S), Dynamic Gait Index (DGI), Timed up & Go Test (TUG) and Range of Motion (ROM).

Study procedures

Firstly, the participants were asked to mark their level of pain on the 0-10 point VAS scale. Following this, the patient's QOL and level of physical function were assessed by the KOOS tool: a questionnaire comprising five subscales regarding pain, symptoms, sports/recreation, QOL and activity of daily living. After KOOS

assessment, the patient's degree of KROM (knee ROM) in both the right and left leg was assessed by a goniometer. Patient mobility was assessed by the TUG test.

The balance and mobility of the patients was determined using the CBM&S tool. The dynamic balance and fall risks were measured with the DGI questionnaire, in which patients were asked to perform eight tasks. Pain was assessed by VAS. The symptoms, functions in daily living, sports and recreation, and knee-related QOL was measured with the KOOS. KROM was measured with a goniometer, dynamic balance with the TUG test.

All four groups received conventional treatment followed by appropriate interventions. The intervention was performed three times a week for six weeks for all groups. The outcome variables were assessed at baseline, and at the end of six weeks after the intervention. The procedure and dosage for various groups are described in Table 1.

The subjects were selected as per the eligibility criteria and randomly distributed into four groups, A-D, by a computer-generated random number table with 1:1 allocation ratio: Group A received conventional treatment, Group B received NEMEX, Group C NMES, and Group D NEMEX in combination with NMES and conventional treatment. Patient allocation was performed using sealed envelopes. The subjects were not informed about their intervention until they were assigned to their respective groups. Enrolment was performed by the investigator.

The subjects were blinded to the intervention: the intervention was described in the sealed envelopes and not revealed to the subjects. No information related to the intervention was included in the informed consent given by the participants. In total, 48 subjects were included in the study; hence, 12 subjects were allocated to each group, meeting the criterion for minimum sample size in a pilot study [27,28].

Statistical analysis

For statistical analysis, IBM SPSS statistics software 21 was used. Descriptive (Mean ± SD) data was analyzed pre and post intervention. To evaluate the quality of the randomization process, the characteristics of the groups were compared at baseline. The one-way ANOVA test was used to evaluate between-group differences. The data was found to be normally distributed (Kolmogorov-Smirnov test). VAS was analysed using the Kruskal-Wallis Test for the between-group comparison, and the Wilcoxon Signed Ranks Test for the within-group comparison. For KOOS, TUG, ROM, CBM&S and DGI results, the one-way ANOVA was used for between-group analysis; if significant, *post hoc* multiple comparisons were performed using LSD Correction.

Results

In total, 61 subjects were screened based on selection criteria. Of these, 51 (83.60%) were found to be eligible and 48 (94.11%) were ready for participation. The Principle of Intention to Treat analysis was used. One participant dropped out of Group C, and his post-intervention data was obtained. The details of the study are described in the CONSORT flow diagram (Fig. 1.). The baseline data of the groups is presented in Table 2.

Pre- and post-intervention data were used to determine the viability of the outcome measures. As 47 of 48 subjects completed the intervention period (six weeks), fully-powered RCT is feasible. Our findings demonstrate strong acceptability to the intervention. A significant improvement in VAS was noted after six weeks

Tab. 1. Procedure and dosage for various groups

Groups	Intervention
Group A	Conventional treatment that included hot pack, isometric quadriceps exercises, high sitting knee extension, and straight leg raise, 10 repetitions once a day, three times a week for six weeks.
Group B	Forward and backward stepping, sideways exercises (3 sets of 10 repetitions), hip muscle strengthening, standing isometric abduction (2 sets of 5 repetitions), knee muscle strengthening (3 sets of 10 repetitions), step-ups & down (3 sets of 10 repetitions), balance exercise for two minutes three times a week for six weeks [26].
Group C	NMES with the following parameters: pulsed current, asymmetrical, frequency 50 Hz, pulse duration 250 μs, contraction time 10 s, rest time 30 s every 20 minutes; current intensity maximum tolerated by each patient for thrice a week for 6 weeks [15].
Group D	Combination of NEMEX, NMES and conventional treatment three times week for six weeks.

NEMEX – Neuromuscular Exercise, NMES – Neuromuscular Electrical Stimulation

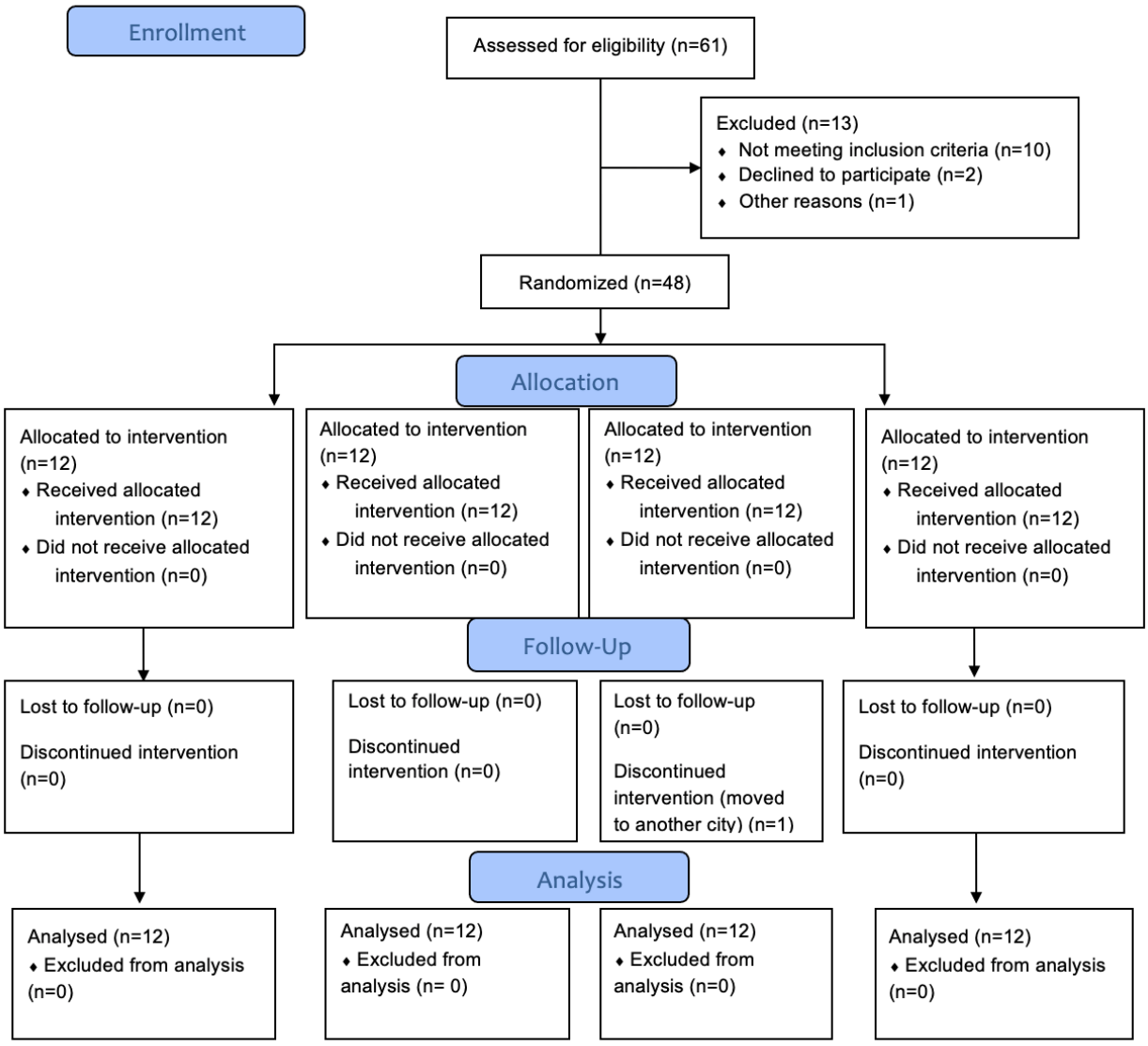

Fig. 1. The CONSORT Flow Diagram

Tab. 2. Baseline characteristics of the participants in the four groups

		Group A (n = 12)	Group B (n = 12)	Group C (n = 12)	Group D (n = 12)
Age	Mean ± SD	52 ± 6.51	55.33 ± 7.01	53.00 ± 8.50	55.17 ± 8.83
Height		154.92 ± 7.91	154.17 ± 8.26	160.08 ± 10.57	156.92 ± 7.40
Weight		72.42 ± 6.13	72.42 ± 5.05	74.00 ± 5.06	70.00 ± 4.18
BMI		30.18 ± 1.38	30.51 ± 1.37	28.99 ± 1.97	28.47 ± 1.25
Gender					
Male	Number	2	2	5	2
Female		10	10	7	10

BMI – body mass index, n – number of subjects in each group, SD – standard deviation.

of treatment in Group D (p = 0.0001) as compared to Group A (Fig. 2.). The between-group analysis for VAS is described in Table 3.

After six weeks of treatment, significant between-group differences were found for the KOOS sub variables and TUG test (p = 0.0001), ROM (R) (p = 0.001), ROM (L) (p = 0.001) and CBM&S and DGI (p = 0.0001) in Group D. Significant differences were found in all variables in Group D compared with Group A after six weeks of intervention. In the within-group comparison, all variables apart from KOOS ADL were found to change significantly in Group A over the six-week intervention. The between-group analysis for all variables is presented in Table 4.

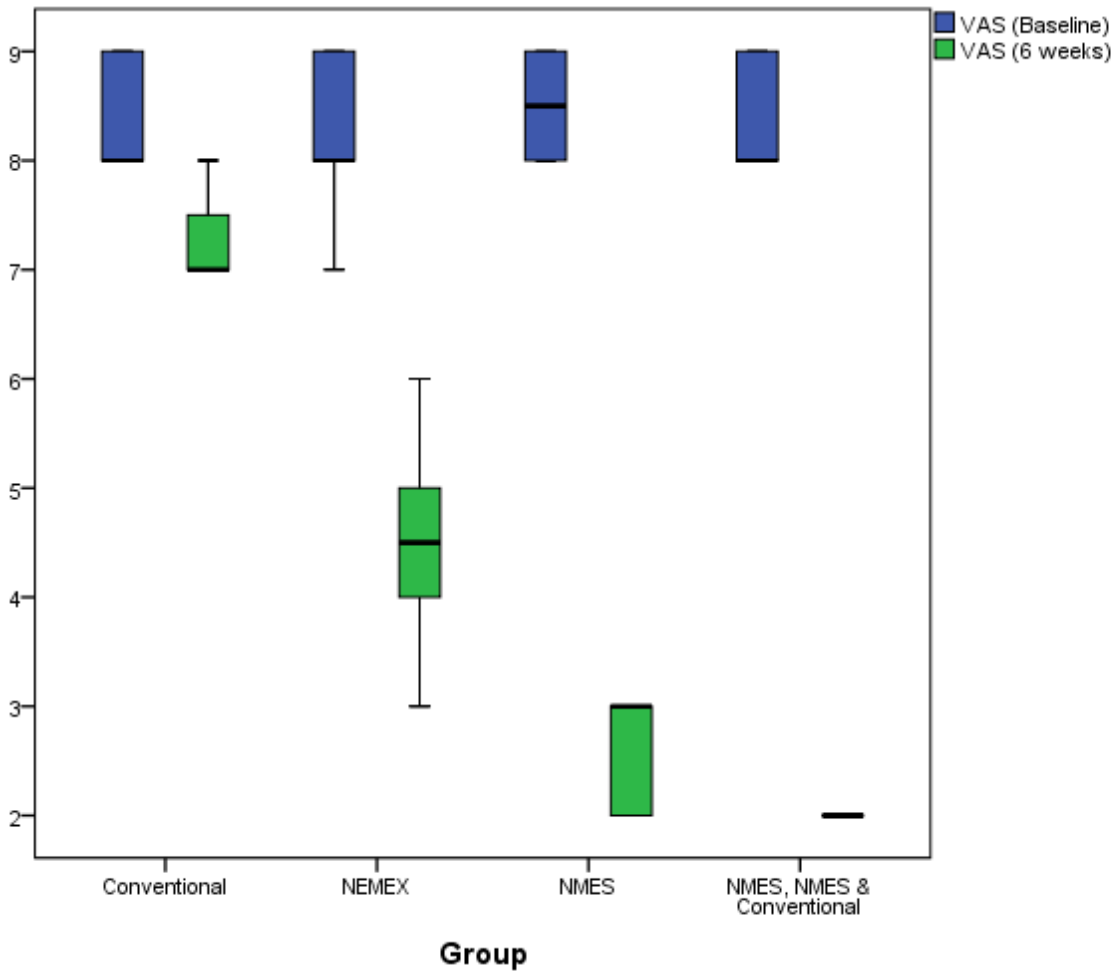

Fig. 2. VAS in various intervention groups at baseline and at 6 weeks

Tab. 3. Between-group analysis for VAS

		Groups				Kruskal-Wallis	p-value
		Group A (n = 12)	Group B (n = 12)	Group C (n = 12)	Group D (n = 12)		
VAS (Baseline)	Median	8.00	8.00	8.50	8.00	1.257	0.739
	Quartile-I	8.00	8.00	8.00	8.00		
	Quartile-III	9.00	9.00	9.00	9.00		
VAS (6 Weeks)	Median	7.00	4.50	3.00	2.00	42.998	0.0001*
	Quartile-I	7.00	4.00	2.00	2.00		
	Quartile-III	7.50	5.00	3.00	2.00		

N – number of subjects in each group, VAS-visual analogue scale, * – statistically significant.

Tab. 4. Shows between group analysis for all variables

Variables	Group A		Group B		Group C		Group D		Between-groups (Baseline)		Between-groups (six weeks)	
	Baseline	Six weeks	Baseline	Six weeks	Baseline	Six weeks	Baseline	Six weeks	F-value	p-value	F-value	p-value
KOOS Pain	39.08 ± 4.10	45.17 ± 5.46	36.25 ± 7.06	58.83 ± 8.18	33.92 ± 8.31	57.42 ± 7.57	41.5 ± 10	64.9 ± 10.02	2.268	0.094	12.924	0.0001**
KOOS symptom	40.67 ± 5.96	34.75 ± 6.30	44.92 ± 5.84	64.25 ± 4.96	43.25 ± 5.40	66.17 ± 4.97	46.67± 6.62	66.5 ± 5.99	2.195	0.102	92.096	0.0001**
KOOS ADL	40.75 ± 3.33	41.67 ± 7.38	42.92 ± 6.52	64.33 ± 5.93	37.83 ± 4.32	58.42 ± 4.06	45.17± 10.24	65.92± 9.51	2.651	0.060	30.054	0.0001**
KOOS Sport/Rec	22.83 ± 3.59	25.83 ± 3.59	26.25 ± 10.82	48.83 ± 13.75	27.00 ± 7.69	51.25 ± 7.42	33.7 ± 13.67	56.8 ± 11.96	2.666	0.059	22.364	0.0001**
KOOS QOL	33.92 ± 9.10	39.17 ± 10.02	36.33 ± 8.92	61.67 ± 7.57	36.42 ± 7.17	62.08 ± 6.40	39.1 ± 8.61	63.6 ± 8.02	0.768	0.518	24.927	0.0001**
TUG	18.27 ± 0.97	13.62 ± 1.21	19.83 ± 2.19	11.11 ± .55	18.38 ± 1.51	14.30 ± 2.08	18.8 ± 2.31	10.9 ± 0.49	1.831	0.155	22.357	0.0001**
ROM (R)	94.80 ± 4.13	97.03 ± 3.82	98.08 ± 7.82	102.8 ± 7.64	99.61 ± 4.86	102.9 ± 4.79	96.4 ± 6.91	107.8 ± 6.94	1.372	0.264	6.480	0.001**
ROM (L)	103.0 ± 2.67	105.3 ± 2.64	105.0 ± 7.94	109.6 ± 7.75	104.6 ± 5.12	107.8 ± 4.87	102.3 ± 8.62	114.1± 8.01	0.462	0.710	4.212	0.011*
CBM&S	28.50 ± 4.72	33.58 ± 4.01	26.58 ± 2.43	50.25 ± 2.70	25.08 ± 4.19	46.17 ± 4.09	29.4 ± 6.22	58.8 ± 6.10	2.146	0.108	68.52	0.0001**
DGI	14.58 ± 1.56	17.67 ± 1.61	14.92 ± 3.00	22.75 ± 0.75	14.92 ± 2.57	17.42 ± 2.64	14.9 ± 1.73	22.8 ± 0.58	0.063	0.979	42.05	0.0001**

CBM&S – Community Balance & Mobility Scale, DGI – Dynamic Gait Index, KOOS – Knee Injury Osteoarthritis Outcome Score, KOOS ADL – Knee Injury Osteoarthritis Outcome Score Activity of Daily Living, KOOS sports/rec – Knee Injury Osteoarthritis Outcome Score sports and recreation, KOOS QOL – Knee Injury Osteoarthritis Outcome Score Quality of life, ROM (L, R) – Range of motion (Left & Right), TUG – Timed Up & Go test, *statistically significant at 0.05; **statistically significant at 0.001.

Post hoc multiple comparisons for all five KOOS sub variables (pain, symptoms, ADL, sports/recreation and QOL), TUG, ROM (R, L) CBM&S and DGI in Group D showed significant improvement as compared to Group A: MD = –19.75000 (p = 0.0001), MD = – 31.75000 (p = 0.001), MD = – 24.25000 (p = 0.0001), MD = –31.00000 (p = 0.0001), MD = –24.50000 (p = 0.0001), MD = 2.68833 (p = 0.0001), MD = –10.77500 (p = 0.0001), MD = –8.74167 (p = 0.0001), MD = – 25.25000 (p = 0.0001), MD = –5.16667 (p = 0.0001), respectively.

Discussion

The present study is the first to compare the effect of two different interventions, NEMEX and NMES, with different mechanisms of action on pain, function, balance, fall risks and mobility skills, in treating KOA. Our findings support the performance of future RCTs assessing the effect of NEMEX and NMES, both alone and in combination, on knee osteoarthritis. The recruitment rate of the present study was 94.11%; therefore, a full-powered RCT is feasible. A 100% retention rate was achieved. In addition, 97.91% of participants completed all 18 sessions of treatment, which is a successful adherence rate. Our findings confirm that the combination of NEMEX with NMES results in an improvement of KROM, dynamic balance, mobility and reduction in pain and fall risks. All outcome variables were improved after six weeks of treatment.

Patients with KOA experience loss of proprioception, which may affect postural stability and risk of fall. Quadriceps femoris muscle (QFM) weakness decreases joint stabilization and shock absorption, hastening the progression of osteoarthritic changes. There is scarcity of literature on the feasibility and advantages of NEMEX in patients with KOA. The only study to investigate the effect of NEMEX in early stage KOA found it to be beneficial in improving knee adduction moment, with a 14 % increase in leg raising noted; however, the study only included a small number of patients [16].

Providing exercises and hot packs prior to intervention have a modest effect on the joints by reducing pain in patients with KOA; in addition, electrical stimulation can induce 10–30% more contraction in both healthy and weak muscles compared to exercises [29]. Exercises can also improve the joint proprioceptive mechanism,

leading to increased joint excursion and enhanced ROM by inhibiting pain through constant firing of A-beta fibres.

A 2021 study found that combining strength training with NEMEX has an additional effect on pain in patients with KOA [29]. NEMEX increases the proteoglycan content of the cartilage immediately after the exercise intervention, which increases its ability to withstand load [30]. Previous findings indicate that the combination of NEMEX with an educational programme yielded significantly greater pain-relieving effects with regard to mean knee pain (VAS) and during function after 12 weeks of exercise [31].

Exercise may exert its pain relief effects by the use of central gating mechanisms, neuroimmune mechanisms and peripheral mechanisms through increased cell density locally at sites with tissue [32]. Exercise is considered a first-line treatment modality for KOA, and can ameliorate pain following acute bouts of exercise, as well as during long-term programmes [33].

Our present findings demonstrate that Group C demonstrated a significant improvement in all variables, *viz.* KOOS sub variables with TUG, ROM (R, L), CBM&S and DGI, compared to Group A. These results are in line with those of previous studies and suggest that exercise is beneficial in patients with knee OA [31,34]. In young and middle-aged people with knee injuries and people who are at high risk of knee OA, NEMEX training programs have been found to be effective in improving function and reducing symptoms [35].

NEMEX treatment has also yielded positive results in physical function in patients waiting for total joint replacement. Neuromuscular Exercises are performed in a closed kinetic manner, which increases compressive forces and muscular co activation, which ultimately improves joint congruency by unloading the ligaments of the knee joint; this is helpful in maintaining knee joint stability [36]. NEMEX seemed helpful in improving function and reducing pain in patients with KOA. A preoperative neuromuscular exercise programme improves activities of daily living and reduces pain in patients receiving total joint replacement at six weeks postoperatively [37].

NMES is an emerging method for strengthening muscles based on causing involuntary contractions in the muscles with electrical impulses. Previous studies have found NMES to have beneficial effects in the management of knee OA and in the rehabilitation of knee arthroplasties, as well as during the pre-rehabilitation period [38]. Previous studies have suggested that NMES treatment may increase quadriceps femoris strength in patients with KOA. Applying the NMES to the quadriceps muscle can increase the modulation of pain and self-reported functional ability in patients with knee OA [39]. A previous study with 63 patients found that NMES appears to play an important role in improving quadriceps muscle strength and reduces pain in patients with KOA [40].

NMES targets and selectively increases recruitment of type II muscle fibres, which helps increasing the strength and oxidative capacity of thigh muscles in patients with knee osteoarthritis. A study based on NMES using alternative biphasic waves with a frequency of 75–85 Hz found 20-day treatment to result in an increase in muscle strength; the cohort comprised 16 healthy women aged between 21 to 45 years on the QFM [41].

The present trial has significant clinical and practical implications. Worldwide, around 10% of men and 18% of women aged 60 years and over are living with OA, 80% experience restricted movement, and 25% are unable to do household works. NEMEX has been found to help improve self-reported activities of daily living, pain and physical function in the senior population. It decreases drug dependency, which in turn, prevents associated complications. A previous study concluded that NEMEX is much at reducing pain, knee joint loading and improving function in patients with mild or moderate KOA compared to treatment with analgesic and anti-inflammatory drugs [42]. Therapeutic strengthening and neuromuscular exercises are effective at improving pain scores and function in patients with KOA [43]. This suggests that neuromuscular exercises effectively reduce pain and improve function in patients with knee osteoarthritis by specifically targeting sensorimotor deficits.

The high retention and low drop–out rates in the present study suggest that the intervention is satisfactory and well accepted in managing KOA. The strength of the present study is that unlike previous studies, it combines two different interventions with different mechanisms of action for treating KOA. The combination of NEMEX and NMES can have synergic effects in reducing pain and improving strength and physical function in patients with knee osteoarthritis. In addition, any intake of medications was monitored to avoid any bias that could influence the results of the study. Furthermore, the retention rate was 100% and adherence rate 97.91%.

However, two limitations of the study were its small sample size and the fact that the no long-term follow-up was performed.

Conclusion

The findings of this pilot trial suggest that a full-powered RCT evaluating the effects of NEMEX and NMES in the treatment of KOA is feasible. Our findings also indicate that the combination of NEMEX

with NMES may significantly reduce pain and fall risks, and improve KROM, balance and dynamic mobility in patients with KOA. In addition, administering either of the two interventions randomly in any of the study groups resulted in improved outcome measures.

Funding
This research received no external funding.

Conflicts of Interest
The authors have no conflict of interest to declare.

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