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Effect of Class IV HILTon Pain and Inflammation Among Individuals with Knee Osteoarthritis: A Randomised Placebo Controlled Trial

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Abstract

Background: *Knee osteoarthritis (KOA) is a chronic condition involving the entire joint by the gradual breakdown of cartilage and persistent pain, inflammation significantly contributes to joint dysfunction. Class IV High-Intensity Laser Therapy (HILT) utilizes focused light energy to reduce inflammation and stimulate cellular repair. An exploration is required on therapeutics to alleviate the above problems.*

Aim: *This study aimed to evaluate the impact of Class IV HILT on pain and inflammation in patients with knee osteoarthritis.*

Methods: *This study implemented a double-blinded, randomized, placebo-controlled trial design. 70 participants aged 40–55 with KOA were randomly assigned to either the experimental group (n = 35) or the control group (n = 35). The experimental group received Class IV HILT (10 W, 300 J & 5 W, 3000 J), hot pack, exercises, and knee brace. The control group received a placebo treatment while undergoing the same adjunct therapies. Pain and inflammation were evaluated using the Numeric Pain Rating Scale (NPRS) and C- reactive protein (CRP) levels, measured at baseline and after 10 weeks.*

Results: *Wilcoxon signed-rank test and the Mann–Whitney U test were used for analysis of pain (NPRS score). Student t-test was utilized for CRP levels. There was a significant decrease in NPRS score (mean1.54±0.92), (p=0.0001) and CRP levels (mean 3.83 ± 0.96), (p=0.0001) in the experimental group.*

Conclusion:*Class IV LASER treatment has been found satisfactory in mitigating pain and inflammation, making it a better choice of treatment method for KOA.*

Keywords:*Knee Osteoarthritis, Pain, Inflammation, Class IV Laser*

INTRODUCTION

Osteoarthritis (OA) is a degenerative musculoskeletal condition[1] that predominantly affects weight-bearing joints, with the knee being the most commonly involved, particularly in aging individuals [2, 3, 4]. The most prevalent risk factors for knee osteoarthritis (KOA) include obesity, prior joint trauma, female gender, and increasing age [5].Clinically, KOA is associated with pain, muscle weakness, leading to difficulties in performing daily routine and a decline in overall quality of life [6].By 2020, OA was anticipated to become the fourth leading cause of disability worldwide. According to the latest WHO bulletin, 10 million people in developed countries and 33.5 million in lower-income nations experience moderate to severe disabilities due to OA, emphasizing its substantial medical and socioeconomic burden [7].

Radiographic imaging is commonly used to evaluate the progression and severity of KOA. However, in the early stages, radiographic changes may not be pronounced, making biochemical serum markers an important tool for early diagnosis, monitoring treatment effectiveness, and slowing disease progression. Research indicates that local inflammation contributes to KOA development [8-9].Systemic inflammatory markers are frequently analyzed in KOA research to investigate their potential role in disease progression.

Previously, these markers were thought to be elevated only in inflammatory arthritis, but recent studies indicate that patients with OA may also have mildly elevated bioinflammatory markers. This suggests that inflammation, albeit at a lower level compared to autoimmune conditions, may contribute to OA pathophysiology [5-10].

KOA management involves both pharmacological and non-pharmacological approaches, aiming to relieve pain, preserve physical fitness, and enhance daily activities. Non-pharmacological treatments include patient education and physiotherapeutic interventions such as electrotherapy, low-level laser therapy (LLLT), and exercises, all of which help reduce pain and improve muscle strength [11].

Class IV High-Intensity Laser Therapy (HILT) has been introduced for musculoskeletal disorders and has demonstrated promising outcomes in KOA treatment. Studies have shown that HILT effectively alleviates pain, enhances range of motion, and improves functional performance compared to conventional treatments. Additionally, research suggests that HILT outperforms LLLT in KOA management, likely due to its higher power output, which allows for deeper tissue penetration and rapid energy delivery [12]. However, while its effects on pain and function are well established, there is limited evidence regarding its influence on inflammatory markers.

This research evaluates the outcomes of Class IV HILT on pain and inflammation in individuals with KOA.

METHODS

A double-blinded, parallel group, placebo randomized controlled trial was conducted to examine the efficiency of Class IV HILT versus a placebo laser and conventional therapy. The protocol adhered to SPIRIT guidelines (Standard Protocol Items: Recommendations for Interventional Trials) and complied with the ethical principles outlined in the 2013 revised Declaration of Helsinki and regulations for Biomedical Research Involving Human Participants. The ethical approval was received from the Amity University Ethical Committee with the IEC no. AUUP/IEC/2021-JAN/12 and study is registered in CTRI under reference number CTRI/2021/12/038646. Patients received verbal and written information on the therapy course and preventive measures as per the guidelines set forth by the Ethics Committee. This study was carried out at Jindal Physiocare's outpatient department, under Amity University. This intervention spanned a total of 10 weeks. Both patient and the assessor were blinded for the study.

Using G*Power version 3.1.9.7, a sample size of 46 participants was determined based on an effect size (d) of 0.85, an alpha level (α) of 0.05, and a statistical power ($1-\beta$) of 0.80. To ensure robust results and compensate for an anticipated 30% dropout rate, the sample size was adjusted to 70 [13].

The inclusion criteria comprised diagnosed cases of KOA with Kellgren & Lawrence radiographic stages 2-3, including any compartment, which might be the patellofemoral, medial femorotibial, lateral femorotibial, or all three, with the age between 40 – 55 yrs.

Exclusion criteria were as follows: Patients with a history of knee surgery, any implants around the knee, an infection, cancer, or tumor, or any of these conditions, injuries to the knee, any history of autoimmunity history of using non steroidal anti-inflammatory drugs (NSAIDs) for the same ailment, history of receiving an intra-articular steroid injection within the last three months, history of any uncontrolled cardiovascular or metabolic diseases and any tattoos in the region being treated, Genuvarum/valgum

After accomplishing the inclusion criteria, subjects were randomly distributed in two groups using on on-site computer system sampling method (35 in each group).

Intervention

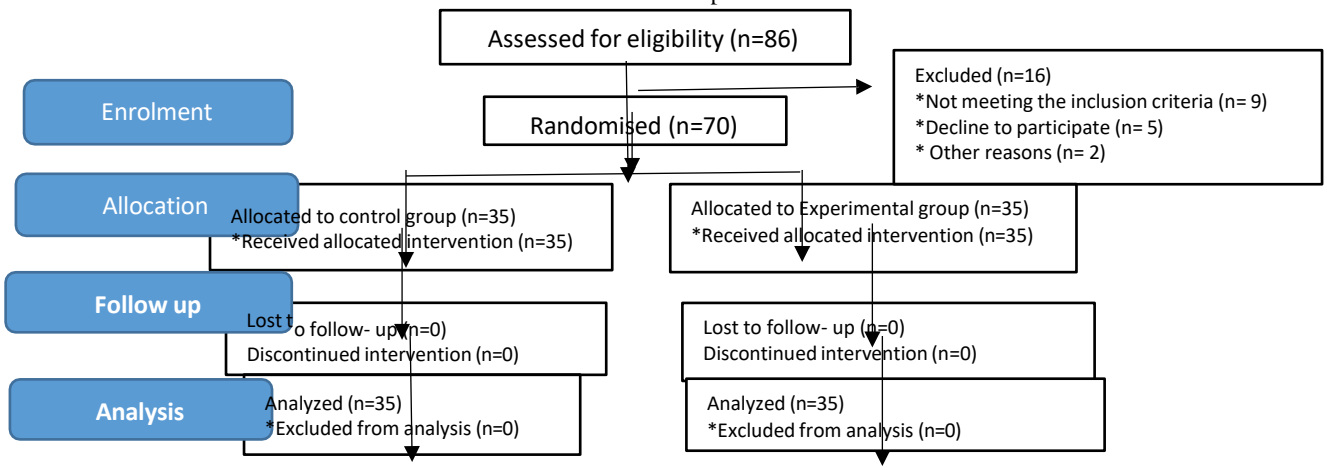
Upon receiving informed consent, participants' demographic details, including age, weight, height, and Body Mass Index (BMI), were documented. Experimental group received BTL-6000 Class IV HILT was applied to the mediolateral and posterior knee regions using an analgesic mode of 10 Watts, 300 J for the mediolateral knee and a bio-stimulation mode of 5 Watts, 3000 J for the posterior knee, with a total laser application time of 14 minutes. In the control group, the Class IV HILT probe was applied for the same time with the intensity turned off, serving as a placebo.

Both groups received conventional therapy as follows: a hot pack applied around the affected knee joint (Temp 40°C) for 10 minutes, followed by a structured exercise program. The exercise regimen consisted of calf and hamstring stretching (three repetitions with a 30-second hold and a 30-second rest), isometric quadriceps and static hamstring exercises (10 repetitions with a 5-second hold and a 5-second rest), straight leg raises, leg raises in side-lying and prone positions (10 repetitions each), as well as bridging,

heel slides, and ankle-toe movements (10 repetitions each). The total duration of one session was 50 min. The intervention was administered three times per week (on alternate days) for 10 weeks in both groups.

Outcome variables

Outcome variables were inflammatory marker C- reactive protein (CRP) value and pain. The Numeric Pain Rating Scale (NPRS) [14] was used to evaluate pain intensity, with scores ranging from 0 (no pain) to 10 (worst possible pain). For the inflammatory marker CRP, patient was asked to give blood sample at the assigned lab National Accreditation Board for Testing & Calibration Laboratories (NABL-accredited). These were assessed before and after the treatment protocol.



CONSORT FLOW CHART

Statistical analysis was conducted using SPSS Statistics Version 23. The Shapiro–Wilk test assessed the normality of the two outcome measures. Given the presence of both normal and non-normal data distributions, parametric and nonparametric statistical tests were applied accordingly. The Wilcoxon signed-rank test was used for within-group comparisons, while the Mann–Whitney U test evaluated between-group differences in NPRS scores. CRP levels were analysed using an independent Student's t-test. A p-value of <0.05 was considered statistically significant.

RESULTS

70 individuals with KOA (24 males, 46 females) participated in the study. Their ages ranged from 40 to 55 years, with a mean ± SD of 46.80 ± 5.09 years. The average weight was 76.15 ± 11.74 kg, height was 166.82 ± 8.28 cm, and the mean BMI was 27.27 ± 2.91 kg/m2.

Both groups demonstrated a significant post-treatment reduction in NPRS scores (p = 0.0001). However, the Class IV HILT group exhibited a more notable decrease in pain levels compared to the control group. Between-group analysis further confirmed a statistically significant difference favouring Class IV HILT, with a mean reduction of 1.54 ± 0.92 (Tables 1 & 2).

Regarding the secondary outcome, inflammatory marker levels (CRP) significantly decreased in both groups by the study's conclusion, with a more substantial reduction observed in the Class IV HILT group (mean reduction: 3.83 ± 0.96, p < 0.0001). Additionally, between-group comparisons showed a further statistically significant improvement in the experimental group (Tables 3 & 4).

Table 1 shows the within-group analysis of NPRS score before and after the study duration.

Pain (NPRS score)		Group					
		Control	Wilcoxon Signed Ranks (z)	p-value	Experiment	Wilcoxon Signed Ranks (z)	p-value
Pre	N	35	5.203	.0001	35	5.192	.0001
	Mean	7.86			7.91		
	SD	.88			.95		
	Median	8.00			8.00		
	Quartile-I	7.00			7.00		

	Quartile-III	9.00			9.00		
Post	Valid N	35			35		
	Mean	3.77			1.54		
	Standard Deviation	1.11			.92		
	Median	4.00			1.00		
	Percentile 25	3.00			1.00		
	Percentile 75	5.00			2.00		
N= Number of participants, WSR= Wilcoxon signed rank, SD=Standard deviation, and NPRS= Numeric pain rating scale							

Table 2 shows between the group analyses of the NPRS score before and after study duration.

Pain (NPRS score)		Group		Mann-Whitney U (z)	p-value
		Control	Experiment		
Pre	N	35	35	.359	.720
	Mean	7.86	7.91		
	SD	.88	.95		
	Median	8.00	8.00		
	Quartile-I	7.00	7.00		
	Quartile-III	9.00	9.00		
Post	Valid N	35	35	6.268	.0001
	Mean	3.77	1.54		
	SD	1.11	.92		
	Median	4.00	1.00		
	Percentile 25	3.00	1.00		
	Percentile 75	5.00	2.00		
N= Number of participants, SD=Standard deviation, and NPRS= Numeric pain rating scale					

Table 3 shows within-group analyses of CRP levels among both groups.

CRP level	Group									
	Control					**Experiment**				
	N	Mean	SD	t-value	p-value	N	Mean	SD	t-value	p-value
Pre-Treatment	35	5.60	1.18	11.151	0.0001	35	6.29	1.67	8.729	0.0001
Post Treatment	35	4.81	0.98			35	3.83	0.96		
N= Number of participants, SD=Standard deviation, and CRP= C-reactive protein										

Table 4 shows between-group analyses of CRP level among both groups

CRP level	Group						t-value	p-value
	Control			**Experiment**				
	N	Mean	SD	N	Mean	SD		
Pre-Treatment	35	5.60	1.18	35	6.29	1.67	1.983	0.051
Post Treatment	35	4.81	0.98	35	3.83	0.96	4.211	0.0001
N= Number of participants, SD=Standard deviation, and CRP= C-reactive protein								

DISCUSSION

This study explored the therapeutic effects of Class IV HILT on inflammatory pain. We found its effectiveness on reducing inflammation and easing pain, confirmed by changes in inflammatory markers. Considering its effectiveness Class IV HILT has emerged as the modern and reliable treatment modality for clinicians.

The placebo intervention involved a simulated application of Class IV HILT, replicating all procedural elements without delivering actual laser energy. This approach ensured that participants perceived the intervention as authentic, thereby maintaining the integrity of the blinding process. Consequently, participants were unable to self-evaluate treatment efficacy and prognosis, effectively minimizing expectancy effects and psychological bias.

The analgesic effects of Class IV HILT are attributed to several mechanisms. Firstly, Class IV HILT modulates pain by promoting the release of beta-endorphins and serotonin at peripheral nociceptors. These opioids bind to nociceptors, blocking external noxious stimuli and diminishing pain perception. Secondly, Class IV HILT also interferes with pain signal transmission by decreasing ATP synthesis, restricting calcium influx into dorsal root ganglion neurons, and enhancing intracellular reactive oxygen species levels, which disrupts pain action potential propagation [15, 16, 17].

The pain-relieving effects of Class IV HILT are further supported by the gate control theory and its impact on nerve fiber regeneration. Through its photochemical and photothermal mechanisms, it enhances blood flow, stimulates cellular metabolism, encourages Schwann cell proliferation, and facilitates nerve fiber rejuvenation [17].Class IV laser therapy, when applied with a longer wavelength over an extended period, delivers a higher therapeutic dosage to the tissue, effectively stimulating cellular activity [18]. This process enhances tissue healing, supports sustained recovery, and helps maintain the achieved tissue repair by improving circulation and reducing inflammation.

Class IV HILT not only alleviates pain but also plays a role in reducing inflammation. Beyond its analgesic and anti-inflammatory effects, Class IV HILT enhances bio-stimulation in KOA, supporting tissue healing and regeneration. Alayat et al. (2017) examined the effects of Class IV HILT and reported an improvement in synovial thickness [19]. Similarly, Alkatan et al. (2021) found a notable increase in cartilage resurgence in the knee joint with high-intensity laser therapy [20]. These findings support that HILT may help mitigate intraarticular cartilage loss, a key pathological feature of knee OA. This can be achieved when inflammation is reduced at the tissue level [21]. Prolonged application of a Class IV laser with a wavelength exceeding 1000 nm results in the delivery of a higher therapeutic dosage to the target tissue. This increased energy density can effectively stimulate cellular activity, thereby contributing to pain reduction and decreased inflammation. This approach may enhance the quality of life for individuals with KOA by delaying the degenerative process.

In contrast, several studies have shown no effect of LLLT in KOA, particularly when using a diode laser with 50 mW power output [22, 23, 25]. This underscores the importance of considering both power output and wavelength when selecting laser therapy as a treatment option. In the current study, a semiconductive neodymium Class IV laser with 1064 nm wavelength and 12 W power was used. This high-power laser provides deeper penetration, making it more effective for reducing inflammatory marker values and alleviating pain

[13, 19]. There is a notable gap in the literature regarding the role of Class IV HILT in modulating inflammatory markers.

Despite these encouraging results, the limitations of current research must be acknowledged. A wider age range and inclusion of Grade 4 OA patients could improve the applicability of findings. Moreover, assessing proinflammatory markers such as IL-6, IL-1β, and TNF in synovial fluid and membrane changes may offer valuable insights into HILT's biological effects [21, 24]. Long-term safety and efficacy remain key concerns, necessitating larger randomized controlled trials (RCTs) with extended follow-up. Additionally, comparative studies with established OA treatments could further clarify HILT's effectiveness and its potential as a primary treatment option.

This study provides strong evidence supporting the efficacy of Class IV High-Intensity Laser Therapy HILT in controlling inflammatory pain associated with KOA. Its therapeutic benefits stem from its ability to modulate inflammatory markers, alleviate pain, and promote tissue regeneration. Class IV HILT emerges as a compelling treatment option for clinicians. The findings corroborate existing research, highlighting its potential to address key pathological features of OA, including cartilage degradation. Nevertheless, further investigation is required, particularly through large-scale RCTs with extended follow-up periods, to confirm its long-term safety, efficacy, and comparative effectiveness against traditional treatments. With continued research, Class IV HILT could well become an integral part of

OA management protocols; also its further effect on other joints and related musculoskeletal conditions can be studied.

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