



Knee Osteoarthritis: Pharmacological & Therapeutic Management

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ABSTRACT

Osteoarthritis (OA) is the most common degenerative joint disorder and is linked with a high load of personal as well as socio-demographic. The objectives of this review article are to focus the current treatment for knee osteoarthritis. Although there is no any permanent treatment that prevent cartilage deterioration and prevent final joint replacement in the advanced disease stage. The present review was prepared according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines (figure 5). Randomized controlled trials (RCT) were searched in PubMed, Google scholar, Springer link and PEDro databases using key words like- Knee Osteoarthritis, Advancement & Physiotherapy management. We included past 10 years' RCT articles published in the English language only from 2011 to 2020. This research was carried out from February 2021 to June 2021. Articles were examined, 100 articles were chosen based on the inclusion and exclusion criteria using the keywords Knee pain, Knee Osteoarthritis. Advancement & Physiotherapy management. Out of 100 studies, 85 studies were selected according to eligibility criteria. 15 studies were rejected as they were found in more than one database. Further 25 articles were rejected because either they were not in full text, objectives not available, there was no control group or they didn't meet the exclusion and inclusion criteria. Finally, 15 articles were included in the collection

Keywords: Osteoarthritis, Physiotherapy, Inflammation, Cartilage, Pain

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INTRODUCTION

Osteoarthritis is defined as a progressive deterioration of an articular cartilage, bone erosion and synovitis. Typically, it is a persistent deteriorating joint disease in older adults, although it can be seen in young people also. At the age 45, greater risk of developing osteoarthritis advances [1]. According to recent studies, based on radiographic evidence about 80% of older adults aged 55 years and older have osteoarthritis. It is estimated that 60% of these older adults experience symptoms. Post-menopausal women have a highest rate of occurrence of knee osteoarthritis as compared to men [2].

Etiology

The cause of this disorder is idiopathic. The most common risk factors for osteoarthritis such as: older age, obesity, joint injuries, repeated stress on the joint, bone deformities and hypermobility.

Epidemiology

According to recent studies, it is obvious that asymptomatic knee OA has higher prevalence rate as it is estimated that 250 million individuals worldwide suffer with OA. 60 years of age or older women are most commonly affected as compared to men. According to global burden of disease 2015, about 85% of the burden of Knee osteoarthritis in the world, ultimately this will make most frequent cause of years of

life lived in less than full health [3].

Mechanism of Osteoarthritis Pain

According to large number of observational studies from investigative procedures such as magnetic resonance imaging concluded that osteoarthritic pain is due to mainly structural changes such as presence of Subchondral cyst like lesions (BMLs) and inflammation of the synovial membrane. According to recent studies, Synovitis, which is a common finding & can be seen in initial phase of the disease. Synovitis is correlated with severity of osteoarthritis. In OA, Multiple inflammatory mediators including plasma proteins (C-reactive protein) , prostaglandins, leukotrienes, cytokines & growth factors, nitric oxide and complement components seen in synovial fluid . These components can produce matrix metalloproteinases and other hydrolytic enzymes (including cyclooxygenase two and prostaglandin E) to prevent cartilage degradation. On the contrary, some evidences suggested that changes in neural networking results in knee OA pain.[4]

Structural Changes in OA

Deterioration in articular cartilage is the hallmark sign of knee OA which is commonly seen in X-Rays as a joint space narrowing. Loss of cartilage and joint derangement lead to bone spurs (abnormal bone structure) and bony changes in the earliest stages of osteoarthritis with bone marrow lesions (BMLs) seen in MRI imaging technique.[5]

Nociception With in the Joint

Free nerve endings or nociceptors are also affected as these are extensively distributed in the skin, muscles and joints. Although Cartilage is avascular as it has no nerve supply. On that account, it is not a primary source of mild & moderate OA pain. The Degranulation of bony and cartilaginous debris by cells lining the synovial membrane activate inflammation and pain from synovitis.

a) Bone Marrow Lesions

80% of individuals are having symptomatic OA as observed by MRI imaging technique. According to histopathological examination, subchondral bone marrow lesions are characterised by steatonecrosis , myelofibrosis and trabecular microfractures

b) Synovitis

On arthroscopic examination, 50% of patients have painful knees due to synovitis as observed by using MRI. Those patients were also reported who did not have any radiographic imaging technique, although it was noted that they had extensive inflammation of synovial membrane lead to knee pain. Supportive evidences suggested that OA pain is due to inflammation in synovial membrane is still unclear, but some theories reported that the inflammatory mediators that trigger sensory nerves, or by any nociceptors become sensitized to mechanical stimulation by synovial membrane inflammation may stimulate OA pain.[6]

Signs/Symptoms & Radiological investigations

The patients suffering from osteoarthritis exhibit various signs and symptoms that are being explained in figure 1 according to American College of Rheumatology [7] and various radiological investigations [8] being carried out for the diagnosis of same are summarized in figure.



Figure 1: Signs & Symptoms of Knee osteoarthritis [6]

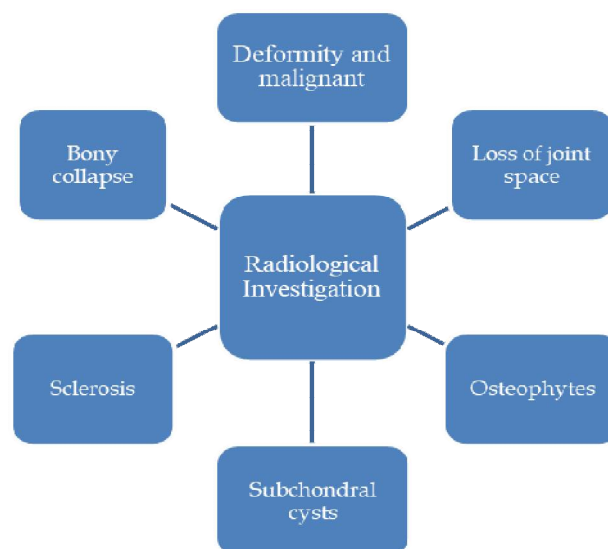


Figure 2: Features of Radiological Investigation [7]

Management of Knee OA [9]

Current treatment of knee OA focus on symptomatic treatment and in severe cases, surgical procedure is preferred. Different guidelines given by academicians and professionals proposed suitable treatment strategies and are explained in Table 1.

Table 1: Societies Recommendations about Osteoarthritis :

TREATMENT	OARSI	ACR	AAOS
Exercise	Suitable	Definite	Definite
Transcutaneous Electrical nerve stimulation	Unknown	Restricted	Indefinite
Weight management	Suitable	Clearly	Limited
Chondroitin or Glucosamine	Not Recommended uncertain	Approved against apply	Approved against apply
Duloxetine	Appropriate	No recommendation	No recommendation
Oral & Topical NSAIDS	Without comorbidities, appropriate with comorbidities, not appropriate	Conditional Recommendation	Strong recommendation
Intra-articular corticosteroids	Suitable	Dependent or Limited suggestion	Indefinite
Intra-articular Visco supplementation	Undetermined	Inappropriate	Suggested against apply

Table 2: Methodological classification assessed by physiotherapy evidence database scale

Criteria	Liao et al	Scharf et al	Usma n et al	Dantal et al	Wagec k et al	Arslal et al	Eftekh ar sadat et al	Nazar i et al	Odol e et al	Fukud a et al	Cost a et al	Nejati et al	Marc elo et al	Mansm ann et al	Palm er et al	Cumulative score
Random allocation?	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	14/15
Concealed allocation?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15/15
Baseline comparability?	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	12/15
Blind participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15/15
Blind therapist?	Yes	Yes	No	No	No	No	No	No	No	Yes	No	No	Yes	No	No	4/15
Blind assessors?	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	0/15
Follow-up?	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	10/15
Intention - to - treat analysis?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15/15
Group comparisons?	No	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	10/15
Point and variability measures?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15/15
Cumulative score	8	9	6	8	8	5	8	6	5	8	9	6	7	9	8	7.3

Table 3: Description of the included studies

Author/year	Study design	Subject/age	Interventions	Study duration	Outcome measures	Result
Liao et al[10]	LLLT , a non-invasive substitutive therapy with RDBMS	n=33 >50 years Gender not reported	Expermental group A active laser treatment ALT(n=16) Group B:- Placebo laser treatment PLT (n=17)	4 weeks (3 times per week)	VAS, PPT and Lequesne index were used.	Statistically significant reduction in the Lequesne index, conscious 4 weeks after treatment and the exercise and increase was noted in PPT in ALT group compared with PLT group.
Usman et al[11]	RCT	n=60 Gender and age not reported	Participants in the combination group w with re treated with continuous US and IFC at the tactile threshold intensity on painful knee area.	12 weeks	The VAS , WOMAC & Short Form Health Survey Questionnaire	Combination therapy group had significant effects as decrease in pain and improvement in functional level and well being as compared to the IRG.
Lucas Ogura Dantas et al[12]	RCT	n=188 Age between 40 & 75 years Gender not reported	Cryotherapy in the form of ice pack was given to 3 experimental groups. The control group received the identical therapy as the experimental group, but with sand-filled sham packs.	4 consecutive days (once a day)	VAS & WOMAC	In persons with knee OA, short-term cryotherapy had no effect on pain or quality of life when compared to a sham group.
Arslan et al[13]	RCT	n=38 Age between 50 to 75 years Gender not reported	The participants were allocated into treatment (received NMES & combined therapy) and control groups on random basis.	5 sessions a week for 6 months for 2 weeks.	Physical performance tests, VAS Scale, WOMAC Index, Nottingham Health Profile and Tampa Scale of kinesiophobia were applied.	Statistically significant effects were seen in treatment group .
Nazari et al [14]	RCT	n=90, Male n=41, Female n=49, age between 50 to 75 years	Participants received treatment from High intensity laser therapy, Conventional physical therapy & exercise therapy.	12 weeks	VAS, WOMAC, knee range of motion , Timed Up and Go test , 6-min walk test	Both after treatment and after 12 weeks, high intensity laser therapy (HILT) was considerably more successful than traditional physical therapy and exercise therapy in lowering VAS, increasing FROM, and improving WOMAC scores.
Odole et al[15]	RCT	n=50, Males n=26, Females n=24, age between 37 to 72 years.	Two groups were assigned : Clinical group (CG) and the other. Tele physiotherapy group (PG)	12 months	VAS for pain & Ibadan Knee/Hip Osteoarthritis Outcome Measure (IKHOAM) for level of physical function.	At the baseline, between the two groups of people with knee OA, there was no significant difference in pain or physical function.

Fukuda et al[16]	RCT	n=121, age between 60 to 70 years Gender not reported.	Participants were divided into four groups at random: control (35), placebo effect (23), low dose PSW (32) and high dose PSW (32). (31)	12 months	An 11-point numerical pain rating scale and the KOOS	Short-term improvement was seen in low & high dose PSW Group. When compared to the control and placebo groups, both treatment groups demonstrated a significant reduction in pain and a gain in function.
Renata Alqualo-Costa [17]	RCT	n=184, gender and age not reported	168 patients were selected and divided into 4 groups (42 in each group): interferential current, photobiomodulation, interferential current plus photobiomodulation or placebo groups.	6 months	VAS, Timed up & Go test, WOMAC questionnaire, Isokinetic dynamometer.	In comparison to placebo and interferential current, interferential current , photobiomodulation resulted in a considerable reduction in pain.
Nejati et al[18]	RCT	n=56, older than 65 years, gender not reported	Two groups of 56 individuals with knee OA were randomly assigned. Patients in the exercise group got non-steroid anti-inflammatory medication (NSAID)-assisted knee strengthening exercises as well as 10 sessions of acupuncture and physiotherapy. . Except for the exercise programme, the non-exercise group received similar care.	12 months	VAS, knee and osteoarthritis outcome score (KOOS) & questionnaire and functional tests (4 steps, 5 sit up, and 6 min walk test) before and after treatment (1 and 3 months after intervention), and 1 year later at the follow-up.	Pain, disability, walking, stair climbing, and sit-up speed all improved considerably in the exercise group during the first and second follow-ups.
Shirin Assar et al[19]	RCT	n=60, age between 68 and 74, gender not reported	36 patients were divided into 3 (12 in each) groups: Aquatic, Resistance exercises & Control group.	8 weeks	VAS, Berg Balance Scale (BBS), quadriceps strength by dynamometer, knee flexion range of motion (ROM), WOMAC	The results showed that KI, VAS, and BBS improved considerably over time in both the TRX and aquatic groups. Only WOMAC (stiffness), knee flexion range of motion, and quadriceps strength improved significantly in the TRX group over time.
Palmer et Al[20]	RCT	n=224, Male n=37%, Female n=43 %, age 61 years	3 groups were divided:- TENS and Knee groups (n=73), sham TENS and Knee group (n=74) and knee groups (n=77).	24 weeks	WOMAC function subscale.	Significant improvement in knee groups

Pharmacological management:

Pharmaceuticals represent an essential pillar of therapy, whereby a wide range of very different drugs, especially non-steroidal anti-inflammatory drugs (NSAIDs) such as Acetaminophen, Metamizole, Naproxene, Ibuprofen, Diclofenac, Etoricoxib, Celecoxib etc in combination with other medications (e.g.

proton pump inhibitors), opioid analgesics, potentially cartilage active agents and phytopharmaceuticals, have all found use. Intra-articular therapies such as Gluco-corticoids, Hyaluronic acid, Slow Acting Drugs in Osteoarthritis (SADOAs) such as Glucosamine and chondroitin sulphate. Topical agents are also popular since they exert fewer systemic side effects and enjoy a high level of acceptance amongst patients. In addition, glucocorticoids and hyaluronic acid preparations number amongst those medications used for intra-articular OA therapy.[21]

Non-pharmacological management:

This management is mainly focused for the treatment of knee osteoarthritis to improve functionality and well-being. Inactivity, disuse & absence of mechanical stimulation are three factors to induce a more rapid cartilage degeneration, reduction of constituents of polysaccharides (glycosaminoglycan), diminished joint kinetics and flexibility. Weight loss is considered in management of knee OA. Weight loss can be achieved by having balanced diet having low caloric intake. Exercises (only Light-to-moderate intensity) should be incorporated in patient’s daily living activities to reduce the risks of diabetes, cardiovascular risks, falls, impairment, mood enhancement and self-awareness (Sharma M et al, 2019). Physiotherapy plays a significant role in management of osteoarthritis and various tools and techniques incorporated for the same are explained in figure 3,4.[22,23]

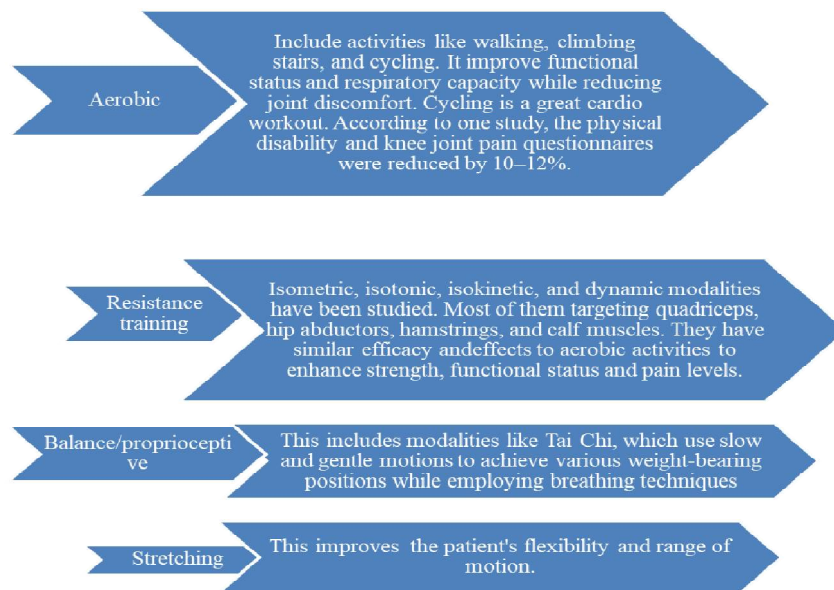


Figure 3: Different exercises for Knee OA

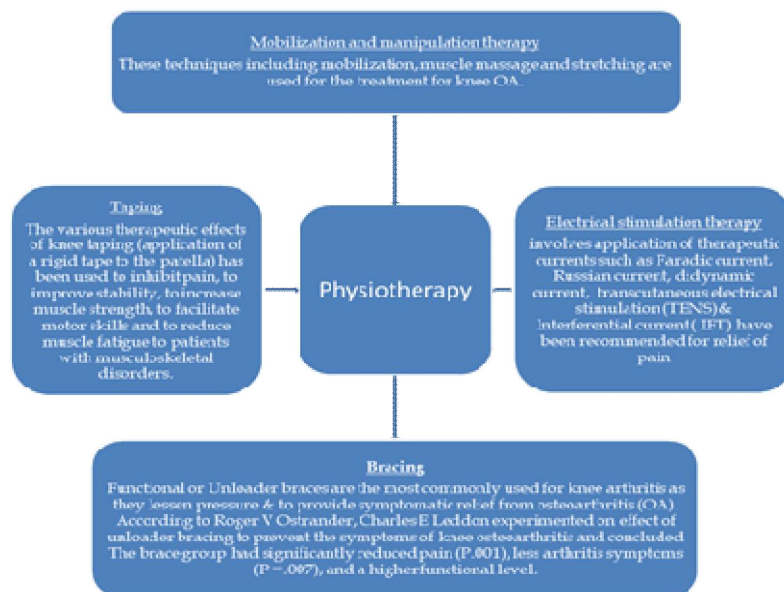


Figure 4: Physiotherapy Management of Knee OA

MATERIAL AND METHODS

Search strategy

The present review was prepared according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines (figure 5). Randomized controlled trials (RCT) were searched in PubMed, Google scholar, Springer link and PEDro databases using key words like- Knee Osteoarthritis, Advancement & Physiotherapy management. We included past 10 years' RCT articles published in the English language only from 2011 to 2020. This research was carried out from February 2021 to June 2021.

Inclusion Criteria

The inclusion criteria involves the PEDro process, and the articles having randomized control trial study and comparative studies will only be included.

Exclusion Criteria

The studies in other languages other than English will be excluded to avoid the translation difficulty and articles older than 2000 will be excluded.

Quality Assessment

The PEDro Scale, which consists of questions in two dimensions, was used to evaluate the methodological quality of a few studies. Internal validity and criteria 2–9 are assessed. Criteria 10–11 evaluate statistical data. Each question is scored based on whether it appears in the study under consideration or not. All positive responses are added together to determine the final score. According to Moseley *et al.*, studies of good quality score a 5 (5/10). As a result, all included studies with a score of 5 were determined to be of good methodological quality in our review. PEDro scale was used to evaluate the investigations (Table 2)

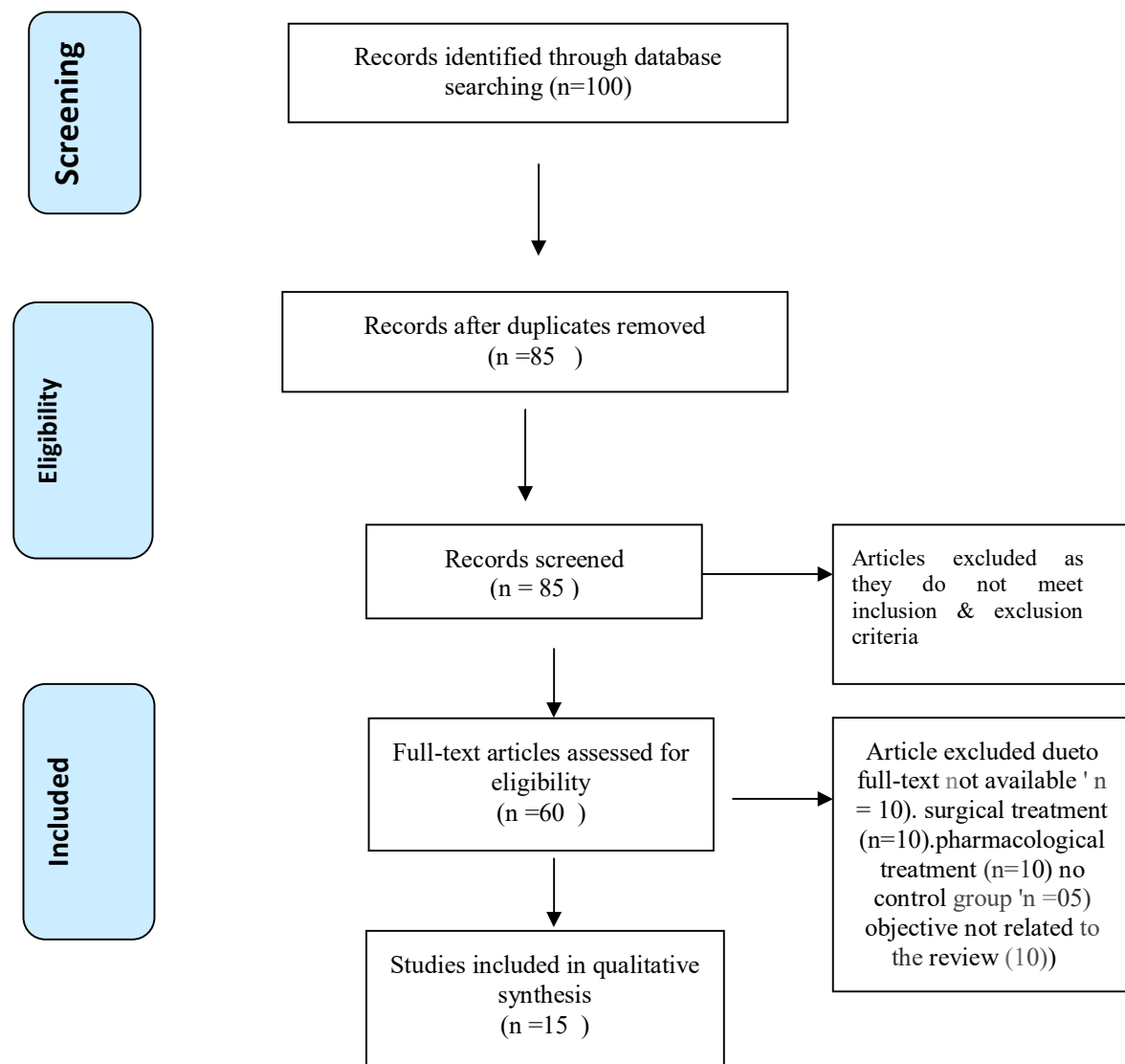


Figure 5: PRISMA flow diagram for study selection

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Data analysis

Included articles were screened including author-year, study design, age of participants, interventions, study duration, outcome measures, and outcomes by investigator.

RESULTS

Articles were examined, 100 articles were chosen based on the inclusion and exclusion criteria using the keywords Knee pain, Knee Osteoarthritis. Advancement & Physiotherapy management. Out of 100 studies, 85 studies were selected according to eligibility criteria. 15 studies were rejected as they were found in more than one database. Further 25 articles were rejected because either they were not in full text, objectives not available, there was no control group or they didn't meet the exclusion and inclusion criteria. Finally, 15 articles were included in the collection. The characteristics of included studies are explained in Table 3.

Quality Assessment of study

Average PEDro score of 15 selected articles was 7.3/15, as shown in Table 2. This score might be due to biasing lead to variations in result. Common limitations were dearth of concealed allocation and blinding of therapist, or assessor. Five trials were unable to accomplish their group comparison criterion, the follow-up condition for participants was not met in five trials, the therapist blinding requirement was not met in eleven studies, all trials failed to meet assessor blinding criterion, the baseline comparability requirement was not met in three trials while the randomization criteria was not met in one trial.

DISCUSSION

The purpose of this systematic study was to determine the efficacy of traditional physical therapy to decrease pain, to increase functionality and to improve well-being in patients with knee OA. 15 research papers of RCTs were evaluated according to Pedro scale. It is observed that first line of treatment in physiotherapy for knee osteoarthritis is electrotherapeutic modalities along with exercises only. One research article revealed TENS therapy, whether combined with or without therapeutic exercise, had no additional benefits in terms of reducing pain and improving function in individuals with knee OA. One study conducted to show the positive effects of exercise (strengthening & proprioceptive), NSAIDS, acupuncture and physiotherapy modalities (TENS & IR) as compared with non-exercise group. High quality articles favored combination therapy including electrotherapy and exercise therapy.

CONCLUSION

It is concluded that exercise therapy combined with high-intensity diode laser therapy is more effective.

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