Section: Orthopedics

Original Research Article

EFFICACY OF SHRESHTHA KNEE EXPERT TREATMENT STRATEGY (SKETS) FOR CORRECTION OF JOINT SPACE WIDTH (JSW) IN OSTEOARTHRITIS (OA) OF KNEE: OBSERVATIONS FROM A MULTICENTRE STUDY

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Received *: 02/07/2024*
Received in revised form *: 21/08/2024*
Accepted *: 05/09/2024*

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DOI: 10.70034/ijmedph.2024.3.131

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2024; 14 (3); 732-740

ABSTRAC

Background: Shreshtha Knee Expert Treatment Strategy (SKETS) is a 21-day therapy approach involving the traditional Ayurvedic system of medicine in India. **Objective:** This study assessed the improvement in joint space width (JSW) of the knee osteoarthritis (OA) with 3-week SKETS therapy. Secondary outcomes were change in composite symptom scores (CSS), and scores for crepitus, shin pain, and range of motion (ROM) of the knee joint.
Materials and Methods: This exploratory study presents the retrospective analysis of data of 93 patients (170 treated joints) with knee OA treated with Shreshtha Knee Expert Treatment Strategy (SKETS) from four clinics. Joint space width was assessed using ImageJ® software on the digital radiographic images. Symptoms were assessed on a four-point Likert scale of 0=no symptom, 1=mild symptom, 2=moderate symptom, and 3=severe symptom.
Results: There was a 75.9% increase in JSW with SKETS therapy after 3 weeks. The mean (SD) joint space increased from 2.57 (0.83) mm at baseline to 4.34 (1.59) after therapy. SKETS therapy significantly ($p<0.001$) improved the cartilage damage in 77.6% (132/170) joints, and significant improvement in the CSS, and other scores was seen. There was improvement in ROM.
Conclusion: SKETS therapy significantly increases the Joint Space Width (JSW) and helps cartilage regeneration in osteoarthritis of the knee. It improves the signs and symptoms of knee osteoarthritis, provides significant pain relief, and has the potential to improve the overall quality of life in osteoarthritis of the knee.
Keywords: SKETS, osteoarthritis, joint space width, composite symptom score.

INTRODUCTION

Osteoarthritis (OA) is the most common chronic disease affecting knee and hip joints and has a huge economic and social burden.[1] Worldwide it has been recently estimated that there is an overall prevalence of about 300 million for hip and knee OA.[2] A report from the global burden of disease (2010) ranked OA of hip and knee OA as the 11th highest contributor to global disability with an age-standardised prevalence of 3.8% for knee OA and 0.85% for hip OA.[3] Treatment goals of OA include symptom relief and improve the quality of life (QOL).[4] Despite availability of multiple therapies, most patients

eventually need joint replacement, which is the financial burden. Report suggests approximately 33% of patients with knee osteoarthritis (OA) end up having total knee replacement surgery.[5]

According to the World Health Organization (WHO), Ayurvedic therapies can represent effective treatment options for certain diseases.[6] In February 2022, new benchmarks for training and practice in Ayurveda were published by the WHO. [7,8] Existing clinical evidence from well-designed exploratory and confirmatory studies, indicate significant clinical effectiveness of Ayurved therapies in the treatment of OA.[9]

Ancient Ayurveda described Sandhigatvata a disease which resembles to osteoarthritis in present era.[10] As per ayurveda, it is type of Vata Vyadhi characterised by pain on and swelling in joints in old age, all Dhatus undergo Kshaya, thus leading to Vata Prakopa. [11,12] Ayurvedic medicines are known to be useful in painful and inflammatory disorders.[13] Shreshtha Knee Expert Treatment Strategy (SKETS) is a new therapeutic approach involving the principles of traditional Indian medicinal systems of Ayurveda. [14,15]

SKETS is a holistic approach to deal with OA inculcating the use of local therapies with oral medication targeting the Knee joint as a complete organ.[16] Formulations have been crafted (proprietary medicines of TechClinic Connect) using the principles of Ayurveda dealing with Agnideepan, Pachan, Shodhan and Bruhan with focus on Asthi-Majja Dhatu Pachak, Bruhan, and Rasayan Dravyas. The use of natural - herbal and herbomineral supplements along with local therapy of fomentation and Dhara was applied to alleviate the symptoms of Sandhigata Vata.

Many patients have benefitted from the SKETS therapy at the Shreshtha Knee Clinics across Maharashtra, and this retrospective study reports the observations from data of four such clinics.

MATERIAL AND METHODS

Study design, setting and ethics

This is a 3-week treatment period, multi-centre, retrospective data analysis of patients treated at four Shreshtha Knee Clinics located in Thane (Naupada, Kalwa and Manpada) and Mumbai (Ghatkopar) region of Maharashtra, India.

The study protocol and documents were reviewed and approved by an Independent Ethics Committee (No: DYP/IECBH/2024/423; dt. 26/08/2024). The study was conducted in compliance with ICH-GCP E6(R2) 2016 (Step 4) guidelines, New Drugs and Clinical Trials Rules (2019), and Declaration of Helsinki (Taipei 2016). This being a retrospective analysis of data, waiver of consent was obtained from the IEC. However, the patient's written informed consent was obtained wherever possible.

Study participants

The study includes data of 93 patients suffering from symptomatic OA of the knee (unilateral or bilateral) who were treated with SKETS. Data of patients of either gender, between 18 to 70 years of age, and diagnosed with osteoarthritis (OA) grade II to IV using the Kellgren–Lawrence (KL) classification (of one or both) knee joints was included. The diagnosis was based on typical history, clinical examination and classical radiological findings. Those who reported substantial pain and difficulty in performing daily activities at first visit, and completed therapy (3-4 weeks) with SKETS were included for analysis. Data of patients with a history of trauma to knee joint, severe bony defects, and joint infection (active or past) and inadequate clinical and radiographic data were excluded. Patients with a history of alcohol, tobacco dependence, or any substance abuse were also excluded.

Shreshtha Knee Expert Treatment Strategy (SKETS)

Shreshtha Knee Expert Treatment Strategy (SKETS) is a combination of local therapy and oral therapy for 21 days. Local therapy consists of Detox therapy, local *Shreshtha Pottali* (dressing) for upto 40 minutes for 5-7 days, depending upon *Saamata*. Later as *Saamata* gets reduced completely, Regeneration Therapy by Regeneration Oil *Dhara* (pouring) on both Knees (upto 25 minutes each knee i.e. 50 minutes), which was continued for the remaining of the 14-16 days, as daily sessions. Oral therapy consists of a tailored combination of ayurvedic drugs. Regeneration therapy serves as an internal as well as an external intervention for patients with osteoarthritis.

The primary objective is to facilitate the regeneration of the damaged cartilage and meniscus. Before initiating the primary regeneration therapy, a detoxification therapy is administered to alleviate the condition of *Saamta* (flare). *Saamta* is characterized by morning stiffness, local shin and knee tenderness, heaviness and restriction in range of motion (ROM), and associated digestive issues such as *amlapitta* (bloating, burping, a white-coated tongue, and anorexia).

The knee expert regeneration therapy of the SKETS is a 21-day (3 weeks) therapy administered systemically in three distinct phases based on the patient's conditions: 1) Detoxification therapy; 2) Intermediate therapy; and 3) Regeneration therapy.

The detoxification therapy comprises external treatment in the form of *Pottali Upakarma*, alongside the administration of oral medications with *Deepana* (bright), *Pachana* (digestive), and *Anulomak* (regulation). Detoxification therapy is administered during the *Saamta* condition (flare) to reduce inflammation at the microcellular level. The application of *Shuddhi Lepa* is exclusively performed during detoxification therapy.

Intermediate therapy is administered following the reduction of the *Saamta* (flare) condition to confirm the attainment of *Niramata* (remission). This

involves external application of Til Oil *Dhara Upakrama* and the internal administration of medicines having *Balya* (force) and *Bruhana* (mega) properties, complemented by medications having mild *Deepana* (bright), *Pachana* (digestive), and *Anulomak* (regulation) properties.

Regeneration therapy is the cornerstone of the SKETS treatment protocol, designed to promote the regeneration of the damaged meniscus cartilage. Externally, this therapy involves *Dhara Upakarma* using *Bala-Ashwagandhadi* oil. Internally, it includes the administration of oral medications with *Bruhana* (mega) and *Balya* (force) properties, provided in gradually increasing doses. The internal medications included tablets *Saatvik Shuddhi, Atulya Shuddhi, Asthijeevanam, Asthi Oorjitam, Mahatiktam Ghrutam, Praval Panchamrit, Pranayu, Kaishor Guggul,* and *Asthi Majja Pachak Vati*. The *Patra Pottali* provided was dipped in warm *Erand-Shunti* oil (34℃- 37 ℃) and applied immediately to the knees in circular anticlockwise motion for 10 minutes minimum which was extended up to 30 minutes as per participant's endurance to heat over the region. Shreshta Regeneration Oil was warmed up to 38℃ and using a *Dhara Patra* it was poured onto the affected knee joint, on the medial side of the joint. These medications are well documented in ayurveda literature.[17] They have analgesic, anti-inflammatory, and immunomodulatory properties which promote positive health, and have been widely used by Ayurvedic physicians to promote health and treat immunoinflammatory and degenerative disorders. Enhancing the digestion and metabolism is a key goal in management of arthritis as per the principles of Ayurveda. [18]

Diagnosis as per Ayurveda

Ayurvedic diagnosis of patients was done on baseline visit. It involves assessing the imbalances or "*dushti*" (vitiation) in the body's tissues and systems. Each term reflects a specific type of imbalance that can contribute to various health conditions, including osteoarthritis.

1. *Rasdushti*: Imbalance in the *Rasa Dhatu* (the plasma or the nutrient fluid). This can lead to poor nourishment of tissues and sluggish circulation, contributing to weakness and general fatigue.
2. *Raktadushti*: Vitiation of *Rakta Dhatu* (the blood tissue). This can lead to inflammatory conditions, skin disorders, and circulatory issues.
3. *Mansdushti*: Imbalance in *Mamsa Dhatu* (the muscle tissue). This can lead to muscle weakness, stiffness, or excessive muscle bulk.
4. *Medhdushti*: Vitiation of *Meda Dhatu* (the adipose or fat tissue). This often leads to obesity, metabolic issues, and excess body weight.
5. *Asthidushti*: Imbalance in *Asthi Dhatu* (the bone tissue). This can cause issues like brittleness of bones, joint pain, and other skeletal problems.
6. *Majjadushti*: Vitiation of *Majja Dhatu* (the bone marrow and nervous tissue). This can lead to conditions affecting the nervous system and a decline in the quality of bone marrow.
7. *Jatharagni Mandya*: Weakness or impairment of *Jatharagni* (digestive fire). This leads to improper digestion and assimilation of food, causing *Ama* (toxins) accumulation.
8. *Grahani*: A condition related to improper functioning of the digestive system, particularly the small intestine, often associated with chronic digestive issues.

Clinical diagnosis of osteoarthritis (OA)

Clinical diagnosis of osteoarthritis (OA) in patients with Grade II-IV, based on the Kellgren–Lawrence (KL) classification, affecting one or both knee joints.[19] Joints with grade-0 have no joint space narrowing (JSN) or reactive changes; grade-1 has doubtful JSN, possible osteophytic lipping; grade-2 has definite osteophytes, possible JSN; grade-3 have moderate osteophytes, definite JSN, some sclerosis, possible bone-end deformity; andgrade-4 joints have large osteophytes, marked JSN, severe sclerosis, definite bone ends deformity.

Radiograph of knee joints

X-ray radiographs for Joint Space Width (JSW) were taken on baseline and end of the study. JSW is the first structural indicator of knee osteoarthritis. The reduction of JSW occurs due to the wear and tear or because of inflammatory processes taking place in the microenvironment of the joint. For the visualization of Knee cartilage,[20] radiography has similar efficiency in diagnosing and representing the correct structural features of the knee joint.[21] Bilateral knee X-Ray in (AP weight-bearing view) were recorded for all patients at the clinics at beginning and end of therapy. The knee AP (Antero-posterior) weight-bearing view is a specialized projection to assess the knee joint, distal femur, proximal tibia and fibula and the patella.[22]

Primary outcome

The primary outcome is the change in joint space width (JSW) of the affected knee joint from baseline to one week after completion of SKETS therapy (3 weeks). Radiography is useful for the visualization of knee cartilage,[23] and radiography is reported to have good efficiency in diagnosing and representing the structural features of the knee joint.[24] The joint space width was measured based on the radiological images of the treated joint. The knee AP (Antero-posterior) weight-bearing view is a specialized projection to assess the knee joint, distal femur, proximal tibia and fibula and the patella.[25] It provides values for joint space width (JSW), meniscal regeneration, which is good representation of disease progression.

High-resolution images AP (antero-posterior) view of the knee joints were obtained and uploaded onto the Microsoft Windows based software FIJI version 2.9.0 (ImageJ, developed by NIH).[26] Image J is commonly used for analysis of images to measure various dimensions in the image.[27,28,29,30] Resolution of image was 1200 X 1000 pixels and measurement scale was set at 1000 NM (nanometre). Vertical dimensions were measured (millimetres) at 5 points

(T1 to T5) on the joint space to measure joint space width. T1 was measured at the widest space on the medial side and T5 at the lateral side of the knee joint. T3 was measured as the widest space in the midline of the joint, whereas T2 and T4 were measured as midpoints of T1-T3 and T3-T5 respectively. Thus, a total of 5 width spaces were measured and the mean joint space width (JSW) was calculated as arithmetic mean (average) of the five width spaces.

Secondary outcomes

The secondary outcomes were improvement (change) from baseline in the composite symptom score (sum of scores for symptoms of joint pain, swelling, tenderness, and joint stiffness), crepitus score, shin pain score, and range of motion (ROM) of the knee joint.

Data of all symptoms scores were collected for baseline, week1, week 2 and week 3 (end of treatment). The symptoms (joint pain, swelling, tenderness, joint stiffness, crepitus on palpation, tibia pain and shin pain) severity was recorded by the clinicians during patient visit on a four-point Likert scale of 0=no symptom, 1=mild symptom, 2=moderate symptom, and 3=severe symptom. The range of motion (ROM) of the knee joint was recorded as 0=no movement restriction (free movement), 1=slightly restricted movement, 2= moderately restricted movement, and 3=severely restricted movement.

Patient data

Baseline demographic data of patients (age, gender, weight), dietary habits, and personal habits were collected. Data of the patient's comorbid conditions, any past medical conditions or surgical procedures was collected.

Data for laboratory investigations done for the patients was collected for baseline and end of treatment (week 3-4). Data were collected at baseline and end of study (Week 3 or 4) as per the availability. Haematology included hemoglobin, CBC (Complete blood count), HbA1C (for diabetics). General biochemistry includes Serum Uric acid, C- Reactive Protein (CRP), ANA (Antinuclear Antibody), ANCA (Antineutrophil Cytoplasmic Antibodies), RA factor (Rheumatoid Factor), LFT (Liver Function Tests), RFT (Renal Function Tests) and Urine examination.

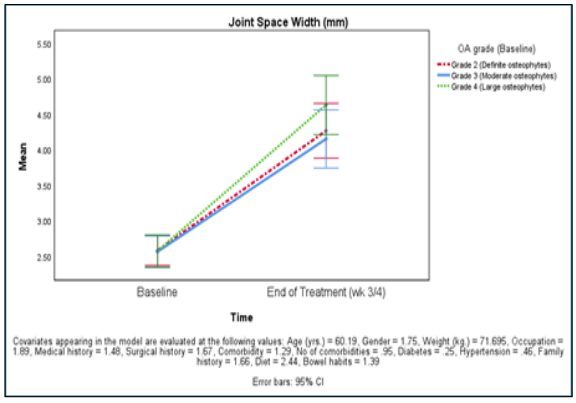
Sample size

Records of all patient's data collected from the four participating clinics were screened for eligibility to include for analyses. We screened 102 patient records who were treated for OA of knee between the period May 2022 to July 2024.Of the 102 patient records, data was incomplete for 09 patients, and data of at least one knee joint was available for 93 patients. These 100 patient records were included for final analysis with a total number of 170 joints (93 right and 77 left knee joints). This being an exploratory study, the sample size is not based on any assumptions and calculations.

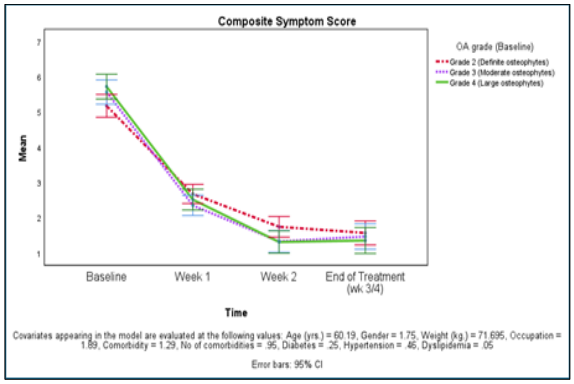
Statistical methods and data analysis

Data for age, body weight, JSW and symptom scores are presented as means with SD, whereas categorical and nominal data presented as numbers and percentages (proportions). 95% confidence intervals (C.I.) presented wherever applicable. Baseline values for JSW and symptom scores were compared to post-treatment values and scores for the different parameters using the subject to repeat measures analysis of variance (ANOVA). Post-hoc individual comparisons were done using t-test. A general linear model (GLM) was used to estimate the values for JSW and CSS adjusted for age, gender, body weight, occupation, comorbidity, number of comorbidities, and presence of comorbidities (diabetes, hypertension and dyslipidemia). Ranking data were analyzed using the Wilcoxon test for baseline and EoT comparisons. All analyses were done using two-sided tests at alpha 0.05.

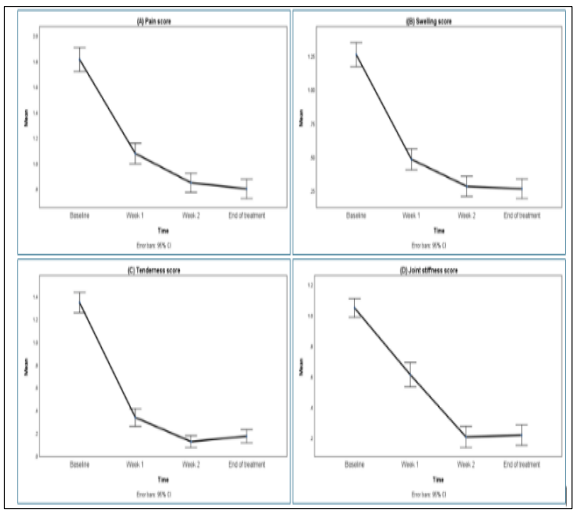
RESULTS



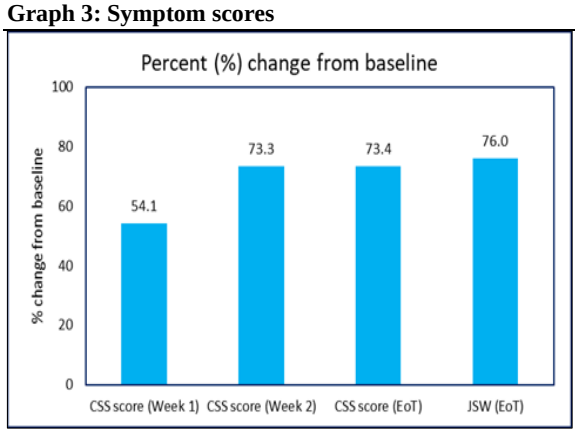
Graph 1: Joint space width (mm) at baseline and end of treatment



Graph 2: Composite symptom scores (CSS) at baseline, follow-up and end of treatment



Graph 3: Symptom scores



Graph 4: Percent change from baseline in composite symptom score (CSS) and joint space width (JSW) – mm

Table-1 presents the demography and profile of patients (n=93) who completed 3-weekSKETS therapy.

Table-2 presents the descriptives (unadjusted and adjusted for age, gender, body weight, occupation, comorbidity, number of comorbidities, and presence of comorbidities) for JSW at baseline and end of treatment.

Composite symptom scores (sum of scores for joint pain, swelling, stiffness and tenderness) reduced significantly ($p<0.001$) from baseline to end of treatment (table-3).

Radiological assessment of meniscal cartilage condition is presented in table-4. Laboratory data was not available for all patients, and no changes in laboratory data were observed at the end of therapy (data not presented).

Table 1: Profile of patients with osteoarthritis of knee (n=93)

		Mean	***SD***
Demography	Age (yrs.)	60.18	9.37
	Weight (kg.)	71.89	12.88
		No.	*%*
Gender	Male	25	26.9%
	Female	68	73.1%
Occupation	Housewife	45	48.4%
	Service	24	25.8%
	Retried	18	19.4%
	Business	1	1.1%
	N/A	5	5.4%
OA grade (KL)	Grade 2 (Definite osteophytes)	33	35.5%
	Grade 3 (Moderate osteophytes)	30	32.3%
	Grade 4 (Large osteophytes)	30	32.3%
History	Medical history	48	51.6%
	Surgical history	31	33.3%
	Family history	31	33.3%
Comorbidity	Present	66	71.0%
	Absent (No comorbidity)	27	29.0%
No of comorbidities	No comorbidity	27	29.0%
	One Comorbid	45	48.4%
	Two Comorbid	20	21.5%
	Three Comorbid	1	1.1%
Comorbid condition	Diabetes mellitus	23	24.7%
	Hypertension	43	46.2%
	Dyslipidemia	5	5.4%
	Respiratory disorders	2	2.2%
	Thyroid disorders	11	11.8%
	Others	4	4.3%
Diet	Vegetarian	21	22.6%
	Non-Vegetarian	10	10.8%
	Mixed	62	66.7%
Bowel habits	Normal	61	65.6%
	Constipation	29	31.2%
	Diarrhoea	2	2.2%

	Other(s)	1	1.1%
C-Reactive protein	Elevated	64	37.6%
	Normal	106	62.4%
RA factor	Negative	163	95.9%
	Positive	7	4.1%
Anti-nuclear antibody (ANA)	Borderline	4	2.4%
	Negative	150	88.2%
	Positive	16	9.4%

* JSN: Joint space narrowing; KL: Kellgren–Lawrence; N/A: not available; OA: osteoporosis; RA: Rheumatoid arthritis; SD: standard deviation

Table 2: Joint space width (mm) in osteoarthritis of knee (n=170)

	N	*Mean*	*SD*	*Adjusted Mean#*	*95% C.I. for adjusted mean*	*p**
Baseline						
Grade 2 OA	62	2.61	0.83	2.58	2.37 to 2.79	-
Grade 3 OA	54	2.56	0.86	2.56	2.34 to 2.78	-
Grade 4 OA	54	2.54	0.83	2.57	2.35 to 2.80	-
All patients	170	2.57	0.83	2.57	2.45 to 2.69	-
End of Treatment						
Grade 2 OA	62	4.30	1.46	4.26	3.88 to 4.65	<0.001
Grade 3 OA	54	4.09	1.45	4.15	3.74 to 4.56	<0.001
Grade 4 OA	54	4.65	1.84	4.63	4.21 to 5.04	<0.001
All patients	170	4.34	1.59	4.35	4.12 to 4.57	<0.001
Change from baseline		*Mean change*	*SD*	*% change*	*SD*	
Grade 2 OA	62	1.69	1.09	70.15	56.64	-
Grade 3 OA	54	1.53	1.13	65.37	56.62	-
Grade 4 OA	54	2.11	1.64	93.27	81.18	-
All patients	170	1.77	1.31	75.98	66.14	-

Adjusted for Age (yrs.) = 60.19, Gender = 1.75, Weight (kg.) = 71.695, Occupation = 1.89, Comorbidity = 1.29, No of comorbidities = 0.95, Diabetes = 0.25, Hypertension = 0.46, Dyslipidemia = 0.05.
* p: repeat measures ANOVA (baseline versus end of treatment)

Table 3: Symptom scores for knee joint in osteoarthritis (n=170)

						Change from baseline		
		Mean	*SD*	*Min.*	*Max.*	*Mean*	*SD*	*p**
Joint Pain	Baseline	1.81	0.615	1	3	-	-	-
	Week 1	1.08	0.533	0	3	-0.74	0.68	<0.001
	Week 2	0.85	0.499	0	3	-0.96	0.75	-
	EoT	0.80	0.506	0	2	-1.01	0.81	-
Swelling	Baseline	1.26	0.589	0	3	-	-	-
	Week 1	0.48	0.513	0	2	-0.78	0.72	<0.001
	Week 2	0.28	0.489	0	2	-0.98	0.70	-
	EoT	0.26	0.481	0	2	-0.99	0.66	-
Tenderness	Baseline	1.34	0.587	0	3	-	-	-
	Week 1	0.34	0.510	0	2	-1.01	0.69	<0.001
	Week 2	0.12	0.347	0	2	-1.22	0.68	-
	EoT	0.17	0.377	0	1	-1.17	0.67	-
Stiffness	Baseline	1.05	0.404	0	3	-	-	-
	Week 1	0.61	0.524	0	2	-0.44	0.58	<0.001
	Week 2	0.21	0.460	0	2	-0.84	0.56	-
	EoT	0.22	0.442	0	2	-0.83	0.62	-
Crepts	Baseline	0.88	0.323	0	1	-	-	-
	Week 1	0.65	0.479	0	1	-0.235	0.525	<0.001
	Week 2	0.60	0.491	0	1	-0.282	0.477	-
	EoT	0.55	0.499	0	1	-0.335	0.510	-
Shin Pain	Baseline	0.42	0.660	0	3	-	-	-
	Week 1	0.12	0.330	0	1	-0.300	0.704	<0.001
	Week 2	0.11	0.309	0	1	-0.318	0.692	-
	EoT	0.13	0.337	0	1	-0.294	0.676	-
Tibia Pain	Baseline	0.23	0.475	0	2	-	-	-
	Week 1	0.11	0.327	0	2	-0.124	0.524	<0.001
	Week 2	0.07	0.257	0	1	-0.159	0.491	-
	EoT	0.08	0.276	0	1	-0.147	0.494	-
ROM	Baseline	0.35	0.600	0	3	-	-	-
	Week 1	0.14	0.426	0	3	-0.212	0.588	<0.001
	Week 2	0.09	0.331	0	2	-0.259	0.579	-
	EoT	0.02	0.152	0	1	-0.329	0.594	-

Composite Symptom Score	Baseline	5.46	1.283	3	9	-	-	-
	Week 1	2.51	1.045	1	7	-2.95	1.28	<0.001
	Week 2	1.46	1.152	0	6	-4.00	1.52	-
	EoT	1.45	1.315	0	6	-4.01	1.69	-

ROM: Range of motion
* p: repeat measures ANOVA (baseline versus end of treatment)

Table 4: Meniscal cartilage condition for knee joint in osteoarthritis (n=170)

	Baseline		EoT		
	No.	*%*	*No.*	*%*	*p**
Normal	0	0.0%	14	8.2%	<0.001
Mild irregularity	25	14.7%	96	56.5%	
Moderately irregular	75	44.1%	58	34.1%	
Severely irregular	70	41.2%	2	1.2%	

* p: Wilcoxon test (baseline versus end of treatment)

DISCUSSION

Structural damage to the meniscal cartilage is quite significant in OA, and cartilage repair is quite challenging. Most of the non-surgical and surgical techniques of cartilage repair are not efficient in restoring the normal anatomy and function of the meniscus.[31] Thus, evolving new and effective strategies for OA are necessary to establish feasible therapeutic solutions. The emergence of regenerative medicine using stem cells and growth factors have shown some promise in pre-clinical models. [32,33] However, several challenges remain which limits their usefulness in clinical practice. [32]

The pathophysiology of OA is multifaceted, and chronic inflammation of joint plays a major role in disease onset and progression.[34] This inflammation is mediated through a variety of immune cells such as T cells, neutrophils, and macrophages.[35] Since cytokines and chemokines are responsible for cartilage damage, treatment with NF-kB pathway inhibitors like BAY11-7082 may restore IL-1b-inhibited chondrogenesis of cartilage stem cells and delays progression of OA.[36] However, these therapies may only prevent cartilage damage, and unable to repair existing damage. To the best of our knowledge, there are no reports of evidence of meniscal cartilage repair with any pharmacological therapy in osteoarthritic joint damage.

Shreshtha Knee Expert Treatment Strategy (SKETS) is a unique 21-day therapy approach involving the traditional Ayurvedic system of medicine in India. This involves a combination of local therapy (dressing with traditional *Pottali* with medicated oils) and oral therapy. Therapy starts with detoxification to alleviate the inflammation of *Saamta* (flare), and associated digestive issues such as *amlapitta* (bloating, burping, a white-coated tongue, and anorexia). This is followed by the intermediate therapy to attain a state of *Niramata* (remission). This involves external application of *Til* Oil *Dhara Upakrama* and the internal administration of medicines having *Balya* (force) and *Bruhana* (mega) properties, complemented by medications having mild *Deepana* (bright), *Pachana* (digestive), and *Anulomak* (regulation) properties. The regeneration therapy involves a combination of drugs to reduce inflammation and regenerate cartilage. These medications are customized as per the patient's profile assessed using Ayurveda principles.[37] These drugs have analgesic, anti-inflammatory, and immunomodulatory properties, widely used by Ayurvedic physicians to promote health and treat immunoinflammatory and degenerative disorders. Ayurvedic principles focus on gastrointestinal tract, and enhancement of digestion and metabolism is a key goal in the management of arthritis.[38]

This exploratory study presents the retrospective analysis of data of 93 patients (170 treated joints) with knee OA who were treated with Shreshtha Knee Expert Treatment Strategy (SKETS). Data of patients of either gender with grade II-IV OA grade (Kellgren–Lawrence) was included for final analysis. We excluded patients having trauma, bone defects and infection. The joint space width was assessed using ImageJ software on the digital radiographic images of knee joints. Although, cartilage and meniscal T2 mapping using Sodium MRI (Magnetic Resonance Imaging) can be used as a non-invasive biomarker to diagnose and monitor the meniscal cartilage repair. [39,40] However, our study was a retrospective analysis, we evaluated digital radiographs of knee joint for assessment of meniscus. We observed an 75.9% increase in joint space width with SKETS therapy at the end of 3-4 weeks after starting therapy. The study by Jain et al. (2021) reports the mean medial and lateral joint space width of healthy Indian adult knee joints to be 5.34 (1.26) mm and 5.21 (1.04) mm respectively on left side, and similar JSW measurements on right side.[41] In our study, the mean (SD) joint space width was narrowed to 2.57 (0.83) mm in joints affected with OA. This width increased ($p<0.001$) by 1.77 (1.31) mm to 4.34 (1.59) at the end of 3-week therapy. Thus, SKETS therapy was able to regenerate cartilage repair and increase JSW to near normal. SKETS therapy significantly improved ($p<0.001$) the cartilage damage in 77.6% (132/170) joints at the end of therapy. Also, there was significant improvement in the composite symptom scores (sum of scores for joint pain, swelling, stiffness and tenderness), and

scores for joint crepitus, shin pain, and tibial pain. There was significant improvement in the range of motion of the knee joint with SKETS therapy. We observed pain relief of 50% or more in 73.5% patients at the end of therapy.

The strength of this study includes its design where the real-world data of patients treated in multiple clinics was included for analysis. The limitation of this study is its retrospective design, and empirical sample size and convenience sampling based on data availability. However, post-hoc power analysis yielded adequate power of >90% for analysis of the primary outcome i.e. joint space width.

Since there are no pharmacological options for cartilage regeneration in OA affected joints, SKETS therapy seems to be a promising approach to improve joint anatomy, function and overall quality of life.

CONCLUSION

Shreshtha Knee Expert Treatment Strategy (SKETS) therapy is a combination of local therapy and oral therapy significantly increases the Joint Space Width (JSW) and helps cartilage regeneration of the knee joints in patients with osteoarthritis of knee. The 3-week SKETS therapy also improves the signs and symptoms of knee osteoarthritis and provides significant pain relief. SKETS therapy has the potential to improve the overall quality of life in osteoarthritis of the knee, and further prospective, comparative studies in larger and diverse populations would confirm the findings of this study.

Conflict of interest

The authors are business owners/employed with Shreshtha Knee Expert.

Acknowledgements

Authors would like to acknowledge Clinsearch Healthcare Solutions for data management and statistical analysis of the data.

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