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Original Research Article

A Hospital-Based Evaluation of the Therapeutic Effectiveness of Nutraceuticals in Treating Osteoarthritis

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Conflict of interest: Nil

Abstract

Aim: Assessing the therapeutic effectiveness of nutraceuticals in treating osteoarthritis.

Material and Methods: The present observational study was conducted at Department of Orthopaedics, Jannayak Karpoori Thakur Medical College and Hospital, Madhepura, Bihar, India. Patients were recruited from Department of Orthopaedics, Jannayak Karpoori Thakur Medical College and Hospital, Madhepura, Bihar, India for 1year. Aged between 19 to 75 years with the clinical diagnosis of osteoarthritis of the knee based on the American College of Rheumatology (ACR) criteria and at least moderate pain in the knee (rated at 5 or greater by the subject on a visual analog scale) during the most painful knee movement during the last month. Patients who had uncontrolled diabetes, hypertension, hepatic disorder, pregnant & lactating women, acute joint trauma of knee were excluded from the study.

Results: Out of 151 patients, 78% patients had comorbidities such as hypertension, anxiety, diabetes mellitus, thyroid disorders etc. All the subjects selected during the study received TriNyros capsule two times daily for three months. At the baseline the mean WOMAC combined score was 39.62 $\pm$ 11.95 ($p< 0.05$) which was reduced significantly to 13.36 $\pm$4.82 ($p< 0.05$) at the end of study. From the baseline 66.80% improvement observed in the patient after treatment with TriNyros. Further sub-group analysis shows that, total WOMAC score in OA patient with comorbidities reduced from 39.37 $\pm$ 11.52 to 13.34 $\pm$ 4.48 ($p< 0.05$) & in patient without comorbidities reduced from 40.08 $\pm$ 12.82 to 13.40 $\pm$ 5.43 ($p< 0.05$) after 90 days treatment with TriNyros. The subgroup analysis revealed that TriNyros reduces pain on palpations significantly from 1.98 $\pm$ 0.64 to 0.66 $\pm$ 0.52 (63.94%) in OA patient without any other disorder and 2.12 $\pm$0.63 to 0.77 $\pm$ 0.47 (66.67%) ($P< 0.05$) in OA patient with co-morbidities.

Conclusion: The findings of the current phase IV post marketing surveillance suggest that TriNyros act synergistically to exert anti-inflammatory/anti-arthritic activity. Cap TriNyros efficaciously reduces joint pain and improves the physical functional ability of OA patient. Furthermore, Cap. TriNyros shows similar efficacy in OA patients with comorbidity and without comorbidity.

Keywords: Osteoarthritis, aflapin, devils claw, anti-inflammatory, NSAIDs, cytokines.

Introduction

Osteoarthritis (OA) is a prevalent degenerative joint disease characterized by the progressive erosion of articular cartilage, subchondral bone remodelling, and synovial inflammation, leading to chronic pain and functional disability. The increasing prevalence of OA, particularly among the aging population, poses a significant burden on healthcare systems worldwide. Traditional pharmacological treatments, including non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics, offer symptomatic relief but are often associated with adverse effects, particularly with long-term use. This has spurred interest in alternative therapies, including nutraceuticals, which are dietary supplements purported to have therapeutic benefits. [1-3] Nutraceuticals, derived from food sources with extra health benefits beyond their basic nutritional value, are gaining popularity as complementary or alternative treatments for OA. Common nutraceuticals used in OA management include glucosamine, chondroitin sulfate, omega-3 fatty acids, curcumin, and various

botanical extracts. These agents are believed to modulate inflammatory pathways, protect cartilage, and improve joint function, potentially offering a safer long-term treatment option for OA patients. [4,5] Recent studies have explored the clinical efficacy of these nutraceuticals with mixed results. A 2022 systematic review and meta-analysis by Bertrand Lussier and Eric Troncy examined fortified foods and nutraceuticals in canine and feline OA, finding significant clinical analgesic efficacy for omega-3-enriched diets and omega-3 supplements, though chondroitin-glucosamine combinations showed a marked lack of effect. [6] Andriana Kaliora et al. investigated a phenolic compound and ascorbic acid supplement in knee OA patients, demonstrating significant pain relief and improvement in joint function compared to controls. [7] Smith et al. highlighted modest but statistically significant improvements in pain and joint function with glucosamine and chondroitin sulfate compared to placebo, with a favourable safety profile. [8] Despite promising findings, the clinical efficacy of nutraceuticals in OA remains a topic of debate due to variability in study designs, dosages, and formulations. High-quality, large-scale randomized controlled trials are needed to establish standardized guidelines for their use in clinical practice. This introduction sets the stage for a comprehensive review of the latest evidence on the role of nutraceuticals in OA management, aiming to elucidate their therapeutic potential and guide future research and clinical application. Devils claw also known as *Harpagophytum procumbens* is a traditional African plant & it has been used as an anti- inflammatory agent in OA. It contains different acetylated phenolic glycosides, terpenoids and iridoid glycosides and primarily marketed as pain killer and anti-inflammatory agent in rheumatism and other joint disorders. IridoForce™ is the standardized extract of devils claw used in OA. [9] Aflapin is selective inhibitor of 5-LOX enzyme obtained from *Boswellia serrata* gum resin. It exerts its anti-inflammatory action by inhibition of 5-LOX & suppression of leukotrienes. [10]

Table 1: Composition of TriNyros

Constituents	Concentration
Rosehip	275 mg
IridoForce™	100 mg
Aflapin®	50 mg

In current research, we evaluated the marketed product TriNyros (combination of Rosehip, IridoForce™, Aflapin) (Nutragenix Healthcare Pvt. Ltd.) (Table 1) as an additive treatment in OA patients and its effect in patients with & without comorbidity.

Material and Methods

A phase IV post marketing surveillance study of Cap. TriNyros (Nutragenix Healthcare Pvt. Ltd.) was conducted at Department of Orthopaedics, Jannayak Karpoori Thakur Medical College and Hospital, Madhepura, Bihar, India for 1year. Patients were recruited from DepartmentDr of Orthopaedics,Jannayak Karpoori Thakur Medical College and Hospital, Madhepura, Bihar, India aged between 19 to 75 years with the clinical diagnosis of osteoarthritis of the knee based on the American College of Rheumatology (ACR) criteria and at least moderate pain in the knee (rated at 5 or greater by the subject on a visual analog scale) during the most painful knee movement during the last month. Patients who had uncontrolled diabetes, hypertension, hepatic disorder, pregnant & lactating women, acute joint trauma of knee were excluded from the study. During the study, the enrolled subjects were treated with TriNyros capsule [Rosehip 275 mg, Irido Force TM (Devil`s claw extract) 100 mg and Aflapin® 50 mg] twice daily for 3 months. All patients were advised not to consume other ayurvedic, herbal and homeopathic treatment during study period. The record of concomitant medication was maintained during study.

At screening, baseline, day 15, 30, 60, and 90, data was obtained using standard case report forms. The primary objective was to evaluate the OA symptoms, WOMAC score, and Pain during the study. Pain on palpation, limited mobility, joint crepitus, edema, and redness were all graded on a 4- point scale (0 = not at all, 1 = mild, 2 = moderate, 3 = severe). The Western Ontario and McMaster Universities (WOMAC) osteoarthritis index was used to quantify the severity of osteoarthritis symptoms, with a higher WOMAC score indicating more severe symptoms. The subjects rated their discomfort on a 10-mm visual analogue scale (VAS). At days 0, 15, 30, 60, and 90, the WOMAC, pain, and OA symptoms were evaluated. On day 90, the patient's global assessment and the physician's global assessment were to be evaluated.

Statistical Analysis

Demographic data were analyzed using descriptive statistics using SPSS version 21. For distribution free data, the Mann Whitney U test was used. All tests were carried out at 5% significance.

Results

During the study total 151 patients were selected

based on inclusion and exclusion criteria in which comprises 44 (29.14%) males and 107 (70.86%) females. The mean age of the subject was 56.80 years, and 71.52% patients belong to the age group above 50 years. Out of 151 patients, 78% patients had comorbidities such as hypertension, anxiety, diabetes mellitus, thyroid disorders etc. All the subjects selected during the study received TriNyros capsule two times daily for three months.

At the baseline the mean WOMAC combined score was 39.62 ± 11.95 ($p< 0.05$) which was reduced significantly to 13.36 ±4.82 ($p< 0.05$) at the end of study. From the baseline 66.80% improvement observed in the patient after treatment with TriNyros. Further sub-group analysis shows that, total WOMAC score in OA patient with comorbidities reduced from 39.37 ± 11.52 to 13.34 ± 4.48 ($p< 0.05$) & in patient without comorbidities reduced from 40.08 ± 12.82 to 13.40 ± 5.43 ($p< 0.05$) after 90 days treatment with TriNyros. The change in effect was 66.12% & 66.57% in patients with and without co-morbidities respectively. The WOMAC score comparison shows that TriNyros shows similar changes in normal OA patients as well as in OA patients with co-morbidities. The improvement in WOMAC score of OA patient observed within 1 week after treatment with TriNyros.

After 90 days treatment with TriNyros, total ED-5D score significantly improved from 47.46 ± 8.10 to 81.64 ± 8.60 ($p< 0.05$). From the baseline, 72.01% improvement was observed in patients treated for three months. In sub-group analysis, total EQ-5D score significantly improved from 47.31 ± 7.65 to 80.34 ± 14.45 ($p< 0.05$) in OA patients with co-morbidity and 47.69 ± 8.99 to 79.23 ± 14.60 ($p< 0.05$) in OA patients without co-morbidities. The% improvement in total EQ-5D score was found at 69.83% & 66.13% from baseline respectively in OA patient with comorbidity and without comorbidity.

During analysis of clinical symptoms parameters such as joint line tendinitis on palpations, limitation of mobility, joint crepitus, swelling and redness were included in the study. The treatment with TriNyros for 3 months leads to 62.63% reduction in pain on palpations of OA patient (Table 2). The subgroup analysis revealed that TriNyros reduces pain on palpations significantly from 1.98 ± 0.64 to 0.66 ± 0.52 (63.94%) in OA patient without any other disorder and 2.12 ± 0.63 to 0.77 ± 0.47 (66.67%) ($P< 0.05$) in OA patient with

co-morbidities (Table 3). After treatment with TriNyros, 64.86% improvement (reduction from 2.07 ± 0.63 to 0.73 ± 0.49) was observed in limitation of mobility (Table 2). Sub-group analysis revealed that 68.70% & 70.83% reduction in OA patient with comorbidity and without comorbidity respectively (Table 3).

Table 2: Clinical symptoms score at baseline and 90 days treatment with TriNyros

Parameters	Before TriNyros at baseline (Mean + SD)	After TriNyros at Day 90 (Mean + SD	% Change after 90 days of treatment
Pain on Palpations	1.97 + 0.69	0.74 + 00.46	62.63%
Limitation of Mobility	2.07 + 0.63	0.73 + 0.49	64.86%
Joint Crepitus	1.34 + 0.63	0.41 + 0.52	69.46%
Swelling	1.44 + 0.68	0.24 + 0.43	83.41%
Redness	0.69 + 0.59	0. 09 + 0.28	87.50%

Movement of a joint affected by OA may cause a crackling or grating sensation called "crepitus". OA treatment with TriNyros for 90 days, reduces joint crepitus from 1.34 ± 0.63 to 0.41 ± 0.52 (69.46%) (Table 2). The reduction rate for joint crepitus is similar in OA patient with comorbidity (70.83%) & without comorbidity (68.70%) (Table 3).

Table 3: Clinical symptoms score changes in OA patient with comorbidity and without comorbidity after treatment with TriNyros

Parameters	At baseline	After 90 days	% Change after 90 days of treatment	Significance
Pain on Palpation				
With comorbidity	1.98 + 0.69	0.72 + 0.47	63.40%	
Without comorbidity	1.94 + 0.69	0.75 + 0.43	61.17%	
Limitation of mobility				
With comorbidity	2.12 + 0.63	0.77 + 0.47	63.94%	
Without comorbidity	1.98 + 0.64	0.66 + 0.52	66.67%	
Joint crepitus				
With comorbidity	1.34 + 0.61	0.42 + 0.54	68.70%	$P< 0.05$

Without comorbidity	1.36 + 0.68	0.40 + 0.49	70.83%	
Swelling				
With comorbidity	1.44 + 0.67	0.22 + 0.45	84.40%	
Without comorbidity	1.43 + 0.69	0.26 + 0.45	81.58%	
Redness				
With comorbidity	0.74 + 0.55	0.08 + 0.28	88.89%	
Without comorbidity	0.60 + 0.66	0.09 + 0.30	84.38%	

OA usually occur in elderly patient which causes wearing down of the cartilage and leads to joint swelling and redness. After treatment with TriNyros, swelling and redness reduced from 1.44 ± 0.68 to 0.24 ± 0.43 (83.41%) and 0.69 ± 0.59 to 0.09 ± 0.28 (87.50%) respectively (Table 2). During the study, swelling improved by 84% and redness improved by 88.89% from baseline after treatment in patients with co- morbidity (Table 3).

VAS score is generally used to determine the intensity of pain in patient. TriNyros treatment reduces VAS score from 6.41 ± 1.09 to 1.39 ± 0.78 (78.27%) after 90 days in OA patient. Furthermore, sub-analysis evaluation revealed that 79.37% & 76.15% reduction observed respectively in patient with and without comorbidity (figure 3). The changes in VAS score is observed after 1 week of treatment with TriNyros.

The patient & physician global assessment of osteoarthritis activity is vital component of various measures of disease activity. During three-month, 92.05% of OA patients as well as physicians were satisfied with TriNyros treatment. No patients and physician reported any non-compliance with TriNyros during the study.

Discussion

This phase IV post surveillance study investigated the clinical efficacy of TriNyros in patients with osteoarthritis We found that administration of TriNyros for three months leads to improvement in WOMAC score, Total EQ-5D score, VAS score, pain on palpation, limitation of mobility, joint crepitus, swelling and redness in OA patient. Further subgroup analysis revealed that, TriNyros shows similar efficacy in OA patient with & without comorbidity. The improvement in OA was observed in early 1st week after initiation of treatment with TriNyros. Patient and physician global assessment revealed that TriNyros is highly accepted and shows no non- compliance during the study. The results obtained in the current study are in line with the previously published study performed by Anand *et al*. (2020)[11] In the previous study 58.82% reduction in WOMAC score, & 67% reduction in VAS score was observed in OA patient treated with TriNyros for 90 days. [11]

Osteoarthritis is a progressive disability disorder that affects 10 to 15% of the Indian population above 60 years. However, age is a key risk factor. Osteoarthritis treatment possess a huge cost with the restrictions in physical performance and discomfort. [12] Despite this burden and the high prevalence of osteoarthritis, little has been done to alter the disease's course and ameliorate symptoms. The current conventional treatment is nonsteroidal anti-inflammatory drugs (NSAIDs), which relieve symptoms such as pain but do not change the course of cartilage loss and joint degeneration. Furthermore, NSAIDs are linked to a high prevalence of gastrointestinal, cardiovascular, and renal adverse effects, all of which are potentially lethal. [12,13]

Innovations that provide symptomatic relief as well as change the course of the disease are desperately needed, and nutraceutical techniques have piqued interest as an alternative to pharmacological approaches. TriNyros is the mixture of *Rosa canina* L. (Rosehip), Boswellia serrata and Harpagophytum procumbens (Devil`s claw) extract, which are most commonly referred in traditional herbal system. Oral administration of *Rosa canina* L. for three months significantly reduced WOMAC score & stiffness in OA patients. It also reduced the consumption of rescue medication required during OA treatment. [14] The use of Rose hip powder for 4 weeks also found to be effective in reducing blood CRP levels and exert its anti-inflammatory action in arthritis patient. [15,16]

Bosewellia serrata extract consist of 3-O-Acetyl-11-keto-beta- boswellic acid (AKBA) which contribute to its anti- inflammatory action by inhibiting 5-lipoxygenase. Aflapin is a novel composition derived from Bosewellia serrata and Vishal AA *et al*. 2011 shows that it is more effective in alleviating pain, joint stiffness and improves physical functioning of patients with OA. [17] The meta-analysis of 28 studies revealed that Bosewellia serrata extract are safe and effective in OA patient. [18]

IridoForce™ is a trademarked extract from Devil's Claw's secondary roots (storage tubers), which contain more harpagoside than the primary roots. IridoForce™ is able to provide an extract with the highest concentration of Harpagoside thanks to a patented technique (up to 20 percent Harpagoside by HPLC or 40 percent by UV). Two high- quality studies (Lecomte *et al*. and Chantre *et al*.) found that Devil's Claw extracts were effective in reducing pain in a review of 28 clinical trials. Adverse events were reported at a very low rate of around

3%. Mainly mild gastrointestinal symptoms occurred and were similar with placebo. In the approved dosage, long-term usage of Devil's claw looks to be safe. [19,20]

There are some limitations of the current study. To begin, no established drugs, such as NSAIDs, were used to evaluate the effects of TriNyros to standard treatment. Secondly parameters such as body weight & body mass index (BMI) are not considered during the study. Obesity is important factor in the symptomatic OA as it has an important effect on the treatment. Finally, only one fixed dose of TriNyros was used during the study to evaluate its efficacy; hence we could not validate effect of different doses on safety and efficacy in OA patient. Further clinical trials with larger sample numbers and varied dosages are needed to establish safety and efficacy.

Conclusion

The findings of the current phase IV post marketing surveillance suggest that TriNyros (Nutragenix Healthcare Pvt. Ltd) act synergistically to exert anti-inflammatory/anti-arthritic activity. Cap TriNyros efficaciously reduces joint pain and improves the physical functional ability of OA patient. Furthermore, Cap. TriNyros shows similar efficacy in OA patients with comorbidity and without comorbidity.

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