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Evaluation of "Ostolief" (Polyherbal Formulation) in the Management of Osteoarthritis: A Double-blind, Randomized, 12-Week Comparative Study

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Abstract

Osteoarthritis (OA), a degenerative form of arthritis, is a disease that leads to considerable disability, especially in the geriatric group of patients. In fact, in certain populations, OA is now assuming epidemic proportions among the elderly. Since the drug therapy of OA involves long-term medication with drugs such as NSAIDs, it is fraught with unwanted adverse effects. In this scenario, plant-based formulations provide a unique modality of treatment as they are safe and possibly have a disease-modifying action. The present study was conducted to evaluate the efficacy of a herbomineral formulation "Ostolief" in comparison with valdecoxib in reducing the pain, stiffness and immobility, characteristic of OA. One hundred patients suffering from OA who needed drug therapy were divided into two groups: one group received tablet Ostolief in a dose of one tablet twice daily, while the other group received tablet valdecoxib 10 mg twice daily for a period of 12 weeks. A total of 94 patients completed the trial. In the Ostolief group, the average pain score at rest on visual analog scale decreased from 49.56 ± 10.37 at

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Osteoarthritis is a debilitating disease in geriatric age group.

baseline to 26.08 ± 9.77, while in the valdecoxib group, it fell from 48.02 ± 13.66 to 26.02 ± 8.53. The pain on joint use decreased from 42.97 ± 12.09 to 24.02 ± 11.38 in patients on Ostolief, while in patients in the valdecoxib group, it decreased from 45.30 ± 13.70 to 25.51 ± 10.66. The reduction in the Western Ontario and McMaster (WOMAC) score in the Ostolief group was from 14.13 ± 1.93 at baseline to 9.30 ± 2.83 at 12 weeks. The corresponding reduction in the valdecoxib group was 13.91 ± 2.10 at baseline to 8.97 ± 2.99 at 12 weeks. Both the drugs were well tolerated. It was concluded that Ostolief showed a comparable efficacy vis-a-vis valdecoxib. On all evaluation parameters, Ostolief and valdecoxib showed similar results. Although patients on valdecoxib showed slightly greater reduction in pain scores, if the safety aspect is considered, Ostolief definitely has an edge while having an equivalent efficacy.

Introduction

OA is a degenerative arthritis of chronic progression and is one of the most debilitating diseases faced by an ever increasing geriatric population. It leads to chronic -sometimes severe - pain mostly in knees and lower back, restricted mobility and a markedly reduced quality-of-life. In many cases, it interferes with normal daytime activities and the joint pains may keep patients awake at night.

OA has a particularly large impact on the health of middle-aged and older women. Before the age 50, men have a higher prevalence of OA, but both the prevalence and incidence are higher in women after the age of 50.[1] The risk of knee, hip and hand OA in women increases dramatically after menopause[2-5]. Older women are more likely to report joint symptoms when radiographic OA is present, and hip OA atleast appears to progress more rapidly in older women compared with older men[6].

Numerous studies suggest that the prevalence of joint pain rises markedly with age in the general population, but for reasons not fully understood may decline somewhat after the age of 75 or 80.[7] Recent data from a variety of sources across the globe suggest that populations are now experiencing an epidemic of knee pain, with one in 4 or one in 3 persons aged 55 and older having chronic knee pain[8,9]. Most studies suggest that knee pain is more common in older women than in older men.

The basic pathology in OA is a thinning of the articular cartilage, due to a decrease in the synthesis of cartilage tissue, relative to the wear and tear. Currently available measures to manage OA include NSAIDs, physiotherapy, supportive belts, etc. Unfortunately, the drug therapy of OA involves long-term medication with drugs such as NSAIDs, and therefore, is fraught with side effects.

In this study, we focus on a novel treatment option of Ostolief for OA. Ostolief is a standardized, multi-ingredient herbal formulation, which not only relieves the symptoms of osteoarthritis , but is also postulated to delay its progression. Ostolief contains Shallaki (*Boswellia serrata*) and Ashwagandha (*Withania somnifera*), which reduce the degradation of glycosaminoglycan and delay the progression of OA. Gokshur (*Tribulus terrestris*) and Guduchi (*Tinospora cordifolia*) are powerful antioxidants and thus exhibit anti-inflammatory action. Bala (*Sida cordifolia*) and Kupilu (*Strychnos nux vomica*) are potent anti-inflammatory and analgesics. Moreover, Guduchi (*T. cordifolia*), Bala (*S. cordifolia*), Gokshur (*T. terrestris*) and Ashwagandha (*W. somnifera*) have anti-aging properties, which have a positive impact on preventing bone degeneration. In this study, we compared the efficacy and tolerability of Ostolief with valdecoxib during a 12-week treatment in a randomized, comparative, double-blind trial.

Materials and methods

One hundred patients (50 in each group), diagnosed as suffering from chronic OA, who needed drug therapy were enrolled after obtaining informed written consent. Each patient received either tablet Ostolief or tablet valdecoxib (10 mg). The two preparations looked

identical. Patients were randomized according to a computer-generated randomization chart. The drugs were packed in sealed bottles with patient serial numbers on them. The patients were enrolled and assigned a serial number in a chronological order. Both study treatments were administered in a dose of one tablet twice daily for a period of 12 weeks. A diary was provided to each patient for recording symptoms. Compliance was checked at every visit.

Evaluation of the patients was performed every 3 weeks. Patients, who were taking other medications for OA, were given a 15-day washout period, following which the study drugs were administered.

Hemoglobin, ESR, total leucocyte count, differential leucocyte count, fasting blood sugar, blood urea, creatinine, bilirubin, alkaline phosphatase and X-ray of the affected joint was performed at baseline on enrollment and at the end of 12 weeks of study period.

Results

Of the 100 patients enrolled in the study, 94 (46 in the

Table 1

Radiological findings in the two treatment groups [number of patients]

Parameter	Ostolief (n = 46)	Valdecoxib (n = 48)	χ^2-test
Marginal lipping	44	41	$\chi^2 = 0.007$; 3 d.f. p = 0.999 (NS)
Narrowing of joint space	41	47	
Sharpened articular margins	12		
Sclerosis	34	45	
Bone cysts	0	0	

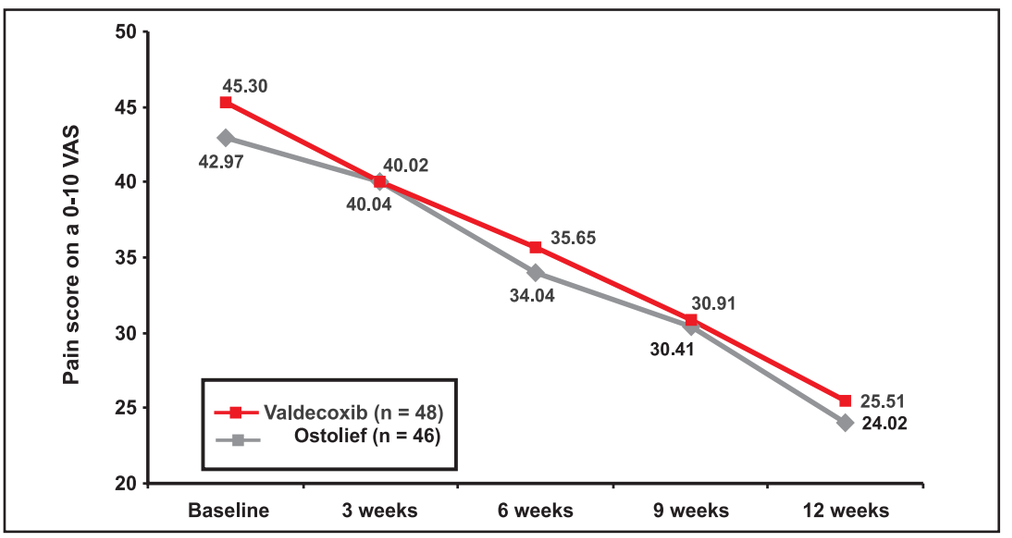

Figure 1. Pain on a 0-10 visual analog scale (VAS) during joint use/mobility in two treatment groups at baseline and after 3, 6, 9 and 12 weeks of therapy.

Table 2

Joint tenderness on a four-point rating scale in the two treatment groups (Number of patients) at enrollment and after 3, 6, 9 and 12 weeks

	Ostolief (n = 46)				Valdecoxib (n = 48)				Mann-Whitney
	Nil	Mild	Moderate	Severe	Nil	Mild	Moderate	Severe	'U' test (p)
Baseline	14	29	3	0	24	17	7	0	p > 0.05 (NS)
3 weeks	15	29	2	0	27	14	7	0	p > 0.05 (NS)
6 weeks	19	27	0	0	27	14	7	0	p > 0.05 (NS)
9 weeks	25	21	0	0	37	8	3	0	p < 0.05 (Sig.)
12 weeks	34	12	0	0	36	6	3	0	p < 0.05 (Sig.)
	p < 0.01 (Sig.) Kruskall-Wallis test				p < 0.01 (Sig.) Kruskall-Wallis test				-

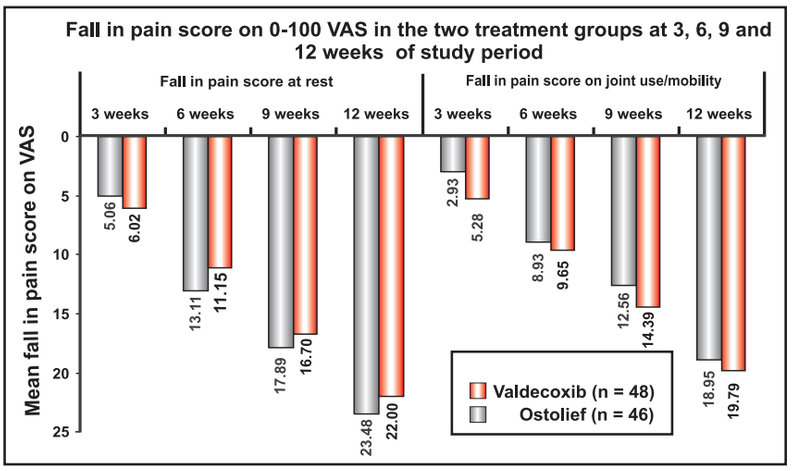

Figure 2. Fall in pain score on 0-100 VAS in the two treatment groups at 3, 6, 9 and 12 weeks of study period.

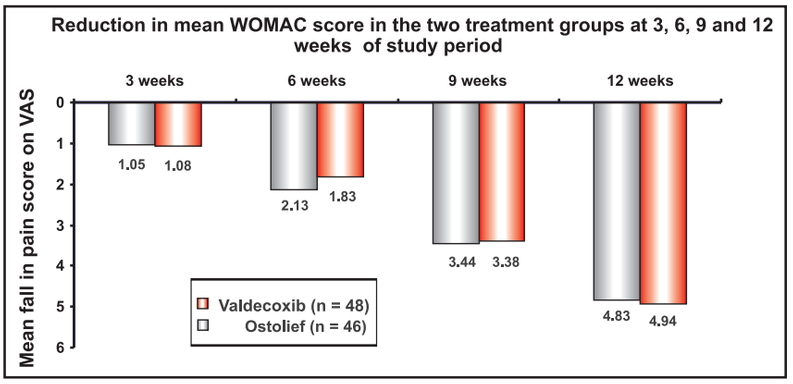

Figure 3. Reduction in the mean WOMAC score in the two treatment.

Ostolief group and 48 in the valdecoxib group) completed the study as per the study protocol.

Marginal lipping and joint space narrowing were the prominent radiological findings in both groups (Table 1).

The pain score on joint use decreased from 42.97 ± 12.09 to 24.02 ± 11.38 in patients on Ostolief after 12 weeks therapy, while for patients in the valdecoxib group, it decreased from 45.30 ± 13.70 to 25.51 ± 10.66. Here again, the reduction in the pain score was significant within both groups ($p < 0.0001$), while there was no difference in the reduction in pain scores observed between the two groups (Fig. 1).

Although the fall in the pain scores were similar in both the groups, the group receiving Ostolief showed a greater fall in the pain score at rest while the group receiving valdecoxib showed a greater fall in the pain scores on joint use/ mobility (Fig. 2).

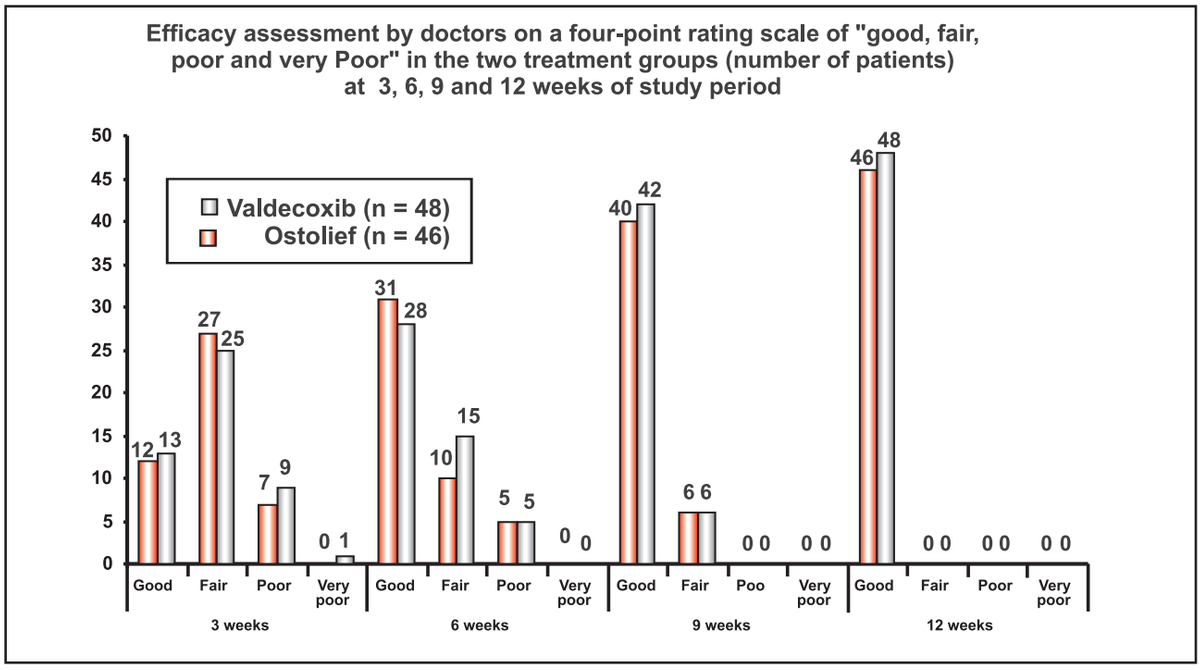

Figure 4. Global efficacy assessment by the physician.

Joint swelling and tenderness

Joint tenderness was also rated on a four-point scale similar to joint swelling. After 12 weeks of treatment, both the groups showed significant reduction in the tenderness (Table 2).

WOMAC score

The WOMAC score for OA showed significant reduction, comparable in the two groups. The mean score in the Ostolief group reduced from 14.13 ± 1.93 at baseline to 9.30 ± 2.83 at 12 weeks. The corresponding reduction in the valdecoxib group was 13.91 ± 2.10 at baseline to 8.97± 2.99. Thus, the reduction in the mean WOMAC score was comparable in both the groups (Fig. 3).

Morning stiffness

In the Ostolief group, only 11 patients complained of morning stiffness at the end of the study, compared to 28 at baseline.

However, in patients in the valdecoxib group, 12 patients complained of morning stiffness after 12 weeks treatment, as compared to 21 at baseline.

Global efficacy assessment by the physician

Overall, physicians rated the response as good in all the 46 patients in the Ostolief group after 12 weeks therapy. It was observed that as the duration of the therapy increased, the response to therapy improved (Fig. 4).

Safety and tolerability

Laboratory investigations such as hemogram and liver and kidney function tests were performed in all the patients before and after the therapy. Both the medications were found to be safe and did not lead to any significant alteration in the liver and kidney functions. Similarly, both the medications were well tolerated by the patients.

Discussion

Long-term use of NSAIDs is a common practice in the management of mild-to-moderate OA. Patients suffering from OA are also known to consume higher doses of NSAIDs, and misuse of NSAIDs is fairly common. Therefore, such patients are especially vulnerable to the distressing side effects of NSAIDs. The severity and morbidity caused by the side effects of NSAIDs can

assume grave proportions especially in long-term users.

NSAID use is a very common cause of upper gastrointestinal (GI) bleeding. Even cyclooxygenase (COX)-2 inhibitors, which are believed to have lesser GI side effects compared to other NSAIDs, have been shown to produce gastric ulcers. The recent findings of cardiac adverse events with the use ofCOX-2 inhibitors, especially rofecoxib, have further highlighted the problem of severe side effects that can force discontinuation of therapy.

In addition to these issues, NSAID therapy offers no advantage in terms of reversing the basic pathological mechanisms in OA, namely destruction of intra-articular cartilages and progressive loss of the articular surfaces of the bones.

Therefore, in the management of OA, it is important to use a therapeutic tool that provides relief from the disabling symptoms, does not cause distressing side effects and also arrests or reverses the degenerative changes that cause OA.

A structure-modifying treatment for OA

Nearly all treatments for OA in the current therapeutic arsenal can be considered symptom-modifying drugs. These include aspirin, analgesics and NSAIDs. Even currently popular nutraceutical treatments, such as glucosamine sulfate - touted as the "arthritis cure" - may only primarily modify symptoms rather than change the underlying disease process and protect the joint from further structural damage. *Recent studies which have been published in "The New England Journal of Medicine" have demonstrated that glucosamine and chondroitin sulfate alone or in combination are similar to placebo and do not reduce pain effectively in patients with OA of the knee*[10]. Therefore, it is very important to initiate therapy with drugs that not only manage symptoms but also favorably affect changes in joint structure over long-term treatment periods and thus slow or arrest disease progression - the so-called disease- or structure-modifying treatments.

Ostolief is one such multi-ingredient formulation that contains ingredients like Shallaki (*B. serrata*), Ashwagandha (*W. somnifera*), Gokshur (*T. terrestris*), Guduchi (T. cordifolia), Bala (*S. cordifolia*) and Kupilu (Strychnos nux vomica). Owing to this unique combination of drugs that act on OA through various mechanisms, Ostolief emerges as a disease-modifying therapy with potent anti-inflammatory and analgesic activity. Shallaki reduces the degradation of glycosaminoglycan and delays the progression of OA. Guduchi, Bala, Gokshur and Ashwagandha have been used in the Ayurvedic system of medicine as *rasayanas* that have anti-aging properties. Herbs that act as *rasayanas* exert their anti-aging effect through rejuvenating/revitalizing all the body tissues (*dhatus*). Since bones are one of the seven *dhatus* (*asthi*), *rasayanas* also have a positive impact on preventing bone degeneration. *Rasayanas* are also powerful antioxidants and thus exhibit anti-inflammatory action.

In this study, it was found that the study medicine, Ostolief, showed good efficacy in all the evaluation parameters. The efficacy of Ostolief was comparable to that of valdecoxib- a COX-2 inhibitor. None of the patients reported any adverse effects with the formulation. The need for rescue medication was also low, indicating that patient satisfaction with this formulation was high.

Conclusion

From this trial, it can be concluded that the clinical efficacy of Ostolief tablets is comparable to that of valdecoxib. Ostolief can be prescribed to patients with mild-to-moderate OA. The patients in this trial reported no side effects of Ostolief.

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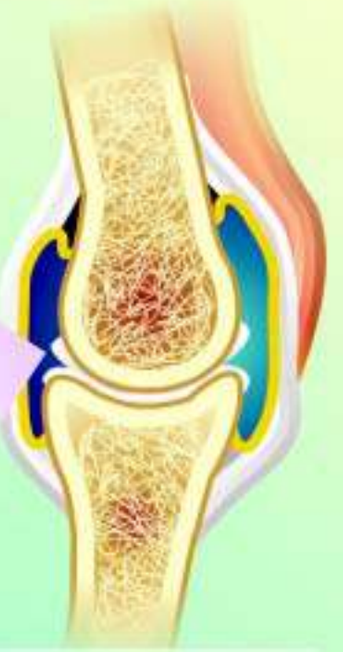

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