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CLINICAL PERSPECTIVES OF INDIAN HCPS ON ACECLOFENAC, PARACETAMOL, AND SERRATIOPEPTIDASE USE IN OSTEOARTHRITIS MANAGEMENT

Orthopaedics

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ABSTRACT

Background: Osteoarthritis (OA) is a leading cause of pain and disability, with its prevalence rising due to aging populations and lifestyle factors. Effective pain management strategies are crucial to improving patient outcomes. The present study analyzed the clinical perspectives of Indian HCPs on the use of a fixed-dose combination (FDC) of aceclofenac, paracetamol, and serratiopeptidase in OA management. **Methods:** A digital questionnaire-based study was conducted among healthcare professionals (HCPs) treating OA patients across India. The study assessed prescribing patterns, patient response, safety, and HCP perceptions of the FDC's efficacy compared to other treatments. **Results:** A total of 140 HCPs participated in the study. The majority (37.86%) reported that 5–7 out of 10 OA patients had used non-steroidal anti-inflammatory drugs (NSAIDs) prior to initiating the FDC, with 32.14% noting NSAID use in all patients. Post-treatment, 58.58% of patients experienced a reduction in pain severity (visual analogue scale [VAS] score ≤5), and 51.43% showed improved mobility. Gastritis (62.14%) was the most common adverse effect. Overall, 54.29% of HCPs reported high patient satisfaction (6–8/10), while 96% expressed willingness to prescribe the FDC again. Additionally, 60.71% of HCPs indicated that serratiopeptidase was preferred over trypsin-chymotrypsin in specific conditions such as post-operative recovery and severe swelling unresponsive to NSAIDs. **Conclusion:** The current study highlights the widespread acceptance of the aceclofenac-paracetamol-serratiopeptidase combination in OA management, demonstrating significant pain relief, improved functional outcomes, and a favorable safety profile.

KEYWORDS

INTRODUCTION

Osteoarthritis (OA) is a broad term encompassing various joint disorders characterized by progressive structural changes affecting the entire joint. These involve cartilage loss, subchondral bone alteration, synovial inflammation (acute and chronic), osteophyte formation, and synovial fluid composition changes. Pain remains the main symptom, having a great impact on clinical practice and healthcare consumption [1, 2]. With the population aging, growing rates of obesity, and rising incidence of joint injury, prevalence of OA is increasingly on the rise, touching an estimated 250 million individuals across the globe [1]. Asia is expected to double its elderly population from around 6.8% in 2008 to 16.2% by 2040 [3]. After reaching 65 years, the majority of individuals are already radiographically showing evidence of OA, and by 75 years, almost 80% present similarly. Although it has a profound public health burden, OA remains a serious issue for epidemiologists [4]. In India, OA is estimated to be the fourth leading cause of disability in the elderly with a prevalence of as much as 56.6%. In OA prevalence in older adults is 56.6% in general, 32.6% in rural and 60.3% in urban areas. Also, females are more frequently affected than males [5].

Osteoarthritis management should focus on reducing pain and stiffness, preserving functional capacity, and preventing joint damage progression to improve quality of life. Treatment strategies include non-pharmacological, pharmacological, and surgical approaches. In the early stages of OA, pain and stiffness are the primary concerns. Paracetamol is recommended as the first-line oral analgesic due to its safety, effectiveness, and affordability [6]. It primarily acts centrally, inhibiting prostaglandin synthesis in the central nervous system (CNS), with a minor peripheral effect on blocking pain impulse generation. When symptoms worsen or joint inflammation is present, non-steroidal anti-inflammatory drugs (NSAIDs) are introduced for better symptom control [7].

Among NSAIDs, aceclofenac is widely used for painful inflammatory conditions, benefiting over 75 million patients worldwide [8]. It effectively reduces synovial prostaglandin E2 levels, relieving acute knee pain and synovial effusions, and is well tolerated in OA, rheumatoid arthritis, and ankylosing spondylitis. However, long-term NSAID use carries a risk of gastrointestinal (GI) complications, including bleeding, ulcers, and perforation, whereas paracetamol has a lower GI risk [6, 7]. A combination of paracetamol and aceclofenac enhances analgesic efficacy while minimizing dose-dependent side effects. Their synergistic action, with paracetamol targeting the CNS and aceclofenac acting peripherally, results in faster and more effective pain relief. This combination is particularly useful in managing acute OA flare-ups, leading to better patient outcomes [7, 9].

Additionally, serratiopeptidase, a proteolytic, an anti-inflammatory enzyme effective in relieving swelling [10]. It further amplifies the therapeutic effect when combined with paracetamol and aceclofenac. It possesses mucolytic, fibrinolytic, and wound-healing properties and interacts with COX-1 and COX-2, modulating inflammatory mediators such as interleukins, prostaglandins, and thromboxane. This triple combination not only provides faster and sustained relief but also improves safety and tolerability, helping mitigate NSAID-induced side effects [2].

The rationale of the present study was to validate the clinical benefits of this combination therapy in a real-world patient population and compare its effectiveness with previous treatments. By analyzing patient responses across multiple parameters, this study aimed to assess the efficacy and safety of the fixed-dose combination (FDC) of aceclofenac, paracetamol, and serratiopeptidase in managing OA-related knee pain.

Method

Study Design

This questionnaire-based study was conducted among healthcare practitioners (HCPs) in India, including general HCPs, orthopedic specialists, and rheumatologists, from [Study Period]. Participation in the study was entirely voluntary. All study-related information, including the questionnaire, was thoroughly explained to participants, and verbal consent was obtained before participation. The study process, including data collection and analysis, ensured the confidentiality and anonymity of the HCPs and their patients. The study was conducted in accordance with ethical principles that are consistent with the Declaration of Helsinki, International Conference on Harmonisation-Good Clinical Practices and the study protocol was

approved by the ACEAS Independent Ethics committee on 30th July 2024.

Study Questionnaire

This questionnaire-based study was designed based on existing literature, clinical guidelines, and expert opinions. It consisted of 17 questions focusing on various aspects of OA management, including prior NSAID and paracetamol use, pain and swelling severity, impact on sleep, treatment duration, post-treatment outcomes, adverse effects, and patient satisfaction. Additionally, it assessed practitioner perspectives on FDC efficacy, likelihood of re-prescription, and comparisons between serratiopeptidase and trypsin-chymotrypsin, including its role in post-surgical healing.

Inclusion And Exclusion Criteria

Healthcare practitioners with at least two years of OA treatment experience, managing patients with bilateral knee pain, and prescribing the FDC for at least four weeks were included. Healthcare practitioners with less experience, cases with FDC use under four weeks, and incomplete patient data were excluded.

Data Collection

Healthcare practitioners participating in the study were provided with a concise overview of the study's objectives and the process for completing the questionnaire. The questionnaire was given to the HCPs either in-person, via phone calls, or through online platforms, as per the HCP's convenience.

Data Analysis

The responses of HCPs were entered into Microsoft excel and descriptive statistics, such as frequencies and percentages, were employed to present data.

Study Outcomes

The study assessed the effectiveness of the FDC of aceclofenac, paracetamol, and serratiopeptidase in OA related knee pain. Key outcomes included pain relief, mobility improvement, patient satisfaction, and swelling reduction. It also evaluated sleep improvement, HCP preferences, post-surgical healing benefits, and safety, including adverse effects and impact on comorbid conditions.

RESULTS

A total of 140 HCPs participated in this study. Total 37.86% of HCPs reported that 5-7 out of 10 patients with OA and bilateral knee pain had used NSAIDs as a prior treatment. Similarly, 37.86% of HCPs noted prior paracetamol use in 3–5 out of 10 patients, followed by 24.29% who indicated its use in only 1–3 patients. Pain severity was predominantly rated between 6-8 on the visual analogue scale (VAS0) scale (59.29%), while mild swelling was most commonly observed in these patients, according to 47.86% of HCPs patients. Sleep disturbances due to knee pain were most commonly reported in 3 out of 10 patients, according to 35.71% of HCPs (Table 1).

Table 1: Prior Treatment and Baseline Symptoms in OA Patients

Question	Options	Response (N=140)
Out of these 10 patients with OA and bilateral knee pain, how many patients had taken prior treatments with NSAIDs?	1-3 patient	11(7.86)
	3-5 patients	31(22.14)
	5-7 patients	53(37.86)
	All 10 patients	45(32.14)
Out of these 10 patients with OA and bilateral knee pain, how many patients had taken prior treatments with paracetamol?	1-3 patients	34(24.29)
	3-5 patients	53(37.86)
	5-7 patients	33(23.57)
	All 10 patients	20(14.29)
What was the most common degree of pain in these 10 patients with OA and bilateral knee pain on a VAS scale of 0-10 where 0= No pain and 10 = pain as severe as can be?	0-2	4(2.86)
	3-5	43(30.71)
	6-8	83(59.29)
	9-10	10(7.14)
What was the most common degree of swelling pain in these 10 patients with OA and bilateral knee pain on a VAS scale of 0-3 where 0= No swelling 1= mild swelling, 2= moderate swelling and 3 = severe swelling which makes it difficult for the patient to	0 = no swelling	2(1.43)
	1= mild swelling	56(40.00)
	2= moderate swelling	67(47.86)
	3= severe swelling which makes it difficult for the patient to walk	15(10.71)
In how many of these patients with OA and bilateral knee pain was sleep adversely affected by the knee pain?	1/10 patients	6(4.26)
	2/10 patients	24(17.14)
	3/ 10 patients	50(35.71)
	4/10 patients	34(24.29)
	>4 patients	26(18.57)

Data presented as n (%).
NSAIDs, non-steroidal anti-inflammatory drugs; OA, osteoarthritis; AS, value added services.

The most common treatment duration with the FDC was 10 days (46.43%), followed by one week (37.14%) (Figure 1).

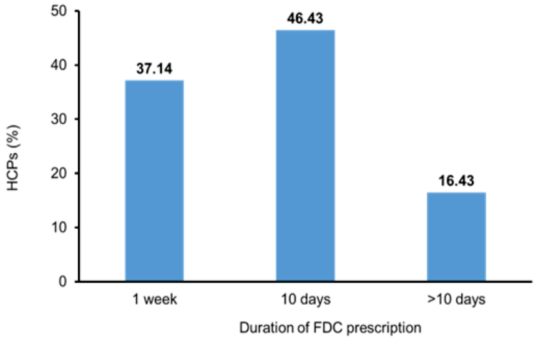

Figure 1: Duration of Prescription for FDC of Aceclofenac, Paracetamol, and Serratiopeptidase in Patients with OA and Bilateral Knee Pain

The majority of HCPs (58.58%) reported that post-treatment with, FDC aceclofenac + paracetamol + serratiopeptidase changed the pain score 5 or lower. Healthcare practionners reported that improved mobility was observed in 51.43% of patients, while 30% could perform routine activities but with some pain. The highest proportion of HCPs (35.71%) reported sleep improvement in more than 4 out of 10 patients with OA and bilateral knee pain. This was followed by 22.14% of HCPs who observed improvement in 3 or 4 out of 10 patients (Table 2).

Table 2: Effectiveness And Safety Of Aceclofenac + Paracetamol + Serratiopeptidase Treatment

Question	Options	Response (N=140)
What was the change in pain score on the VAS scale after treatment of these patients with OA and bilateral knee pain with the FDC of aceclofenac + paracetamol + serratiopeptidase?	0-2	27(19.29)
	3-5	55(39.29)
	6-8	48(34.29)
	9-10	9-10
What was the change in swelling and mobility after treatment of these patients with OA and bilateral knee pain with the FDC of aceclofenac + paracetamol + serratiopeptidase?	Improved mobility	72(51.43)
	Mild impairment of movement	25(17.86)
	Can move and perform routine activities but with pain	42(30)
	Cannot perform routine activities	1(0.71)
In how many of these patients with OA and bilateral knee pain was sleep improved after treatment with the FDC?	1/10 patients	8(5.71)
	2/10 patients	20(41.29)
	3/ 10 patients	31(22.14)
	4/10 patients	31(22.14)
	>4 patients	50(35.71)

Data presented as n (%).
FDC, fixed dose combination; OA, osteoarthritis.

The most common adverse effect was gastritis (62.14%), followed by abdominal pain (9.29%) and nausea (5%) (Figure 2).

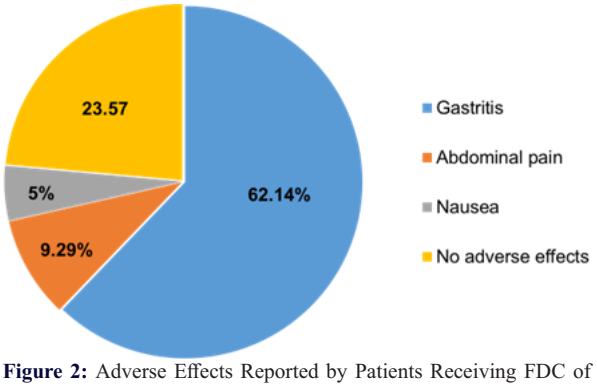

Figure 2: Adverse Effects Reported by Patients Receiving FDC of Aceclofenac, Paracetamol, and Serratiopeptidase

Based on clinical practice, the majority of HCPs (54.29%) reported that 6 to 8 out of 10 patients with OA and bilateral knee pain were satisfied with their pain relief after treatment with the FDC. This was followed by 27.14% of HCPs who observed satisfaction in 5 out of 10 patients. Considering the efficacy and safety of the FDC, the majority of HCPs (51.43%) rated it as "Good," followed by 39.29% who rated it as "Excellent". Furthermore, 95.71% of HCPs indicated a willingness to repeat the treatment in future OA cases. The most common comorbid conditions among patients were hypertension (51.43%), diabetes (43.57%), and ischemic heart disease (5%) (Table 3).

Table 3: Patient Satisfaction And Future Treatment Considerations

Question	Options	Response (N=140)
How many of these 10 patients with OA and bilateral knee pain were satisfied with their pain relief after treatment with the FDC?	2 to 4/10 patients	14(10.00)
	5/10 patients	38(27.14)
	6 to 8 out of patients	76(54.29)
	≥ 9 patients	12(8.57)
Considering the efficacy and safety of the FDC, what rating would you give the FDC of aceclofenac + paracetamol + serratiopeptidase in these patients with OA and bilateral knee pain?	Excellent	55(39.29)
	Good	72(51.43)
	Fair	11(7.86)
	Poor	2(1.43)
Would you consider repeating the treatment with the FDC of aceclofenac + paracetamol + serratiopeptidase in OA with bilateral knee pain?	Yes	134(95.71)
	No	6(4.29)
What were the comorbid conditions in your patients with OA and bilateral knee pain treated with the FDC of aceclofenac + paracetamol + serratiopeptidase?	Hypertension	72(51.43)
	Diabetes	61(43.57)
	IHD	7(5.00)
Data presented as n (%). FDC, fixed dose combination; IHD, ischemic heart disease; OA, osteoarthritis.		

In the comparative analysis, 60.71% of HCPs stated that serratiopeptidase worked better than trypsin-chymotrypsin in certain clinical situations. The primary scenarios where serratiopeptidase was preferred included post-operative recovery (15%), cases with higher adhesion risk (13.57%), and severe swelling not responding to NSAIDs alone (28.57%). Additionally, 37.14% of HCPs supported using serratiopeptidase for one-month post-arthroplasty, while 45.71% preferred its use for 15 days post-surgery (Table 4).

Table 4: Comparative Analysis And Role Of Serratiopeptidase In OA Management

Question	Options	Response (N=140)
How do you compare serratiopeptidase vis-à-vis Trypsin + Chymotrypsin?	They are at par	11(7.86)
	serratiopeptidase is superior	33(23.57)
	In some situation, serratiopeptidase works better	85(60.71)
	Serratiopeptidase is inferior	11(7.86)
If your answer is C in above, then kindly specify those situations:	Post -operative patient	21(15)
	Patients where adhesions are more likely	19(13.57)
	Severe swelling and inflammation not responding to NSAID monotherapy	40(28.57)
	All of the above	60(42.86)
Does Serratiopeptidase FDC help in post-surgery healing in knee arthroplasty?	Yes, post arthroplasty, Serratiopeptidase FDC can be given for one month	52(37.14)
	Yes, post arthroplasty, Serratiopeptidase FDC can be given on and off for 6-18 months depending on prognosis	17(12.14)
	Yes, post arthroplasty, Serratiopeptidase FDC can be given for first 15 days	64(45.71)
	Not Effective	7(5.00)
Data presented as n (%). FDC, fixed dose combination; NSAIDs, non-steroidal anti-inflammatory drugs.		

DISCUSSION

The treatment approach for OA is often influenced by a combination of HCPs' clinical judgment, patient preferences, and the efficacy and safety of available therapies. This study aimed to assess the real-world effectiveness of an FDC of aceclofenac, paracetamol, and serratiopeptidase in managing knee pain associated with OA.

The present study revealed that the significant proportion of patients had previously used NSAIDs and Paracetamol for pain management before initiating treatment with the FDC. This observation aligns with the previous study indicating that certain NSAIDs are among the most effective options for OA pain relief. Among NSAIDs, formulations known for their superior pain relief and tolerability are commonly preferred [11]. Evidence suggests that paracetamol use is associated with significant reductions in pain and improvements in functional capacity, making it a preferred choice [12].

A study conducted by Samma et al. demonstrated that 56.7% of OA patients experiencing severe pain, 38.3% reporting moderate pain, and only 5% having mild pain [13]. The present study also found that pain severity was predominantly rated between 6–8 on the VAS scale (59.29%), indicating moderate to severe pain. These findings highlight the significant burden of knee pain in OA patients.

Prior study had indicated that the aceclofenac-paracetamol combination is both effective and well-tolerated in managing OA flare-up pain, reducing disease severity, and enhancing functional outcomes [7]. Additionally, serratiopeptidase has been shown to further improve pain relief, with evidence suggesting significant reductions in pain scores within a short duration of use [14].

Sleep disturbances due to knee pain, reported in a significant proportion of patients before treatment, showed notable improvement after FDC therapy, reinforcing its role in enhancing overall quality of life. Previously done research indicates that the combination of aceclofenac and paracetamol significantly improves treatment outcomes and quality of life in individuals with arthritis [9]. Serratiopeptidase further enhances this combination by reducing inflammation, improving pain relief, and increasing drug penetration. Its fibrinolytic and wound-healing properties contribute to faster recovery [2].

In this study, gastritis (62.14%) being the most commonly reported adverse event of FDC, followed by abdominal pain (9.29%) and nausea (5%). These findings align to some extent with previous studies on NSAID-related effects. A study by Gundagatti et al. reported similar findings, among aceclofenac users, gastritis was observed in 15%, with abdominal pain and nausea in 2.5% and 7.5%, respectively. In contrast, paracetamol users experienced abdominal pain (21.3%), epigastric pain (6.3%), gastritis (5%), and nausea (43.8) [15]. Among serratiopeptidase-related adverse effects included allergic skin reactions, muscle and joint pain, gastrointestinal disturbances (anorexia, nausea, abdominal upset), and, rarely, pneumonitis [16].

These highlighting NSAID-related gastrointestinal side effects as a primary concern in long-term OA management.

In the current study, 54.29% of HCPs reported high patient satisfaction (6–8/10) with FDC treatment, while 27.14% noted moderate satisfaction. Most rated the FDC as Good or Excellent, with 96% willing to prescribe it again, highlighting its strong acceptance and perceived efficacy in OA management. These findings align with the study by Pant et al. which demonstrated that a similar FDC (Parflex) led to significant reductions in pain scores, with excellent or good global efficacy assessments by 54% of patients and 59% of their treating HCPs [14].

This study assessed the comparative effectiveness of serratiopeptidase versus trypsin-chymotrypsin. More than 50% HCP reported in some situation, serratiopeptidase works better. This finding contrasts with the observations made by chandanwale et al. who stated that trypsin-chymotrypsin produced significantly greater improvements in erythema, local irritation, wound discharge, edema, and pain than serratiopeptidase [17].

The majority of HCPs (60.71%) in this study reported that serratiopeptidase was more effective in post-operative recovery, cases with high adhesion risks, and severe swelling unresponsive to NSAIDs alone, indicating a strong clinical preference for its use in post-surgical care. Previous clinical studies have highlighted its anti-inflammatory, anti-edemic, and fibrinolytic benefits in reducing tissue adhesion and swelling. Widely used in surgery, orthopaedics, ENT, gynaecology, and dentistry, serratiopeptidase remains a valuable therapeutic option for managing inflammation and pain [18]. Previous studies have explored its roles in reducing inflammation, edema, and adhesion formation. A study by Chappi et al. demonstrated that serratiopeptidase effectively controlled swelling and trismus after third molar extractions, showing moderate analgesic activity [19]. Similarly studies by Ai-Khateeb and Nusair as well as Tachibana et al. reported that patients treated with serratiopeptidase experienced significant reductions in post-surgical swelling and pain, including cases of postoperative buccal swelling following Caldwell-Luc antrostomy [20, 21]. These findings support the growing preference for serratiopeptidase in post-surgical and inflammatory conditions.

Limitations

The present study has several limitations. The limited sample size may not fully represent the diverse clinical practices across the country, and a larger sample would enhance the generalizability of the findings. In addition, the data are based on HCPs' perceptions, which may introduce recall bias and limit the accuracy of responses. Moreover, including patients' perspectives would provide a more comprehensive understanding of the efficacy and safety of the montelukast-fexofenadine combination. Finally, the questionnaire-based nature of this study limited responses to predefined options, potentially restricting the depth of insights.

CONCLUSION

This nationwide study explored the perceptions of HCPs across India regarding the FDC of aceclofenac, paracetamol, and serratiopeptidase in managing osteoarthritis-related knee pain. The FDC demonstrated significant pain relief, improved functional capacity, and enhanced patient satisfaction, with a favorable safety profile. Healthcare practitioners widely endorsed its use, with 96% willing to prescribe it again. Additionally, serratiopeptidase was preferred over trypsin-chymotrypsin in specific clinical scenarios, particularly post-operative recovery and severe swelling unresponsive to NSAIDs. These findings highlight the efficacy and acceptance of this combination in OA.

Conflict Of Interest: None

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