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Original Research Article.

Clinical Perspectives on the Effectiveness and Safety of Polmacoxib in Pain Management: A Survey of Clinicians Across India

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ABSTRACT

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for the management of pain and inflammation, and they primarily act through COX-1 and COX-2 inhibition. While selective COX-2 inhibitors provide reduced gastrointestinal side effects, cardiovascular safety is still a concern. Polmacoxib, a novel NSAID, shows dual inhibition of COX-2 and carbonic anhydrase (CA). Thus, it may offer improved safety, but there is a dearth of real-world data in India.

Introduction: The study aimed to assess the clinical use of polmacoxib in India, focusing on effectiveness, side effects, clinicians' satisfaction, and its future potential.

Methods: A structured survey form was distributed to 2,740 clinicians, including general practitioners, orthopaedic surgeons, and other specialists, across India. Data on indications, dosing, side effects, and clinician satisfaction were collected.

Results: Out of all the respondents, 30% prescribed polmacoxib to >20 patients each, with 79.5% prescribing it primarily for chronic pain. Most found it more effective than other analgesics, with 48.1% reporting favourable safety profiles. The most common side effect was oedema (8.8%). High satisfaction was observed among respondents, and they were optimistic about the future of polmacoxib in India.

Discussion: Polmacoxib demonstrated promising effectiveness and safety, particularly for chronic pain management.

Keywords: Analgesic, Anti-Inflammatory Drugs, Pain, Polmacoxib.

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INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for their analgesic, antipyretic, and anti-inflammatory properties. These pharmacological effects are primarily achieved through the inhibition of cyclooxygenase (COX) enzymes. COX enzymes exist in two isoforms: COX-1 and COX-2. COX-1 is responsible for producing prostaglandins and thereby protecting the gastric mucosa and facilitating platelet aggregation. While COX-2 is induced during inflammatory processes and produces prostaglandins contributing to pain, fever, and inflammation.[1]

The conventional NSAIDs are nonselective, inhibiting both COX-1 and COX-2. However, selective COX-2 inhibitors target only COX-2 isoform. This selective action reduces the risk of gastrointestinal side effects by preserving the protective effects of COX-1 on the stomach lining, while still providing anti-inflammatory benefits.[1,2] The Osteoarthritis Research Society International (OARSI) guidelines recommend COX-2 inhibitors for patients with gastrointestinal comorbidities, as they are safer options as compared to nonselective NSAIDs and COX-1 inhibitors.[3] However, the use of COX-2 inhibitors has been associated with an increased risk of cardiovascular side effects, including myocardial infarction and elevated blood pressure, leading to safety concerns.[4,5]

The withdrawal of certain COX-2 inhibitors, such as valdecoxib and rofecoxib, due to their association with cardiovascular risks further emphasises the need for safer alternative medications. This has led to the development of novel NSAIDs that combine effective analgesic effect with a more favourable safety profile, particularly regarding gastrointestinal and cardiovascular health.[6,7]

Polmacoxib, a first-in-class NSAID inhibiting both COX-2 and carbonic anhydrase (CA) enzymes, was first approved in South Korea in 2015 for the treatment of osteoarthritis and colorectal cancer. Unlike traditional NSAIDs, polmacoxib offers a dual mechanism of action. In India, polmacoxib (2 mg) was approved by the Central Drugs Standard Control Organisation on 14

February 2023 for the treatment of idiopathic (primary) osteoarthritis of the hip and knee. This unique dual-action mechanism sets polmacoxib apart from other COX-2 inhibitors, as most do not show significant activity against CA.[2,8-10]

The cardiovascular system has both COX-2 and CA, with CA being excessively present in blood, blood vessels, and cardiovascular tissues. Polmacoxib demonstrates a higher affinity for CA than for COX-2 in these tissues, reducing its COX-2 inhibitory effects in the cardiovascular system. This dual action may help mitigate the cardiovascular risks typically associated with COX-2 inhibition. Furthermore, the low dose of polmacoxib has minimal impact on CA function within the cardiovascular system. Whereas, inflamed tissues, such as those found in osteoarthritic joints, have low levels of CA and increased COX-2 expression. In these areas, polmacoxib effectively inhibits COX-2, thereby reducing pain and inflammation without significantly affecting CA activity.[2,9]

The dual mechanism of action of polmacoxib suggests a potentially improved safety profile, especially in reducing cardiovascular risks compared to traditional COX-2 inhibitors. However, there is limited real-world data on its use, side effects, and overall acceptance among healthcare providers in India. The aim of this study was to fill this gap by surveying clinicians across specialties on their experience with polmacoxib. We evaluated dosing frequency, side-effect profiles, and clinicians' satisfaction with its effectiveness and safety. Additionally, the study explored the opinion of clinicians regarding the future potential of polmacoxib in India.

MATERIALS AND METHODS

A purposive sampling approach was used to collect data for this study. A structured questionnaire was distributed to 2,740 clinicians across various states in India. The various participants included general practitioners, consultant physicians, orthopaedic surgeons, general medicine specialists, diabetologists, endocrinologists, surgeons, gynaecologists, cardiologists, pulmonologists, rheumatologists, otolaryngologists, neurologists, physiotherapists, dermatologists, critical care specialists, pain management and rehabilitation consultants, and spine specialists.

The survey form gathered detailed information on various aspects of polmacoxib treatment, including dosage, duration, indications, observed side effects, and overall treatment outcomes. Participants were also asked to estimate the approximate number of patients they had treated with polmacoxib.

Clinicians who were unwilling to participate were excluded from the study, along with those lacking prior experience with polmacoxib in clinical practice or those actively involved in the research and development of polmacoxib. The responses were systematically recorded, tabulated, and analysed to assess clinicians' attitudes towards polmacoxib.

RESULTS

A total of 2,740 clinicians participated in the study. Analysis of the geographic distribution of participants indicated that a majority of respondents were based in Karnataka (13.68%), Tamil Nadu (12.90%), Uttar Pradesh (10.66%), Maharashtra (10.51%), Andhra Pradesh (7.32%), Gujarat (6.80%), Telangana (6.25%), Rajasthan (5.70%), and Odisha (4.41%). About 58.83% of the respondents were orthopaedic surgeons, 26.50% were consultant physicians, 12.66% were non-surgical medical specialties, 1.79% (gynaecologists and general surgeons) were surgical specialties and 0.22% were classified under miscellaneous clinician category.

Approximately 30% of respondents reported having prescribed polmacoxib to >20 patients each, with all remaining clinicians treating ≥5 patients each with this medication. The survey results were consistent, with most clinicians (79.5%) reporting use of polmacoxib primarily for chronic pain. However, as shown in Table 01, polmacoxib was prescribed for both acute and chronic pain management.

Approximately 76.2% of clinicians found polmacoxib to be more effective in pain management compared to other analgesics, including NSAIDs. Additionally, 48.1% of respondents considered polmacoxib to have favourable renal, cardiac, and gastrointestinal safety profiles, with minimal side effects. The most frequently reported side effect, noted by 8.8% of clinicians, was oedema (generalised, facial, or pedal). Most clinicians (93%) indicated that they prescribed a once-daily dose of polmacoxib, which they believed improved patient compliance. A few clinicians also prescribed polmacoxib twice daily treatment regimen. As shown in Figure 01, clinicians rated their satisfaction with polmacoxib on a scale of 1 to 5 (5 being the highest), with 35% rating it as 5, 44% as 4, and 16% as 3. When asked about the future of polmacoxib in India, only 5% of the clinicians were not satisfied with treatment, rating it as 1 or 2 on the scale as illustrated in Figure 02.

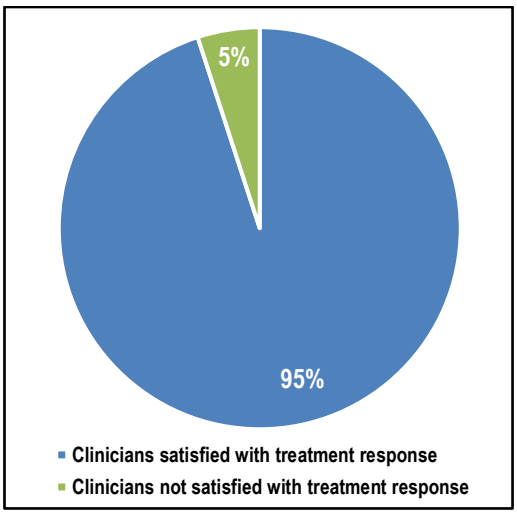

Figure 1: Clinicians' satisfaction with treatment response

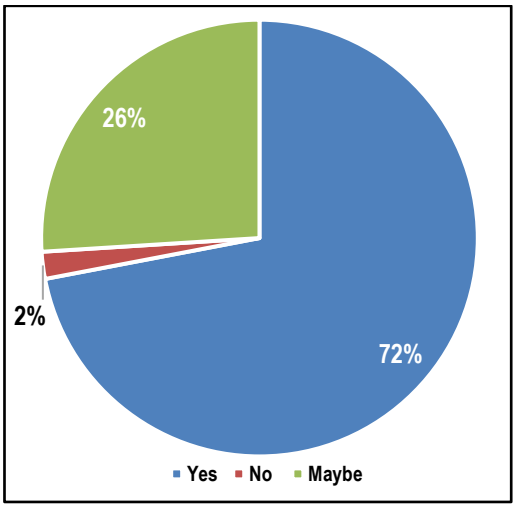

Figure 2: Clinicians' opinion on the future of polmacoxib in India

Table 1: Indications for which polmacoxib was prescribed by clinicians

Indication	Percentage
Acute pain	4.1%
Chronic pain	79.5%
Arthralgia	8.0%
Spine pain	5.0%
Others	3.4%

DISCUSSION

This study provided valuable information about the real-world experiences and perspectives of Indian clinicians on the effectiveness and safety of polmacoxib in managing acute and chronic pain. The results indicates that polmacoxib is more effective than other NSAIDs and has favourable renal, cardiac, and gastrointestinal safety profiles, with minimal side effects. About 93% of the participating clinicians prescribed it once daily that helped them achieve improved dose compliance. Notably, the side-effect profile observed in our study was mild, with oedema being the most frequently reported side effect.

The currently available treatment options have several side effects associated with them and include gastrointestinal complications and toxicity, cardiovascular incidents, nausea, constipation, fatigue xerostomia and decreased appetite. However, polmacoxib has favourable gastrointestinal, cardiovascular, and renal profile. Studies also suggest that the efficacy of polmacoxib is noninferior to traditional NSAIDs and celecoxib indicating the advantage of polmacoxib over the currently used treatment options. The safety advantage of polmacoxib is due to the tissue-selective COX-2 inhibition mechanism of polmacoxib. The gastrointestinal and renal regions are the primary areas where NSAIDs and coxibs affect adversely. However, the COX-2 inhibition with CA binding potential of polmacoxib demonstrates attenuated COX-2 binding in the gastrointestinal tract and kidney, which might lead to fewer side effects associated with COX-2 inhibition in those organs.[10]

Lee M et al conducted a phase III trial and evaluated the safety and analgesic efficacy of polmacoxib 2 mg compared to placebo and celecoxib 200 mg in patients with osteoarthritis. Over six weeks, polmacoxib demonstrated superior efficacy to placebo, with a significant reduction in pain as measured by the Western Ontario and McMaster Universities (WOMAC) pain subscale (treatment difference of –2.5, p = 0.011). However, it was noninferior to celecoxib (treatment difference of 0.6, p = 0.425). At week 3, more patients on polmacoxib were assessed as "much improved" by the physician compared to those on celecoxib or placebo. While gastrointestinal and general disorders were more frequent in the polmacoxib and celecoxib groups, the side effects were relatively mild, suggesting a better tolerability profile than traditional NSAIDs. The open-label extension phase (18 weeks) showed consistent results, supporting the long-term safety and efficacy of polmacoxib. These findings highlight the potential of polmacoxib as an effective analgesic for osteoarthritis with a favourable gastrointestinal safety profile, making it a promising alternative to conventional NSAIDs in managing chronic pain.[9]

Another clinical trial by Schmidt WK et al assessed the safety and efficacy of polmacoxib at high, moderate and low doses [initial loading dose for one day (8 mg, 4 mg or 2 mg, respectively) and maintenance dose for 20 days (1.2, 0.6 or 0.3 mg/day, respectively)]. The results demonstrated a significant improvement in osteoarthritis symptoms compared to placebo, as evidenced by a median value of 37% improvement at Day 21 in the WOMAC score versus median value of 17% for placebo (p = 0.01). The high-dose group also showed significant benefits across secondary endpoints, including WOMAC osteoarthritis scores (p = 0.010) over the entire 21-day treatment period and WOMAC subscales of pain (p = 0.016), stiffness (p = 0.023), and physical function (p = 0.010) over the treatment and follow up period indicating sustained improvements. The rapid onset of action and sustained efficacy of polmacoxib were further supported by statistically significant pain relief at all assessment points (Days 7, 14, 21, and 28, p < 0.05). Importantly, no significant cardiovascular or gastrointestinal side effects were observed, with no instances of gastrointestinal bleeding. These results suggested that polmacoxib offers a promising treatment for osteoarthritis, providing effective pain relief and functional benefits without the common gastrointestinal and cardiovascular risks associated with traditional NSAIDs.[11]

Sinha SD et al conducted a randomized, double-anonymous study in 294 patients with idiopathic knee or hip osteoarthritis and compared the safety and efficacy of polmacoxib 2 mg versus celecoxib 200 mg. The results indicated a significant decrease in WOMAC pain score from 13.24 at baseline to 8.22 (mean difference 4.88; $p \leq 0.0001$) at week 6 of treatment with polmacoxib versus 13.29 at baseline to 8.47 (mean difference 4.49; $p \leq 0.0001$) at week 6 of treatment with celecoxib. The difference between polmacoxib versus celecoxib group in change in mean WOMAC pain subscale score was 0.37 (95% CI: −0.33, 1.07; p = 0.2950). The upper limit of one-sided 97.5% CI (1.07) of the difference in WOMAC pain subscale score between the two groups was within the predefined non-inferiority margin of 2 units. The reduction in VAS were similar between the two groups over the 6-week treatment period. The number of adverse events reported in polmacoxib, and celecoxib group were 18 and 40, respectively, and all the event were mild in nature with no serious event being reported in the study. They concluded that polmacoxib 2 mg demonstrated a positive tolerance profile and was non-inferior to celecoxib in efficacy in Indian patients with osteoarthritis, and polmacoxib presents fewer gastrointestinal side effects than traditional NSAIDs commonly prescribed for osteoarthritis.[12]

The outcome of our study aligns with published clinical trials showing that polmacoxib is effective for the management of pain, and the side effects of polmacoxib are generally limited to minor, reversible symptoms, without the gastrointestinal and cardiovascular risks associated with other NSAIDs. Polmacoxib can be considered a safer option for long-term pain management as compared to other NSAIDs. In addition to the effectiveness and safety, the once-daily dosing regimen was well-received by clinicians, who noted that it promotes patient adherence, a critical factor in managing chronic conditions where compliance is often challenging. The surveyed clinicians expressed optimism about the potential role of polmacoxib in India, suggesting a strong interest in its broader application in pain management. This sentiment is particularly encouraging, given that chronic pain is a major public health concern, with substantial socio-economic impacts and limited long-term therapeutic options that balance effectiveness and safety.

CONCLUSION

This survey provides data about the real-world use of polmacoxib in India, with a diverse group of healthcare professionals across various specialties. These findings suggest that polmacoxib is emerging as a preferred option among clinicians for chronic pain management, particularly in osteoarthritis, and is perceived as more effective than other analgesics, including traditional NSAIDs. The once-daily dosing regimen has contributed to high levels of clinician satisfaction, with most reporting improved patient compliance. Furthermore, polmacoxib appears to offer a favourable safety profile, with minimal side effects, particularly in terms of gastrointestinal, renal, and cardiac health. Given the positive feedback on both its effectiveness and safety, there is optimism about the future role of polmacoxib in the management of pain in conditions like osteoarthritis. Future research, including larger, long-term studies, is required to further confirm these findings.

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