

Original Research Article

The impact of non-steroidal anti-inflammatory drugs use in elderly cardiovascular patients: an observational study from tertiary care in South India

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ABSTRACT

Background: Long-term use of NSAIDs, by patients having cardiovascular conditions, has shown to increase the risk of cardiovascular events and increased risk of death. Hence, the study was conducted to determine the complications related to NSAID use by the elderly patients with cardiovascular disease (CVD).

Methods: The study was a single-center prospective observational study conducted November 2017 to October 2018. Elderly patients (>60 years) suffering from various CVDs and reported NSAID intake daily for at least one month were included. A questionnaire included demographic, treatment related history and complete details of NSAIDs intake including nature, dose, indication, source etc. The same questionnaire was again filled at the end of one-year follow-up.

Results: A total of 100 participants were included in the study. The mean age was 72±8.6 years. Majority of the patients (93%) had hypertension, and 69% of the patient had previous MI. Five NSAIDs (diclofenac, ibuprofen, mefenamic acid, naproxen, and ketorolac) were used routinely. At least one over the counter NSAID used was reported by 86%, 57% were prescribed at least one NSAIDs by their orthopaedics and physicians. At the end of 1-year follow-up, authors found that 71% had MI (2% increase), 4% developed reinfarction, 20% had severe left ventricular failure (4% increase), 7% had atrial fibrillation (1% increase), and 2% patients died and 63% patients reported raise in systolic blood pressure by 5mmHg.

Conclusions: High prevalence of concomitant NSAID use among elderly CVD patients, which might be contributing towards increase in CVS morbidity and mortality.

Keywords: Arterial hypertension, Adverse effect, Cardiovascular disease, cardiovascular risk, Elderly, Heart failure, NSAID

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are most frequently used to treat pain and inflammatory conditions as compared to the other classes of drugs in the geriatric population. The major conditions where NSAIDs are used by elderly people include osteoarthritis,

rheumatoid arthritis, gout, and chronic pain in geriatric population.¹ The mechanism of action of NSAIDs involves inhibiting cyclooxygenase (COX) enzyme. The COX enzymes are responsible for inducing prostaglandins (PG) synthesis which causes pain and swelling in the affected areas.² Although NSAIDs are beneficial agents

which act as analgesic, antipyretic, and anti-inflammatory; they are also associated with different adverse events, especially in the geriatric population.^{3,4}

Long-term use of NSAIDs, by patients having cardiovascular conditions, has shown to increase the risk of hospital admission, reinfarction, atrial fibrillation, cerebrovascular accidents, and gastrointestinal bleeding along with increased risk of myocardial infarction (MI) and death.³

A study by Pawlosky N et al, showed that even a short-term use of NSAIDs for less than 90days could increase the risk of serious coronary conditions.⁵ The study observed relative risk of coronary adverse events with different NSAIDs like ibuprofen (incidence rate ratio (IRR): 1.67; 95% CI: 1.09 - 2.57), diclofenac (IRR: 1.86; 95% CI: 1.18 - 2.92), and rofecoxib (IRR: 1.46; 95% CI: 1.03-2.07). Another study on NSAID reported that long-term use of NSAIDs increases blood pressure by up to 5 mm Hg and also antagonize the action of blood pressure lowering drugs like beta-blockers.⁶ Focusing specifically on the geriatric population with a history of MI or other cardiovascular disorders, a study reported increased risk of cardiac complications and deaths with long-term NSAIDs use.⁷

The present study was designed to assess the prevalence of NSAID usage and to study the incidence of cardiac events with the usage of NSAIDs in an elderly population with cardiovascular conditions (CVS) living in the southern part of India.

METHODS

The single-center study was conducted at Physicians of cardiology and internal medicine department participated in the study as investigators. The study duration was one year conducted from November 2017 to October 2018. Written informed consent was taken from all the participants, and the study protocol was approved by the local ethics committee. The study was conducted in accordance with good clinical practice (GCP) as required by the international conference on harmonization (ICH) guidelines, ethical guidelines for biomedical research on human subjects (ICMR, 2006) and declaration of Hurst SA et al.⁸ A total of 100 patients were selected based on the exclusion and inclusion criteria.

Inclusion criteria

- Patients aged >60 years,
- Attending cardiology department with cardiovascular symptoms,
- Using NSAIDs on a daily basis for at least one month.

Exclusion criteria

- Patient age <60 years,

- Not given consent to the study.

A thorough questionnaire was developed for the study. The demographic data, medical history including prior addictions to smoking, alcohol, history of NSAIDs intake including the name of the medications, frequency of intake, indications of use, duration of use, whether prescribed or taken over the counter and history of concomitant medications were collected from all patients using the questionnaire. The patients were asked to fill the form at both the starting and ending of the study duration.

Statistical analysis

Data was analyzed by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. IBM SPSS statistical software version 21 was used for data analysis.

RESULTS

The mean age of the patients was 72±8.6 years. The majority of the patients (93%) had hypertension, and 69% of the patient had previous MI. 46% of the patients were treated with PTCA. Osteoarthritis was the most common (34%) concomitant condition among the patients who required treatment with NSAIDs. All the baseline demographic and clinical characteristics are summarized in Table 1.

Table 1: Baseline demographic and clinical characteristics of patients.

Characteristics	N=100
Mean age	72±8.6
Males	62 (62%)
Chronic Smoker	17 (17%)
Occasional alcohol use	28 (28%)
Hypertension	93 (93%)
Diabetes	34 (34%)
Renal disorder	22 (22%)
Previous MI	69 (69%)
Severe left ventricular failure	16 (16%)
Atrial fibrillation	6 (6%)
Previous CABG	14 (14%)
Previous PTCA	46 (46%)
Concomitant conditions	
Osteoarthritis	34 (34%)
Rheumatoid arthritis	8 (8%)
Cancer pain	4 (4%)
Gout	11 (11%)

MI: Myocardial infarction; PTCA: Percutaneous transluminal coronary angioplasty; CABG: Coronary artery bypass grafting

The questionnaire revealed that 5 NSAIDs were used routinely which were diclofenac, ibuprofen, mefenamic acid, naproxen, and ketorolac. Diclofenac was used by 72% patients, 10% patients were using ibuprofen, 10%

patients were using naproxen and 4% patients were using Mefenamic acid, and 4% patients were using ketorolac. 86% of the patients were using at least one over the counter drugs without a prescription while 57% were prescribed at least one NSAIDs by their orthopedics and physicians. The majority of the patients were using NSAIDs for knee pain (42%) and low back pain (27%). 16% of the patients were using these drugs for >20 years. The NSAIDs usage information is given in (Table 2).

Table 2: NSAIDs usage information.

Drug usage	N=100
Diclofenac	72%
Ibuprofen	10%
Naproxen	10%
Mefenamic acid	4%
Ketorolac	4%
At least one OTC NSAIDS	86%
At least one NSAID drug prescribed	57%
Indication for use	
Knee pain	42%
Lower back pain	27%
Upper back and neck pain	14%
Leg pain	7%
Hand and wrist pain	7%
Headache	3%

At the end of 1-year follow-up, authors found that 71% had MI (2% increase), 4% developed reinfarction, 20% had severe left ventricular failure (4% increase), 7% had Atrial fibrillation (1% increase), and 2% patients died and 63% patients reported an increase in systolic blood pressure by 5 mmHg. These findings suggest that 13% of the cardiovascular patients taking NSAIDs observed a cardiovascular complication (Table 3).

Table 3: Increase in number of patients with cardiac complication at 1-year.

Cardiac condition	Total (N=100)	% Increase at 1 yr
MI	71%	2
Severe left ventricular failure	20%	4
Atrial fibrillation	7%	1
Reinfarction development	4%	4
Deaths	2%	2
Total increase in complications	13%	
Increase in blood pressure by 5 mmHg	63%	

DISCUSSION

The follow-up at 1 year suggests that 13% of cardiovascular patients taking NSAIDs experiences either exaggeration in their symptoms or develop new cardiovascular complications over the time. Observations

suggest that use of NSAIDs is exaggerated in the Indian population. Even though different variable categories of drugs are available, most patients in India are either prescribed NSAIDs or take NSAIDs without a prescription.⁹ The present study also present the similar data and identified that 86% of the patients in the study were using at least one non-prescribed (OTC) NSAIDs while 57% were prescribed at least one NSAIDs for different conditions.

Pawlowsky N et al, elucidates that the usage prevalence of NSAIDs is higher in the geriatric population as compared to the younger generation because of the different comorbid conditions.⁵ The present study suggested that Indian geriatric patients with CVS diseases are compelled to take NSAIDs to manage muscular and skeletal pains and inflammations related to comorbid conditions like osteoarthritis (34%), gout (11%), rheumatoid arthritis (8%), and cancer pain (4%). These patients had major complaints of muscular or skeletal pain in knees, lower back, upper back, neck, legs, hands, wrists, and head.

While observing the cardiovascular risks in the patients treated with NSAIDs, one must consider the fact that the relative risk depends on the frequency and duration of the therapy. The present study found that the prevalence of MI increased by 2% in the study population, 4% patients had reinfarction and 2% patients died. A large cohort study investigating NSAID use after an MI reported that the hazard ratio for repeat MI and reinfarction increases (HR: 1.56 at 90 days) in CVS patients with increased duration of NSAID consumption.¹⁰

Around 63% patients in the present study experienced an increase in systolic BP by 5mm Hg at one-year follow-up. Multiple studies have identified that NSAIDs antagonize the antihypertensive actions of beta-blockers and thus affect the blood pressure management. This negative impact of the NSAIDs is more prominent in community-dwelling elderly patients. An increase in hypertension-related morbidity and mortality has also been reported in the CVS patients taking NSAIDs.^{6,11,12}

A case-control study done in four European countries found that use of seven traditional NSAIDs (diclofenac, ibuprofen, indomethacin, ketorolac, naproxen, nimesulide, and piroxicam) and two COX 2 inhibitors (etoricoxib and rofecoxib) increases the risk of heart failure, related hospitalization, and death by 1.16 to 1.83 times when they are taken in high doses (>2 times the daily recommended dose).¹³ The present study reflected similar observation as it reported a 4% increase in the case of severe left ventricular failure in the study patients. However, in the present study, authors did not perform a dose-dependent analysis of the complication outcomes.

Atrial fibrillation (AF) is another condition which is reported to exacerbate with the use of NSAID. It has also been reported that newly diagnosed AF patients are at

higher risk of developing exacerbations with concomitant non-aspirin NSAID use.^{14,15}

Authors were surprised to observe that patients were receiving a prescription for non-aspirin NSAIDs (57%) from orthopedics and physicians even though they were aware of their CVS status. Diclofenac (prescribed as well as OTC) which is considered to be a non-safe drug for used in CVS patients was taken by 72% of the study patients. These findings suggest that extensive awareness about NSAID abuse and its impact on overall health status of CVS patients is required.^{13,14}

Citing the recommendations by the American college of rheumatology, we recommend that the CVS patients must discuss their NSAID usage extensively with their cardiologists, orthopedics, and physicians to avoid untoward outcomes.¹⁶

Also, pain management with physical and occupational therapies is must be preferred over pharmacological agents. For pharmacologic therapy, acetaminophen must be prescribed with a daily dose no greater than 4000 mg. Patients who are poor candidates for surgery, who are refractory to opioid analgesics and who are above the age of 75 years must be treated with topical NSAIDs (especially topical diclofenac).

Citing the recommendations of the 2012 American geriatrics society beers criteria, we also advise to avoid indomethacin and ketorolac in CVS patients.¹⁷

The study concluded that the usage of NSAIDs in the patients with CVS ailments increases the prevalence of CVS morbidity and mortality. Use of NSAIDs must be done with caution in such patients and as per the recommendation of reputed clinical authorities. The study did not include a case-control patient cohort to provide a relative risk of the complications.

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REFERENCES

1. Bekkering GE, Bala MM, Reid K, Kellen E, Harker J, Riemsma R, et al. Epidemiology of chronic pain and its treatment in the Netherlands. *Neth J Med.* 2011;69(3):141-53.
2. Thomas MA. Pain management—the challenge. *Ochs J.* 2003;5(2):15-21.
3. Day RO, Graham GG. Non-steroidal anti-inflammatory drugs (NSAIDs). *BMJ.* 2013;346:f3195.
4. Balmaceda CM. Evolving guidelines in the use of topical nonsteroidal anti-inflammatory drugs in the treatment of osteoarthritis. *BMC Musculoskeletal Dis.* 2014;15(1):27.
5. Pawlosky N. Cardiovascular risk: are all NSAIDs alike? *Can Pharm J.* 2013;146(2):80-3.
6. Johnson AG, Nguyen TV, Day RO. Do nonsteroidal anti-inflammatory drugs affect blood pressure? A meta-analysis. *Annals Int Med.* 1994;121(4):289-300.
7. Harirforoosh S, Asghar W, Jamali F. Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications. *J Pharm Pharm Sci.* 2014;16(5):821-47.
8. Hurst SA. Declaration of Helsinki and protection for vulnerable research participants. *JAMA.* 2014;311(12):1252.
9. Chatterjee S, Dureja GP, Kadhe G, Mane A, Phansalkar AA, Sawant S, et al. Cross-sectional study for prevalence of non-steroidal anti-inflammatory drug-induced gastrointestinal, cardiac and renal complications in India: interim report. *Gastroenterol Res.* 2015;8(3-4):216.
10. Schjerning Olsen AM, Fosbøl EL, Lindhardsen J, Folke F, Charlot M, Selmer C, et al. Duration of treatment with nonsteroidal anti-inflammatory drugs and impact on risk of death and recurrent myocardial infarction in patients with prior myocardial infarction: a nationwide cohort study. *Circulat.* 2011;123(20):2226-35.
11. Snowden S, Nelson R. The effects of nonsteroidal anti-inflammatory drugs on blood pressure in hypertensive patients. *Cardiol Rev.* 2011;19(4):184-91.
12. Fosbøl EL, Gislason GH, Jacobsen S, Folke F, Hansen ML, Schramm TK, et al. Risk of myocardial infarction and death associated with the use of nonsteroidal anti-inflammatory drugs (NSAIDs) among healthy individuals: a nationwide cohort study. *Clinic Pharmacol Therapeut.* 2009;85(2):190-7.
13. Arfè A, Scotti L, Varas-Lorenzo C, Nicotra F, Zambon A, Kollhorst B, et al. Safety of non-steroidal anti-inflammatory drugs (SOS) project consortium. Non-steroidal anti-inflammatory drugs and risk of heart failure in four European countries: nested case-control study. *BMJ.* 2016;354:i4857.
14. Guo Y, Tian Y, Wang H, Si Q, Wang Y, Lip GY. Prevalence, incidence, and lifetime risk of atrial fibrillation in China: new insights into the global burden of atrial fibrillation. *Chest.* 2015;147(1):109-19.
15. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation: analysis and implications. *Archives Int Med.* 1995;155(5):469-73.
16. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American college of rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res.* 2012;64(4):465-74.

17. Campanelli CM. American geriatrics society updated beers criteria for potentially inappropriate medication use in older adults: the American geriatrics society 2012 beers criteria update expert panel. *J Am Geriat Soci.* 2012;60(4):616.

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