



USAGE OF NSAIDs AND ITS DRUG INTERACTION WITH OTHER CONCURRENTLY PRESCRIBED DRUGS IN ELDERLY PATIENTS

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ABSTRACT

As the population ages, care of older patients is becoming increasingly important. With age comes an increased incidence of chronic disease and disabilities, often accompanied by pain. Pain control is fundamental to maintaining quality of life, and NSAIDs are commonly prescribed for control of pain and inflammation in elderly patients. It is a highly effective drug class for pain and inflammation; however, NSAIDs are known for multiple adverse effects, including GI bleeding, cardiovascular side effects, and NSAID induced nephrotoxicity. The presence of polypharmacy is more frequent among those who reported diseases of the circulatory system, endocrine, nutritional and metabolic diseases and diseases of the digestive tract which are more common in elderly population and also increases the chances of drug interaction. Self-medication is highly prevalent in elderly people who are unaware of risks involved. However, self-medication may leads to unwanted consequences due to interactions with the prescribed drug therapy for chronic diseases. Knowledge on the part of doctors as well as patients about self-medication practices would help in reducing the chances of any untoward consequences. It is the duty of pharmacist to provide these types of knowledge to doctors as well as patient.

KEYWORDS: Non steroidal anti-inflammatory drugs, Cyclooxygenase, Prescription pattern, Polypharmacy, Drug interaction, Self medication.

INTRODUCTION

Felix Hoffman discovered acetylsalicylic acid in 1897 and the first non-steroidal anti-inflammatory drug (NSAID) was determined. NSAIDs are the frequently used drugs on account of their anti-pyretic, anti-inflammatory, and analgesic properties.^[1] They are one of the most commonly prescribed classes of medications for pain and inflammation control and are also available as over the counter. They account for approximately 5-10% of all medications prescribed each year.^[2] Due to their lenient availability, more than 30 million people throughout world use NSAIDs every day.^[1] However, they have wide range of side effects.^[1] Their chronic use is associated with a well known spectrum of side effects, in particular those involving the gastrointestinal system, cardiovascular system as well as renal system. Certain cyclooxygenase (COX)-2-selective drugs rofecoxib and valdecoxib were withdrawn from the market because of their cardiovascular toxicity.^[3]

Before twenty year, it was presented that the mechanism of action of NSAIDs was through their inhibition of prostaglandin biosynthesis. After that, it

has been accepted that these drugs work by inhibition of the enzyme COX. Now we know that COX has at least two different isoform. One is constitutive isoform, COX-1, and another is inducible isoform, COX-2.^[4] Activation of first one leads to the production of prostacyclin. When prostacyclin released from endothelium it acts as antithrombogenic agent and when released by the gastric mucosa it acts as cytoprotective agent. The later one is induced by inflammatory mediators in migratory and other cells. Hence It is suggest that the anti-inflammatory actions of NSAIDs are due to inhibition of COX-2, and the undesirable effects, such as irritation of the gastrointestinal mucosa, are due to inhibition of COX-1.^[4]

A Brazilian study in elderly patients indicated a mean drug consumption of two to four drugs per person per day.^[5] The elderly consume a disproportionate amount of prescription and nonprescription medications. The increase in drug consumption among the elderly population might be due to the prevalence of chronic diseases, the physiology of aging,

the influence of the pharmaceutical industry on prescriptions and the medicalization that is common in the training of the health professionals.^[5] Thus, inappropriate medication use is highly prevalent among elderly patients (age ≥ 65 years).^[6]

Virtually all medications can produce undesirable side effects. The elderly are more likely to experience adverse drug reactions (ADRs) as a result of age-related increases in the frequency of drug use, sensitivity to drug effects, and prevalence of predisposing conditions that can increase the frequency and severity of ADRs.^[7] Thus, elderly patients are highly susceptible to polypharmacy, which may cause drug-drug interactions (DDIs) and ADR related complications and hospitalizations.^[7] The risk of ADRs is 13% when an individual consumes two drugs, 58% for those who use five drugs and 82% among those who consume seven or more drugs.^[5] Approximately 15% of hospital admissions caused by ADRs are the result of drug interactions and the risk of drug interactions are higher among the elderly population.^[5]

In the elderly, an estimated 29% of fatal peptic ulcer complications may be due to NSAIDs.^[8,9] It is well known that NSAIDs induce gastrointestinal (GI) adverse effects, including serious complications such as upper GI bleeding, perforation, obstruction, and death. So gastro-protective agents like H₂ blockers or proton pump inhibitors should be co-prescribed in patients using these NSAIDs for long time.

In 2015, Ussai *et al.*, did a retrospective study of 3,050 subjects with chronic pain and found that 97% of those with chronic pain took NSAIDs for more than 21 consecutive days.^[10] Considering this professional societies, including American Geriatric Society, American College of Rheumatology, and the European League against Rheumatism, recommend using NSAIDs with caution and limit their use to the lowest effective dose and shortest duration and when used, common gastrointestinal, renal and cardiovascular side effects should be routinely monitored as the prevalence of inappropriate use of NSAIDs is of concern.^[2,11,12]

Appropriate use of medications remains an important goal. ADRs are common and accompanied by a significant risk of morbidity.^[13] Although initially viewed as a safer alternative in this particular population, emerging evidence suggest that the adverse effects on a variety of end organ systems may sometimes outweigh the analgesic benefits.

Prescription pattern analysis

A study conducted on elderly population with a family health program showed that anti-inflammatory and analgesics were used by 28.8% elderly persons.^[14] Among the classes of anti-inflammatory and analgesic, 70.6% ingested non-opioid analgesics, 41.7% ingested NSAIDs, 16.5% used glucocorticoids and 1.4% took

opioid analgesics. Self-perception of health was found to be related to the use of anti-inflammatories and analgesics, with the worse the health reported by the elderly person, the greater the use of medications.^[14] Liver disease and osteoarthritis/arthritis/ rheumatism were found to be associated with the use of anti-inflammatories and analgesics, with 46.0% and 37.5% elderly persons suffering from these conditions, respectively. It was observed that the higher the usage of medications in general, the greater the use of anti-inflammatory and analgesics.

In a study which was conducted in Jordan by Qoul *et al.*, a total of 25,692 prescriptions were reviewed.^[15] 52% of the collected prescriptions had NSAIDs. Out of this, 40.6% was prescribed for elderly patients (aged 60-80). The average number of drugs per prescription was 3.76 with a range of 1-8 drugs. About 72% of the patients used 3 or more medications. 58.3% of NSAIDs were used for osteoarthritis, 20.1% for orthopedic pain, 12.1% for rheumatoid arthritis, and 9.5% for other musculoskeletal disorders. Diclofenac was the most frequently prescribed NSAID with 83.74%. Dosage forms included tablet (58.72%), gel (18.24%), and suppository (5.78%). Ibuprofen tablet and Indomethacin capsule accounted for 5.63% and 3.84% of all NSAID-containing prescriptions respectively. Concomitant therapy with gastro-protective agents were reported in 71.16% of prescriptions. Famotidine was the most commonly prescribed one (86.30%), followed by antacid (10.85%) and omeprazole (2.85 %).

A prospective study on medication prescribing pattern for geriatric patients in a tertiary care teaching hospital found that NSAIDs (diclofenac, mefenamic acid) prescribed to 56.4% of the geriatric patients were regarded as potentially inappropriate.^[16]

Incidence of polypharmacy among NSAID elderly users

In a study conducted in Brazil, 10.30% of the 573 elderly respondents reported the regular use five or more medications.^[17] In terms of health conditions, elderly individuals who used public health services and who described their health as poor or very poor were associated with the use of polypharmacy. The presence of polypharmacy was more frequent among those who reported diseases of the circulatory system, endocrine, nutritional and metabolic diseases and diseases of the digestive tract.^[17]

A study done in United Arab Emirates (UAE) by Mubarek *et al.* reported that 89% of the included participants were exposed to polypharmacy.^[18] The study also found that greater exposure to polypharmacy can lead to comorbidities and the number of drug interactions increased with increasing number of medications taken by elderly patients.

Usage of Gastroprotective Agents (GPA) among chronic NSAID users

A study which dealt with co-prescribing of proton pump inhibitors (PPIs) among chronic users of NSAIDs in the UK found out that of all patients included in the study 9.7% received at least one PPI prescription.^[19] Among PPI users, PPIs were available on ~50% of the days with non-selective NSAID (nsNSAID) therapy. After multivariate adjustment, age ≥ 65 years, history of any hospitalization and co-prescriptions for anti-coagulants or oral corticosteroids increased the odds of any nsNSAID-PPI overlap by 21–68%. Prior gastro-protective agent (GPA) use increased the odds of any PPI use during follow-up by 16-fold and nsNSAID-PPI overlap by 19-fold. Among PPI users, patients with prior use of any GPA had a 2.46 times higher nsNSAID-PPI overlap ratio. In conclusion, it was inferred that although chronic nsNSAID users at high risk for GI events were more likely to receive a PPI prescription than those with low GI risk, PPI supply overlapped only 51% of mean days of nsNSAID supply.^[19] GI safety of nsNSAID-PPI co-therapy observed in controlled trials may therefore not be achieved in clinical practice

Wayne et al conducted a cohort based study on risk of peptic ulcer hospitalizations in users of NSAIDs with gastro-protective co-therapy versus cox-2 inhibitors where they reported that users of NSAIDs with no gastro-protective co-therapy had an adjusted incidence of peptic ulcer hospitalizations of 5.65 per 1000 person-years.^[20] This risk was reduced by 39% for users of NSAIDs with gastro-protective co-therapy and 40% for users of cox-2 inhibitors without such co-therapy. Concurrent users of NSAIDs and proton pump inhibitors had a 54% risk reduction, very similar to the 50% reduction for concurrent users of proton pump inhibitors and cox-2 inhibitors. Based on their results they concluded that co-prescribing a proton pump inhibitor with an NSAID is as effective as use of a cox-2 inhibitors for reducing the risk of NSAID-induced gastropathy.^[20]

Analysis of NSAID drug interactions with other concurrently used drugs

A study conducted in elderly at Trondheim, Norway found that it was a common practice to prescribe NSAID for chronic gout, rheumatoid arthritis/ankylosing spondylitis and gonarthrosis.^[21] Co-prescription was prevalent for gastroprotective drugs, antithrombotic drugs and drugs used for hypertension and/or congestive heart failure, whereas systemic glucocorticoids, methotrexate, SSRIs and lithium were co-prescribed to a lower degree. The study recommended that co-prescription of NSAIDs and interacting drugs in the elderly constitutes a major problem.^[21] Improved educational initiatives directed towards prescribers and enhanced vigilance during all stages of prescription handling may improve this state.

De Lima et al. conducted a prospective, exploratory and

descriptive based study to analyze potential drug interactions and adverse reactions to NSAIDs in elderly.^[5] Their results showed the importance of monitoring the use of NSAIDs among the elderly due to the increased risk of drug interactions and adverse reactions associated with age, concomitant diseases, multi-prescriptions and polypharmacy. Of the 200 prescriptions analyzed, 32.5% contained two drugs and 40.5% contained three drugs, while other quantities were less common. Potential drug interactions were identified in 44.5% prescriptions, giving a total of 104 potential drug interactions, which were most common on prescriptions containing either three or two drugs.^[6] In terms of clinical condition, 23.5% were being treated for systemic arterial hypertension and 9.5% had type 2 diabetes mellitus.

Potential drug interactions were described in 59.6% of the 47 patients with hypertension and in 56 of the 153 patients without hypertension.^[5] 47.4% patients with type 2 diabetes mellitus exhibited potential drug interactions whereas 69 of the 181 participants without diabetes exhibited potential drug interactions. Among the 104 potential drug interactions, 24% were classified as high or severe, with 40.4% moderate and 22.1% low. The authors recommended the importance of monitoring the use of these drugs, given the high potential for drug interactions and adverse reactions among elderly individuals who take those drugs.^[5]

A study which took place in India focusing in elderly individuals practicing self-medication revealed that 88.5% reported self-medication in 6-month recall period.^[22] The researchers concluded that Self-medication is highly prevalent in elderly people who are unaware of risks involved. However, self-medication may lead to unwanted consequences due to interactions with the prescribed drug therapy for chronic diseases. Knowledge on the part of doctors as well as patients about self-medication practices would help in reducing the chances of any untoward consequences.^[22]

CONCLUSION

This review concludes that prescription pattern of NSAIDs should be monitored in elderly patients. There are high chances of polypharmacy in elderly patients as complications are increasing with age. Hence prescription of these type of patients should be properly reviewed otherwise there are high chances of drug interaction. COX – 2 inhibitors alone are more appropriate treatment if the patient has not cardiovascular disease otherwise non-selective NSAIDs with gastro-protective agents are advisable. Although the NSAIDs are most appropriate first line treatment for pain management, the elderly patients with chronic disease like hypertension and diabetes should be monitored. Awareness about the complications of self medication to the patients may help in reducing the chances of any untoward consequences. Awareness of the doctors as well as patients may help in reducing self medication. It

is the duty of pharmacist to provide information regarding drug interactions, adverse drug reactions and self medication to the doctors, nurses as well as patients.

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