

Toxicity Profile of Commonly Used Anti-Inflammatory Drugs in Geriatrics

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ABSTRACT

Background: Anti-inflammatory drugs are commonly used in geriatrics. Geriatrics usually encounter problems of pain and inflammation and are more vulnerable to the toxicity of drugs as compared to young patients. In this review, we aimed to find out the toxic profile of drugs and the pharmacotherapy considerations for geriatric care.

Methods: The electronic databases like Google Scholar, PubMed, ScienceDirect, and different related text books of recent edition were searched using specific keywords for preparing this narrative review. Related experts in the field were also consulted. Papers published in English language were included in the review.

Results: The diseases geriatrics mostly suffered from are osteoarthritis (OA), ankylosing spondylitis, carcinoma, and other degenerative disorders that require anti-inflammatory medicines. Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are mostly used agents for the treatment of inflammation in such population. As the pharmacokinetics of drugs get altered due to alteration in body physiology in geriatrics, the pharmacodynamics also gets affected, and hence toxicity ensues even with normal dose. Depending upon the nature of the drugs, presence of comorbidity, and poly-pharmacy; gastrointestinal, renal, and cardiovascular toxicities occur. Due to this reason, utmost care should be taken for pharmacotherapy practice in geriatrics.

Conclusion: In geriatrics, the anti-inflammatory drugs should be used rationally for the shortest duration possible at the lowest effective dose. The careful evaluation of the beneficial and potential risks of the agents and pharmacovigilance must be considered for pharmacotherapy practice in such populations.

Keywords: Anti-inflammatory agents; Comorbidity; Geriatrics; Inflammation

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INTRODUCTION

The geriatrics mostly face problems of chronic musculoskeletal pain (MSP) as a symptom of different inflammatory diseases like OA especially of knees and hips, gout, ankylosing spondylitis, and other age related degenerative disorders, which are disturbing their quality of everyday life.¹ The pain may also accompany the different types of carcinomas, diabetes, infections, muscle spasms, ulcers, inflammatory bowel disease (IBD), different neuropsychiatric conditions, and headache in such population. Rheumatoid arthritis (RA), though may occur at any age, may pose a risk of toxicity of the drugs used for intervention thereafter. Among such diseases; pain related to OA, RA, IBD, gout, cancer, ankylosing spondylitis, and other age related degenerative disorders are associated with inflammation. It is crucial to deal with such kind of pain. The pharmacotherapy measure to tackle needs drugs with anti-inflammatory properties which cause toxicity in geriatrics.² Different types of medicines are used to treat pain and inflammation. These are NSAIDs, corticosteroids, disease modifying anti-rheumatic drugs (DMARDs), immunosuppressants, and other supplements like chymotrypsin and serratiopeptidase. Among them, NSAIDs and corticosteroids are mostly used agents around the globe.³ Over the counter (OTC) availability of NSAIDs is another reason of maximum use. Therefore, the self-medication practice of such agents has also posed the risk to geriatrics.⁴ This study was carried out with the objectives of finding out commonly used anti-inflammatory drugs, their toxicity profile, pharmacological risks, and to assess pharmacotherapy considerations in geriatrics.

METHODOLOGY

The electronic databases like Google Scholar, PubMed, Science Direct, and different related text books of recent edition were searched using specific keywords like "anti-inflammatory drugs", "geriatrics", "toxicity profile of anti-inflammatory drugs" and "drug toxicity in elderly" for preparing this narrative review. Related experts in the field were also consulted. Papers published in English language were included in the review.

PHARMACOLOGICAL RISKS IN GERIATRICS

As geriatrics are vulnerable to toxicity of anti-inflammatory drugs, utmost care must be given to these patients. The pharmacokinetic profile of drugs gets altered in geriatrics due to exhaustive physiology as compared to that of adults, which

has a direct impact on the pharmacodynamics profile which leads to altered pharmacological effects.^{5,6} Therefore, age-related changes in physiological and hence pharmacokinetic (PK) and pharmacodynamics (PD) profile as well as comorbidity and poly-pharmacy makes the drug therapy complicated in geriatrics.^{7,8,9}

Pharmacokinetic Profile

Pharmacokinetics may be altered in the elderly due to changes in physiology with age. There is an increase in gastric pH, body fat, or decrease in body mass, gastrointestinal tract (GIT) motility, renal function, serum albumin, phase-I enzymes, and total body water that contribute to the alteration of PK profile.¹⁰

Absorption There is delayed absorption due to the change in physiology such as delay in gastric emptying, diminished splanchnic blood flow, increased gastric pH, and impairment in intestinal movement.^{11,12}

Distribution There is a change in distribution of the drugs as well. Geriatrics have decreased water content, thereby decreasing the volume of distribution (Vd) of water soluble drugs. Similarly, Vd of lipid soluble drugs is increased because of high mass of adipose tissue and less lean muscles.^{13,14}

Elimination Due to the decrease in liver mass and perfusion, the hepatic first pass effect of highly cleared drugs through the hepatic route could be reduced in geriatrics, thus some drugs show better bioavailability. The hepatic clearance of some drugs may be reduced by up to 30% and cytochrome P450 (CYP450) - mediated phase I reactions get impaired more likely than phase II reactions in such population.^{15,16}

Renal excretion is decreased up to 50% in about two thirds of geriatrics, but confounding factors such as hypertension and coronary heart disease account also for depressed renal function.^{15,16} Serum creatinine is decreased with age.¹⁷ Drugs eliminated from the kidney can result in increased concentration and subsequent adverse drug reactions (ADR). All renally eliminated drugs should be monitored carefully.¹⁶

Pharmacodynamic Profile

There is a decrease in receptor sensitivity in geriatrics as compared to younger people.¹³ The impact of altered pharmacokinetics may add another burden for disturbing the normal pharmacodynamics profile of drugs. Therefore, the pharmacological effect in geriatrics is more correlated with either

ineffectiveness or toxicity at a dose which is normal in the adult population.¹⁶

ANTI-INFLAMMATORY DRUGS COMMONLY USED IN GERIATRICS

Pharmacotherapy in the management of pain associated with inflammations comprises of drugs of the following categories (Table 1) that modulate or reduce the inflammatory process, thereby decreasing the associated pain.¹⁸

Anti-Inflammatory Drugs Classification^{5,18,19,20}

NSAIDs Diclofenac Na/K, Naproxyn Na, Indomethacin, Aceclofenac, Aspirin, Ibuprofen, Piroxicam, Mefenamic acid, Celecoxib

Corticosteroids Prednisolone, Methylprednisolone

DMARDs Methotrexate, Hydroxychloroquine, Leflunomide, Sulfasalazine, Minocycline, Penicillamine, Auranofin, Etanercept, Infliximab, Adalimumab

Immunosuppressants

Azathioprine, Mercaptopurine, Cyclosporine, Methotrexate, Hydroxychloroquine

Salicylates Sulfasalazine, Mesalazine

Others Chymotrypsin, Serratiopeptidase

DIFFERENT TOXICITY PROFILE OF ANTI-INFLAMMATORY DRUGS

Geriatric patients are at more risk to adverse reactions to drugs. Different studies have suggested that ADR observed in patients above age 65 is more as compared to adults.^{21,22}

Factors affecting ADRs in geriatrics

Since poly-pharmacy, multiple disease states, increased severity of illness, reduced drug elimination, and increased sensitivity to drug are associated with geriatrics, these effects make geriatrics more vulnerable to ADRs.¹⁴

Studies have shown that:

- Patients with numerous medications have a greater chance of experiencing ADRs due

to drug-drug interactions and potential overlapping or synergy between adverse reactions^{8,14}

- Patients with multiple disease states are at higher risk of having disease-drug interactions²³
- There are predictions about the possible change in pharmacokinetic and pharmacodynamic profile with age and ADRs observed¹⁶
- Another issue complicating geriatrics drug therapy includes adherence²⁴
- Factors related to gender, socioeconomic status, sedentary life style, poly-pharmacy, complex regimens of drug therapy are also responsible^{9,25,26,27,28}
- Other complication, which hinders the disease processes, is also responsible for ADRs²⁹
- Improper drug therapy and drug monitoring may add up the ADRs in elderly.³⁰

Anti-inflammatory drugs show toxicity in GIT, kidney, cardiovascular system (CVS), and skin, which are depicted in table 2.

NSAIDs

NSAIDs fall among the mostly prescribed and highly effective anti-inflammatory medications.³¹ However, these have multiple adverse effects such as GIT irritation/hemorrhage, bleeding, CVS side effects, dermatological reactions, and nephrotoxicity. It is very critical to use NSAIDs rationally in geriatrics.³²

PK & PD of NSAIDs

The major therapeutic actions of NSAIDs depend on their ability to block prostaglandins synthesis through cyclooxygenase enzymes (COX-1 and COX-2) inhibition.³³ COX-1 is expressed in normal cells, while COX-2 is induced in inflammatory cells. COX-2 inhibition represents the desired anti-

Table 1: Anti-inflammatory drugs to treat different geriatric diseases

SN	Diseases	Anti-inflammatory drugs for treatment
1	OA and other degenerative disorders	NSAIDs, corticosteroids, chymotrypsin or serratiopeptidase
2	IBD	Salicylates, corticosteroids, immunosuppressant
3	Gout	NSAIDs, corticosteroids
4	RA	NSAIDs, corticosteroids, immunosuppressant, DMARDs, biotechnological agents
5	Cancer	NSAIDs, corticosteroids, immunosuppressant

inflammatory response, while COX-1 inhibition plays a major role in the undesired GIT and renal toxicities.¹⁹

Most NSAIDs are well absorbed in the GIT and have high bioavailability. Some drugs such as diclofenac undergo hepatic first-pass metabolism, while some drugs such as sulindac and parecoxib are prodrugs and need hepatic metabolism to be active.^{34,35,36} NSAIDs are highly bound to plasma proteins and are usually metabolized in the liver, and excreted in the urine.⁵ Common NSAIDs have a variable half-life (0.25-0.3 hours for aspirin or 45-50 hours for piroxicam).^{37,38} All these pharmacokinetics parameters can change with aging since the elderly have low body water compared with adults. Protein binding may be reduced and Vd may be altered. In the case of newer NSAIDs, the most important ADR to be considered is renal damage, which may be irreversible.³⁹ Because they are cleared primarily by the kidneys, these drugs will accumulate more rapidly in geriatrics and especially in the patient whose renal function is already compromised.⁵ There is no evidence that COX-2-selective NSAIDs are safer regarding renal function. Geriatrics receiving high doses of any NSAID should be carefully monitored for changes in renal function.

Toxicity Profile

Renal vasoconstriction and consequently aberrant renal function due to inhibition of prostaglandins and thromboxane synthesis occurs with NSAIDs use. Clinical manifestations of NSAID induced nephrotoxicity include electrolyte imbalance such as hyperkalemia, reduced glomerular filtration rate, chronic kidney disease, acute interstitial nephritis, sodium retention, edema, and renal papillary necrosis. The American geriatric society recommends that all NSAIDs should be avoided in patients with stage IV and V CKD cases (creatinine clearance less than 30 mL/min).³²

Gastrointestinal bleeding and ulceration from NSAIDs use an increase in severity and frequency with increasing age. The mechanism underlying NSAIDs induced GIT adverse effects lies in the fact that these medications inhibit prostaglandin synthesis, causing weakening of the protective gastrointestinal mucosal barrier and predisposing to bleeding.

Since rofecoxib and valdecoxib were withdrawn from the market in 2004 and 2005, respectively, due to CVS adverse events such as edema, myocardial infarction, thrombotic events, stroke and hypertension; concerns regarding all COX-2

inhibitors' the potential for CVS adverse events have been raised.⁴⁰ Thus, all NSAIDs (COX-2 and non-selective) may be associated with increased CVS adverse events and each medications' risk/benefit profile should be considered before prescribing to individual patients.

Non-selective NSAIDs are known to attenuate the antihypertensive effect of some specific antihypertensive agents such as angiotensin-converting-enzyme inhibitors (ACEIs). The mechanism of NSAIDs promoting hypertension is hypothesized to be related to the inhibition of prostaglandin synthesis, which leads to an interference of the renal vasculature which manipulates the regulation of blood pressure. In addition, NSAIDs themselves can cause elevation of serum aldosterone, leading to sodium retention and hypertension.

As there is evidence of inflammation in alzheimer's brain, there have been different studies regarding the use of NSAIDs in such condition. A study conducted by Grodstein et al revealed that the long-term use of ibuprofen was associated with slower rates of cognitive decline.⁴¹ Evidences suggest the linkage of elevated pro-inflammatory cytokines to major depression and NSAIDs may play some role in mitigating the anti-inflammatory effects of depression. In adults over 18 years of age, NSAIDs had a statistically significant antidepressant effect in bipolar depression, however, this effect was not seen in geriatrics with depression. Different studies suggest that NSAIDs may play an essential roles in reducing infection-induced inflammation in this particular scenario.³² NSAIDs seem to be a significant risk factor in falls, which can lead to morbidity and mortality in such population. Data from Walker et al suggested that NSAIDs increase the likelihood of falling by 10 fold. NSAIDs are considered an important group of fall risk-increasing drugs (FRIDs).⁷

In animal models, NSAIDs improved bladder function and decreased micturition frequency. Some studies have found significant improvement in the management of nocturia in benign prostatic hyperplasia (BPH) and overactive bladder in geriatrics.³² Most probably by altering prostaglandins and prostaglandin precursors in the central nervous system, NSAIDs may get associated with psychiatric events in geriatrics, where the common symptoms may be psychosis, agitation, depression, anxiety, paranoia, delirium, mania, and hallucinations.

NSAIDs not only have analgesics of palliative

Table 2: Toxicity profile of anti-inflammatory drugs ^{5,18,19,20}

Organ	Toxic reactions	Drugs responsible
GIT	GIT irritation	NSAIDs, salicylates, corticosteroids
	GIT hemorrhage/Bleeding	NSAIDs, salicylates, corticosteroids
	Ulcer	NSAIDs, salicylates, corticosteroids
	Hepatotoxicity	Methotrexate, aspirin, nimesulide
Kidney	Acute renal ischemia	NSAIDs
	Acute renal failure	NSAIDs
	Acute and chronic interstitial nephritis	NSAIDs
CVS	Edema, myocardial infarction, Thrombotic events, Stroke and Hypertension	NSAIDs, corticosteroids
Skin	Urticaria	Aspirin, NSAIDs
	Fixed drug eruptions	Acetylsalicylic acid
	Bullous pemphigoid	Sulfasalazine, penicillamine
	Angioedema	NSAIDs, corticosteroids

action, but also have the potential to lower the risk of cancers such as endometrial, esophageal, head and neck, prostate, colorectal, ovarian cancer and melanoma. As these agents inhibit COX-2 expression, which plays a major role in tumor initiation, tumor progression, and suppression of antineoplastic immune cells; these can inhibit cancer cells proliferation and apoptosis induction as a direct effect.

Different studies suggest that NSAIDs can increase the risk of stroke, which varies with type of drugs. Compared with naproxen, the least harmful NSAID for CVS outcomes, valdecoxib was associated with the highest risk of stroke. The incident can occur with the use of valdecoxib, diclofenac, aceclofenac, but no such incidence has been reported with naproxen or ibuprofen. Studies suggest that the long-term use of all NSAIDs can increase the risk of stroke by 64% in two years.³² NSAIDs can interfere with vasoconstriction and sodium excretion causing hypertension, a major risk factor of stroke. These medications can also induce platelet aggregation and increase thrombus formation.

Due to poly-pharmacy⁹, comorbidities²³, and physiological changes⁶, geriatrics are more vulnerable to drug interactions as depicted in table 3. It is another crucial factor to use NSAIDs and other anti-inflammatory agents with care in geriatrics.

CORTICOSTEROIDS

Glucocorticoids, as corticosteroids are effective as

a clinical milestone for the treatment of numerous inflammatory and autoimmune diseases including bronchial asthma, COPD, allergy, RA, IBD, and multiple sclerosis. However, the therapeutic benefits of corticosteroids are limited by their toxicity profile, especially in high dose or long term use.⁴³ Corticosteroids are extremely useful in geriatrics who cannot tolerate full doses of NSAIDs. However, these agents consistently cause dose- and duration-related osteoporosis, especially the hazardous toxic effect in the elderly.⁵

PK & PD of Corticosteroids

These are administered by oral as well as parenteral route; intravenous, intra-articular, inhalation, and topical route depending upon the clinical status of patients and the urge of action. There is rapid absorption after oral administration with the peak effect occurring at 2-8 hours. It is due to the influence of impaired PK, including that of hepatic, renal function, and concomitant drugs; the alterations in the pharmacological effects of corticosteroids are more apparent in geriatrics.

These agents impede the access of neutrophils and monocytes to an inflammatory site as a major mechanism to exhibit anti-inflammatory effects.⁴⁴ The consideration of impacts of aging on adrenal function is essential for using corticosteroids in geriatrics. For glucocorticoids, the changes of decreased production and decreased clearance are relatively balanced. The reduction in drug dose in such population of asthenic build is appropriate due to the decrease of muscle mass

Table 3: Interactions of NSAIDs with other agents ^{5,18,19,20,42}

Medications	Interactions
Antiplatelets (aspirin, clopidogrel)	Risk of gastrointestinal bleeding increases
ACEIs and Angiotensin receptor blockers	Blood pressure increases due to attenuation of antihypertensive effects
Beta blockers	Blood pressure increases by attenuation of antihypertensive effects
Calcium antagonists	Blood pressure increases by attenuation of antihypertensive effects
Corticosteroids	Risk of gastrointestinal bleeding increases
Digitalis glycosides	Serum digoxin level increases
Diuretics	
Methotrexate	NSAIDs reduce renal excretion of methotrexate, causing methotrexate toxicity.
Selective serotonin reuptake inhibitors (SSRIs)	Increases risk of gastrointestinal bleeding
Warfarin and other anticoagulants	Increases risk of gastrointestinal bleeding

and volume of plasma with aging. Despite the physiologic changes, the careful and ethical use of corticosteroids can be a rational therapy for the optimization of therapeutic outcome in geriatrics.⁴⁵

Toxicity Profile

Normally, in case of asthma and COPD; geriatrics take corticosteroids through inhalation from a metered dose inhaler or dry powder inhaler. Due to the topical action rather than systemic effects in such cases, these are not that much toxic. Special attention and dose adjustment in geriatrics is needed due to probable age-related changes in hepatic, renal, or cardiac functions. However, steroids like prednisolone, methylprednisolone taken orally can cause the following adverse events⁴⁶ as depicted in table 4, and geriatrics are indeed more vulnerable to these effects.

DMARDs

These are agents indicated as standard of care

for the therapy of RA where they help prevent joint deformities and injuries.⁴⁷ Basically, DMARDs interfere with the cellular signaling cascade that promotes inflammation. These may also be indicated for the therapy of other autoimmune disorders like scleroderma, spondyloarthritis inflammatory myositis, IBD, and systemic lupus erythematosus (SLE) like diseases. Though these have anti-inflammatory activity, these are not the agents mostly being used in geriatrics as RA may occur at any age. However, when it occurs in geriatrics, the condition becomes serious as the toxic profile of drugs may prove dangerous in such patients as compared to adults. By slowing down the joint damage, these agents may induce or maintain remission, reduce the frequency of flare-ups, and ease steroids tapering with sustained control in disease. DMARDs can be administered orally, subcutaneously, or intravenously. These agents have delayed onset of action.

Table 4: ADR profile of corticosteroids ^{5,18,19,20}

System	Toxicity profiles
GIT	Irritation, dyspepsia, hemorrhage, ulcer
Metabolism	Hyperglycemia, cushing's syndrome, weight gain, adrenal suppression
CVS	Fluid retention, edema, hypertension, arrhythmia
Musculoskeletal system	Osteoporosis, myopathy, osteonecrosis
Dermatology	Ecchymosis, skin thinning and atrophy, acne, hirsutism, facial erythema, thinning of hair, and perioral dermatitis
Ophthalmology	Glaucoma, cataract
Neuropsychiatry	Psychosis, akathisia, sleep disturbances
Others	Risk of infection

Close monitoring is essential in case of geriatrics taking DMARDs regarding effectiveness and toxicity profile. The toxicity mostly occurs due to the decreased renal clearance of some DMARDs. Therefore, the therapy is to be adjusted according to the clinical status of individuals such as renal function, co-morbidity, concomitant drug administration, or poly-pharmacy. The dose is to be adjusted to the lowest possible level with effectiveness.⁴⁸ The more common toxicities in early therapy is myelosuppression and hepatotoxicity with DMARD. Therefore, more frequent monitoring is recommended early in therapy.⁴⁹ The toxicity of different agents of DMARDs is specific (Table 5).

IMMUNOSUPPRESSANTS

System	Toxicity profiles
GIT	Nausea, vomiting, diarrhoea
Liver	Hepatotoxicity
Blood	Leukopenia, anemia
CVS	Altered QT interval (Hydroxychloroquine)
Ophthalmology	Ocular toxicity (Hydroxychloroquine)

Immunosuppressants are used in organ transplant cases and auto-immune diseases such as RA, IBD, and cancers. Such type of disease may occur at any age from adults to elderly. These agents may suppress immunity and hence patients may become prone to different diseases. Geriatrics, if use immunosuppressants, may get other diseases very soon due to their altered and weak physiology.^{50,51} So, caution must be given while using such agents to the geriatric population.

In the case of geriatrics, clinically significant alterations in PK parameters occur due to the change in physiology with age. This may lead to higher serum concentration of immunosuppressant. In some cases, such as mycophenolic acid, due to the higher protein binding nature⁵² of the drug and lower albumin level in geriatrics, a higher dose of drug is needed as compared to adults. However, the free fraction of this agent in case of renal insufficiency may cause infections and hematological toxicities.⁵³ Geriatrics need appropriate monitoring of therapy of such agents for adherence issues due to the toxicity profile of such drugs.⁵⁴ Immunosuppressants act to prevent allograft rejection by preventing/inhibiting cell

activation, cytokine production, differentiation, and/or proliferation.⁵⁵ Appropriate selection of immunosuppressants in geriatrics is complex as such population is considered in exclusion criteria in many studies.

Immunosuppressant may cause myelosuppression leading to anemia, thrombocytopenia, and leukopenia. There are other drug specific adverse events such as methotrexate is also associated with hepatotoxicity, mucosal ulceration, folic acid deficiency, and flu like syndrome. Cyclosporine causes hypertension, nephrotoxicity, hypomagnesaemia, hyperkalemia, hyperlipidemia, and diabetes. Azathioprine causes diarrhea, myelosuppression, pancytopenia, neutropenia, nausea, vomiting, rash, pneumonitis, and liver damage.^{5,18,19,20}

OTHERS

Other anti-inflammatory agents like salicylates, biotechnological drugs, chymotrypsin, and serratiopeptidase also cause ADRs that may prove to be more toxic to geriatrics. Therefore, a detailed clinical picture of patients' needs to be taken and used with caution in geriatrics. They have specific toxicity profile depending upon the agents used. For example, salicylates have a toxicity profile similar to NSAIDs along with bone marrow suppression, nephritis, and hepatotoxicity.^{5,18,19,20}

GENERAL PRINCIPLES OF PRACTICE IN GERIATRICS

In the practice of anti-inflammatory agents in geriatrics, care must be taken for the following general principles:

- Start with low dose and reduce slowly⁵⁶
- Due to the reduced renal and hepatic function, the half-life of many drugs will be prolonged in such population¹⁴
- Rapid dose increase prevents the rapid therapeutic dose response, thereby causing the accumulation of drugs in the body, and ADRs may occur more frequently
- The fewest number of drugs should always be used to treat patients. If possible, emphasize on non-pharmacological measures
- Always evaluate possible drug toxicity
- Geriatrics can have typical presentations of ADRs, which may manifest as CNS changes
- Use other agents along with that counteract the ADR of anti-inflammatory drugs.

- Practice pharmacovigilance so that identification, monitoring, and management of ADR can be done in an appropriate manner

Different professional societies, including the American geriatric society, American college of rheumatology recommend using NSAIDs with caution and limit their use to the lowest effective dose and shortest duration along with monitoring of gastrointestinal, renal, and cardiovascular side effects.³² Gastro-protective agents like proton pump inhibitors, H₂ blockers, misoprostol can be used along with anti-inflammatory drugs.³ Another strategy to minimize gastrointestinal adverse effects is to substitute nonselective NSAIDs with selective COX-2 inhibitors (celecoxib, rofecoxib) as these agents cause less damage to the gastrointestinal mucosa. However, there are increase risks of cardiovascular adverse effects with COX-2 inhibitors. Thus, a comparison of a patient's gastrointestinal risk factors versus cardiovascular risk factors is necessary to determine the choice of gastrointestinal protection options for patients on chronic NSAIDs.³² Osteoporosis can be minimized in corticosteroids users by calcium along with vitamin D or bisphosphonates, and frequent exercise.⁵ The estimates of the total cost of anti-inflammatory agents to the geriatrics must be accompanied by the additional costs of gastro-protective agents and related interventions.

CONCLUSION

As the body physiology gets exhausted with age; the altered PK and PD profile lead to the different pharmacological effects of drugs in geriatrics that otherwise would have a normal profile in adults. To provide comprehensive care to geriatrics; it is important to consider the mechanism of action, current guidelines, ADRs, and the pleiotropic effects of common drugs. This should be used for the shortest duration possible at the lowest effective dose, and with careful monitoring of gastrointestinal, renal, and cardiovascular toxicity. The benefits of therapy with such agents must be weighed against their potential risks. Alternative therapies such as physiotherapy, psychosocial counseling may also be practiced as far as possible to relieve pain in such populations. The careful monitoring of therapy, pharmacovigilance, comparatively safer agents, topical therapy, or concomitant use of protective agents is recommended for safety concerns in geriatrics.

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