

# Promoting rational self-medication of nonsteroidal anti-inflammatory drugs in Nepal

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**ABSTRACT**

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a commonly used class of drugs. They are used for self-medication worldwide including Nepal to treat self-limiting conditions, and mild to moderate symptoms associated with disease. Similar degree of care like prescription-only drugs is needed for these drugs as these are also linked with many adverse effects. However, nephrotoxicity remains a major concern with these drugs; other systems such as gastrointestinal, cardiovascular, hematologic, respiratory, and hepatic are also affected. The renal effects of analgesics are pronounced among patients with comorbid conditions, hypovolemic state of body and those with concomitant use of nephrotoxic or other drugs. A number of studies on self-medication all over the world have revealed that NSAIDs are the most commonly used drugs as self-medication. Easy access to these drugs either in pharmacy or in nonpharmacy outlets has become a reason for proper monitoring of over-the-counter use of these drugs. Responsibility remains with all healthcare professionals, either at individual or institutional level, to establish the balance between the benefits and risks associated with these drugs. The consumer who uses the drugs and the policy-framing bodies are others who could intervene in promoting the rational use of NSAIDs.

**INTRODUCTION**

Pain is a common problem experienced by people of all ages. An analgesic is defined as “a compound capable of producing analgesia, i.e., one that relieves pain by altering perception of nociceptive stimuli without producing anesthesia or loss of consciousness.”<sup>[1]</sup> Analgesics are basically of three major types: Nonopioid analgesics (e.g., paracetamol, ibuprofen, and diclofenac), opioid analgesics (e.g., morphine, codeine, and pethidine), and adjuvant analgesics (e.g.,

anxiolytics, antidepressants, and local anesthetics).<sup>[2]</sup> Nonsteroidal anti-inflammatory drugs (NSAIDs) are the drugs which are commonly used for self-medication. They are commonly used by patients for the treatment of pain, fever, headache, inflammation, muscular pain, menstrual cramps, arthritis, etc., most of which are self-limiting conditions. People prefer self-medication with over-the-counter (OTC) drugs instead of seeking medical help from healthcare providers in case the condition is mild to moderate.

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OTC drugs, also known as nonprescription medicines are those drugs which are taken as self-medication without consulting a doctor or without any medical supervision. NSAIDs are the most preferred OTC drugs followed by anticold tablets and vitamins.<sup>[3]</sup> OTC drugs usually have a wide range of safety and lesser adverse effects compared to medicines that require prescription. Inappropriate use of OTC drugs can lead to serious adverse effects, and both drug-drug and drug-food interactions increasing the risk of mortality and morbidity. It can also lead to increased rate of hospital admissions and healthcare costs. A similar level of care should be taken with OTC drugs and prescribed medicines with regard to drug selection, use, and monitoring.<sup>[4]</sup> However, it is the core responsibility of the pharmacist to provide relevant, adequate information about the OTC drug to ensure that the user is aware of and can reduce the risk of adverse effects.

The situation of self-medication is different in developing countries compared to developed ones. In developed countries, the availability of OTC drugs in supermarkets has increased their accessibility. The cost of a doctor consultation is also high but is usually reimbursed by insurance. In developing countries, medical services are poor, and health professionals lack control over the use of pharmaceutical products by patients.<sup>[5]</sup> Drugs classified as prescription-only medicines are often sold without a prescription in developing nations.<sup>[5]</sup> In Nepal, there is a trend of nonqualified personnel selling drugs without clinical indication, without enquiring about drug-related allergies, and preexisting medical problems which can complicate the treatment regimen and medicines used by the patient.<sup>[6]</sup>

Although NSAIDs have been providing benefit by relieving mild to moderate symptoms associated with acute or chronic illness, there is also an increased risk of adverse effects associated with their use. Gastric irritation is the most common problem seen with NSAIDs use. Continuous uses of these drugs as monotherapy or in combination with other drugs over long periods of time are associated with the development of slowly progressive kidney disease.<sup>[7-9]</sup> The mechanism of action of NSAIDs is inhibition of the cyclo-oxygenase enzyme and the production of prostaglandin products of arachidonic acid, the role of which is to maintain renal hemodynamics, fluid, and electrolyte balance and synthesis of renal hormones such as renin and erythropoietin.<sup>[5]</sup>

A study done in Bangladesh among 480 patients showed that misuse of analgesics occurs as a result of wrong indication, and longer duration of use through professional and nonprofessional sources such as friends and relatives.<sup>[10]</sup> The adverse effects of analgesics are more prominent among the elderly who are more likely to have multiple diseases. Increased bleeding with aspirin and interactions with prescription drugs are the main reasons for adverse effects in elderly patients.<sup>[11]</sup> The use of OTC drugs is also common among low-income families and people living in rural areas who find seeking a doctor or hospital is expensive.

## NONSTEROIDAL ANTI-INFLAMMATORY DRUGS USE IN NEPAL

A study done in Nepal in the year 2001 showed that 59% of undergraduate medical students had used self-medication.<sup>[12]</sup> The commonly encountered disease conditions were fever and headache, and the drugs mostly used for self-medication were paracetamol followed by other NSAIDs.<sup>[12]</sup> These NSAIDs were used as self-medication when minor ailments such as headache or fever did not subside within 24 h.<sup>[12]</sup>

A literature search in library, journals, internet search was done but no information was found regarding the official list of OTC drugs available in Nepal. Certain hospitals have created an OTC list for their hospital pharmacies. There is a practice of prescription-only medicine being available OTC. The common NSAIDs which are being sold OTC in Nepal include paracetamol, ibuprofen, paracetamol + ibuprofen, paracetamol + caffeine, aspirin, nimesulide, diclofenac, aceclofenac, mefenamic acid, and indomethacin.

NSAIDs have many prominent adverse effects that affect almost every system of the human body. These have been classified as renal and nonrenal effects and are discussed below.

## GENERAL SIDE EFFECTS OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

### Nonsteroidal anti-inflammatory drugs and associated kidney problems

Widespread use of NSAIDs has raised concern about its nephrotoxicity. The effects are more common among people with comorbid conditions

associated with less intravascular volume as a result of congestive heart failure, liver cirrhosis, diuretic use, salt restricted diet, nephrotic syndrome, and high-level proteinuria.<sup>[13]</sup> In the hypovolemic state, prostaglandins (most importantly prostaglandin E1 and or prostacyclin) oppose the action of the vasoconstrictor autacoids to maintain renal blood flow and glomerular filtration.<sup>[13,14]</sup> The production of the vasodilatory prostaglandins is inhibited by NSAIDs [Table 1]. Furthermore, NSAID-induced nephrotoxicity is significant in patients taking other drugs such as angiotensin-converting enzyme inhibitors and/or potassium-sparing diuretics and salt substitutes.<sup>[13,14]</sup>

The renal effects of NSAIDs are illustrated in Table 2.

### Evidence of self-medication with nonsteroidal anti-inflammatory drugs

Search using the databases Google Scholar, Google, and PubMed using the keywords self-medication, analgesics, developing countries, Nepal, NSAIDs was carried out during September 2014. A number of articles related to self-medication with NSAIDs were found. Studies which provide a clear outline of analgesic use were considered as relevant. Studies done in south Asian countries were given priority. Furthermore, studies done in other developing nations and 2-3 studies in developed countries were also considered as this could help in showing that self-medication of NSAIDs is common in developed as well as developing nations.

Table 3 shows that the use of analgesics as self-medication is popular all over the world. Analgesics and antipyretics account for a major portion of drug categories used OTC in developing countries such as India, Pakistan, and Nepal. The table also depicts that they are also the main OTC drugs in developed nations such as Australia and the USA. Most studies show that analgesics were the most commonly used OTC drugs, and it was found to be common among people of all age groups, gender, and both urban and rural areas [Table 3].

### Importance of monitoring over-the-counter use of nonsteroidal anti-inflammatory drugs

The health professional has less control over the use of the NSAIDs if more of these drugs are available OTC. Some control should be maintained to fix the quantity of the drugs to be dispensed. Otherwise, the analgesics are more likely to cause adverse effects, and the risk of overdose is high.<sup>[15]</sup> During the 1990s, in the United Kingdom, there has been an increase in number of paracetamol poisoning and suicide.<sup>[16]</sup> To

**Table 1: Non-renal effects of NSAIDs**

System	Effects
Gastrointestinal <sup>[17,18]</sup>	Gastrointestinal (GI) effects like dyspepsia, anorexia, gastric and duodenal ulceration, perforation and upper GI hemorrhage are found to occur with analgesics. Above mentioned effects contribute to duodenal and gastric ulcers. Patients with concurrent use of glucocorticoids, <i>Helicobacter pylori</i> infection, heavy alcohol consumption etc., are at high risk for analgesic associated GI effects.
Hematologic <sup>[17,19]</sup>	Hematologic effects like prolonged bleeding time, aplastic anemia, agranulocytosis, inhibition of platelet aggregation are seen.
Respiratory <sup>[17,18]</sup>	Pulmonary effects of analgesics are mostly provoked by the use of aspirin. Patients with previous history of asthma, nasal polyps, and history of rhinitis are at high risk. Aspirin induced asthma is seen among patients who take aspirin. Acute rhinitis, wheezing, bronchospasm, pneumonitis, pulmonary oedema are pulmonary effects seen with analgesics.
Cardiovascular <sup>[17,20-22]</sup>	Unlike low dose aspirin, other analgesics are not thought to afford cardioprotection. Patients at increased risk of cardiovascular disease and thrombosis are more prone to the cardiovascular adverse effects of analgesics. Analgesics like rofecoxib and valdecoxib, the COX-2 inhibitors can cause thrombi formation which increases the risk of cardiovascular events
Hepatic <sup>[17,20]</sup>	Hepatotoxicity occurs after the patient ingests 150 to 250 mg/kg of paracetamol as a single dose. Conditions like cytochrome P450 induction (e.g. heavy alcohol consumption) or glutathione depletion (e.g. fasting or malnutrition) increase the incidence of hepatic injury, even in therapeutic doses. Injury is mostly reversible following the discontinuation of the drug. Jaundice, biochemical abnormalities are other hepatic effects of analgesics.
Dermatological <sup>[20]</sup>	Rash, urticaria and other allergic reactions occur occasionally. Rash is usually erythematous or urticaria, but sometimes they are more serious and may result to drug fever and mucosal lesions

overcome this, legislation was introduced to restrict the pack sizes to 32 tablets from pharmacy and to 16 tablets from nonpharmacy outlets.<sup>[16]</sup>

**Table 2: Renal effects of NSAIDs**

Effect	Comments
Acute renal failure <sup>[7]</sup>	Severe hemorrhage, burn, salt loss and hypoalbuminemia are the risk factors for acute renal failure as these conditions cause volume depletion. During volume loss, circulating vasoconstrictors are released increasing vascular resistance and blood pressure. To counteract the released vasoconstrictors and maintain normal blood flow to the kidney, prostaglandins are released by the kidney. Analgesics are prostaglandin inhibitors which enhance the action of vasoconstrictors predisposing to acute renal failure.
Acute interstitial nephritis and minimal-change glomerulopathy <sup>[7]</sup>	Uses of some analgesics have been reported to be implicated in acute interstitial nephritis with or without minimal change glomerulopathy. This disappears after the offending drug is withdrawn.
Analgesic nephropathy <sup>[8, 9, 23]</sup>	Classic analgesic nephropathy occurs because of slowly progressive interstitial nephritis. Polyuria, leukocyturia and microscopic hematuria are common symptoms of analgesic nephropathy. The disease progression is usually insidious, advanced renal failure may result in the later stage. The exact mechanism is unknown and is thought to be due to medullary ischemia, an effect of reactive metabolites.
Chronic renal failure <sup>[2,7]</sup>	The condition develops in patients who are continuously using analgesics for longer duration of time. Concurrent use of other nephrotoxic drugs (e.g. vancomycin, aminoglycosides) further worsens the situation. Hyperkalemia is a fatal adverse effect that occurs in patients with chronic renal failure. Progressive worsening of analgesic induced papillary necrosis, interstitial nephritis are the other reasons for chronic renal failure.

**Table 3: Selected studies on self-medication with NSAIDs**

Author (s)	Country	Major Findings
Jain <i>et al.</i> , 2012 <sup>[24]</sup>	India	24.8% of drugs requested for self-medication were analgesic/antipyretic.
Patel MM <i>et al.</i> , 2012 <sup>[25]</sup>	India	Of the 330 self medications consumed during the study period, 43.03% was pain relievers.
Shankar PR <i>et al.</i> , 2002 <sup>[12]</sup>	Nepal	Most commonly used drug was paracetamol in 69 instances (43%) followed by other analgesics in 37 instances (23.1%).
Eticha T <i>et al.</i> , 2014 <sup>[26]</sup>	Ethiopia	Analgesics/antipyretics are the most frequently used category of drugs (20.8%).
Maharjan M., 2011 <sup>[27]</sup>	Nepal	Out of 100 mothers being studied, 93% used antipyretics as OTC medication for their children under 5 years.
Ali SE <i>et al.</i> , 2010 <sup>[28]</sup>	Malaysia	148 out of 481 (30.2%) female students use analgesic as self-medication.
Goh LY <i>et al.</i> , 2009 <sup>[29]</sup>	Australia	Analgesics were the most common class of drugs used OTC followed by laxatives and low dose aspirin.
Hussain S <i>et al.</i> , 2011 <sup>[30]</sup>	Pakistan	The most common drugs available for self-medication were analgesics i.e., 66% in rural compared to 34% in urban areas.
Pineles LL <i>et al.</i> , 2012 <sup>[31]</sup>	USA	Analgesics were the most used OTC drugs (47.2%)

All health professionals who deal with drug therapy have an important role in preventing the risks associated with self-medication. They can be in an excellent position to provide information, give advice, provide health education, and different professionals should utilize a

collaborative approach for dealing with self-medication of and other medicines. Pharmacist can play a key role by providing relevant information about the OTC drug, supplying quality drugs, training the healthcare providers, identify the health-related problems associated and raise awareness. At individual and institutional levels, the need for regulation of OTC use of drugs is equally important. Regulations such as selling OTC analgesics with information leaflet and fixing the quantity of drugs to be sold can be made. It is important that the patient taking NSAIDs as self-medication is aware of appropriate dosing, recommended duration of therapy for the medication and any other additional information about an individual drug. Many people are seen using NSAIDs as self-medication for minor ailments which should be strictly controlled. However, there is a need for balancing the benefit and risk for the use of analgesics, as analgesics even in therapeutic dose are likely to produce adverse effects which can lead to hospitalization and economic consequences and even death.<sup>[32]</sup>

### Recommendations

NSAIDs are one of the commonly used drugs for self-medication in many countries including Nepal. A multistage approach may prove beneficial in avoiding/minimizing nephrotoxicity and other adverse effects of NSAIDs. This includes intervention at the following levels.

### Manufacturing

The manufacturers of NSAIDs should ensure that they keep adequate patient information leaflets in



each pack of the NSAIDs and are easily understood by patients and preferably in local language.

### Prescribing

The physician needs to obtain detailed information whether the patients are taking concomitant medicines or are suffering from other disease conditions while prescribing NSAIDs. The interaction of prescription drugs with NSAIDs can also lead to unwanted consequences. They should also counsel their patients about benefits and risks associated with self-medication with NSAIDs.

### Dispensing

In the community and hospital pharmacy settings, pharmacist needs to ensure that patients receive adequate counseling about the medicines they use. Pharmacist can inform about common side effects associated with the drug and steps to follow in case any unwanted effect is seen.

### Consumer

A patient who uses NSAIDs as self-medication should have adequate information on benefits and risks associated with the drug they take. Patients need to know appropriate dose and duration of the drug they are taking.

### Policy

Policies which aim to promote healthy intervention for proper use of NSAIDs should also be made. Restricting pack size, compulsory requirement of information leaflet inside the pack may be some of the steps to be taken.

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### Conflicts of interest

There are no conflicts of interest.

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