## Non-Steroidal Anti Inflammatory Drugs Usage In Orthopaedics And Trauma Practice ----A Guide And Review

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## Abstract

**Background:** Non steroidal anti-inflammatory drugs (NSAIDs) are a group of heterogeneous compounds with anti inflammatory, analgesic and often times anti pyretic properties. They are weak organic acids and are the most commonly used drugs in Orthopaedic/Trauma practice. They provide mild to moderate pain relief.

NSAID share common therapeutic and side effects irrespective of the class or group to which an individual drug may belong. These side effects are many and varied and constitute a major concern in their usage since most of them are life threatening.

The NSAIDs are also one of the most commonly abused drugs. The abuses stem mostly from poor prescription habit by the health professionals.

The poor prescription habit by the professionals and laissez-a-faire attitude to NSAID Usage informed the need for this review which addresses the issues, controversies and preventive strategies to reduce the complications in Orthopedics/Trauma practice.

**Methods:** Literature on the subject was reviewed extensively using manual library internet search. Publications from local and international Journals spanning a period of over thirty years were reviewed. The internet search was done using pubmed and ortholink search engines.

**Results:** NSAIDs act locally at the site of origin of pain by inhibiting the cyclooxygenase enzymes and induce no change in mood and dependency. The inhibition of the Cox enzymes can be reversible or irreversible and leads to inhibition of prostaglandin synthesis. All the therapeutic and most of the side effects of NSAIDs result from the inhibition of the cyclooxygenase pathway.

Thus the Cox-2 selective inhibitors have lesser side effects than the non selective Cox inhibitors; though there is recent evidence linking them with adverse cardiovascular events.

There is paucity of information in literature on the guidelines of the prescription/usage of NSAIDs, and the preventive strategies in orthopedics and traumatology.

**Conclusion**: NSAIDs are the most commonly prescribed group of drugs in orthopedics and trauma practice. They constitute a great asset to any Doctor who

deals with pains associated with inflammation which they relief quite effectively. NSAID Usage is froth with significant life threatening complications. A high index of suspicion of the possibility of occurrence of these complications, adherence to proper prescription guidelines and preventive strategies, change of the laissez-a-faire attitude of the professionals to NSAID prescription and appropriate monitoring of the patients on the drugs are paramount in improving their safety profiles. Orthopedic and Trauma surgeons need to be aware of the serious side effects and the role of preventive strategies in the use of NSAIDs.

*Key words:* NSAID, guidelines, preventive strategies, orthopedics/trauma.

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### Introduction

The proliferation of the NSAIDs in various forms and names and the wide spectrum of their clinical application in Medical practice for the management of musculoskeletal disorders and injuries have created a great niche for the abuse of these potentially harmful drugs by both the health professionals and the general public.

Reports of life threatening and fatal side effects and complications from these drugs are common in literature<sup>1,2</sup>. They are the most commonly used drugs in orthopedics and traumatology. Because NSAIDs are readily available, they are favorite instruments of suicide and a major cause of accidental poisoning in children. The past twenty years has seen an explosion of the number and types of these agents; including the Cox-2 selective inhibitors.

The aim of this study is to review the issues, controversies, complications and the abuses that may arise from their usage and recommend guidelines and preventive strategies that may reduce these problems in orthopedic/trauma practice.

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**Mechanism of Action:** NSAIDs inhibit the cyclooxygenase (Cox) enzymes that catalyze the biosynthesis of prostaglandins (PG) and thromboxanes from the arachidonic acid. This inhibition could explain all the clinical actions (therapeutic and side effects) of the NSAIDs. Prostaglandins (PGD<sub>2</sub>, PGE<sub>2</sub>, PGF<sub>2</sub>, and PGI<sub>2</sub>) are synthesized in the microsomes of all cells except the red blood cells, and are released when cells are damaged or stimulated. They act on cells in the vicinity of their synthesis to exert their actions<sup>3</sup>.

The cyclooxygenase in mammalian cells exist in two isoforms, Cox-1 and Cox-2. They are highly similar in structure and chemical activities; the major difference however lies in their biological roles and genetic regulation. Cox-1 expression is constitutive in most cell types and is thought to carry out house keeping roles in the various tissues; while Cox-2 expression is induced in response to inflammatory and proliferative stimuli<sup>4</sup>.

The individual class of NSAIDs has differing modes of inhibitory activity on the Cox enzymes. Aspirin acetylates a Serine amino acid at the active site of the enzyme while indomethacin inhibition is complex and involves sites different from that of Aspirin.

Based upon their inhibiting mechanisms, Cox inhibitors can be grouped into four classes <sup>4</sup>. The drugs in the first class irreversibly inhibit the Cox enzyme by acetylating the active site of the terminal amino acid. The prototype of this group of drugs is Aspirin. Aspirin is considered Cox-1 selective since doses 10-100 folds higher than those required for Cox-1 are necessary to acetylate the Cox-2 active site <sup>5</sup>.

The second class is reversibly competitive in action. They compete with arachidonic acid for its binding site on the enzyme.

The third class exhibits a slow time dependent inhibition of the Cox isoforms. The delayed kinetics of inhibition by this class probably reflects the time necessary for formation of a salt bridge between the carboxylate of the drug and arginine 120 (Cox-1 numbering). This inhibition is also reversible. The fourth class of Cox inhibitors selectively and reversibly inhibits only Cox-2. They contain larger side-groups which penetrate the larger binding pockets of Cox-2, but their size prevents them from entering the smaller pockets of Cox-1<sup>4</sup>.

Thus the analgesic efficacy of the NSAIDs results from their action at the site of origin of the pain through the inhibition of the prostaglandins.

Other mechanisms of action of NSAIDs may exist; such as inhibition of leukotriene synthesis, lysosomal enzyme

release, lipogenase activity, neutrophile aggregation and various cell membrane functions. Some newer agents such as aceclofenac can also inhibit the release of TNF, IL-1B, IL-6, and inhibit the binding of leucocytes to inflamed tissues by causing shedding of adhesion molecule (L- selectin) and thus stops propagation of inflammatory process<sup>6</sup>.

NSAIDS also have antipyretic effects which they exact by suppressing the effects of the endogenous pyrogens through the inhibition of the prostaglandins synthesis <sup>7</sup>. Fever may be caused by inflection, tissue damage, inflammation, malignancy and graft rejection etc. They produce fever by stimulating the biosynthesis of endogenous pyrogens in the phagocytic cells. The pyrogens cross the blood brain barrier into the pre-optic hypothalamic area where they induce the elevation of body temperature mediated through the release of prostaglandins. The initiation and maintenance of inflammatory response seems to depend on the PGs, especially the E and I types, since the effects produced by the injection of the PGs are strongly reminiscent of inflammation. It appears that PG cannot produce increased vascular permeability and chemostatic response without the participation of other mediators (histamine, 5HT, Bradykinin, leukotriene, chemostatic factor, etc).

The concentrations of NSAIDs that inhibit PG synthesis do not affect migration of inflammatory cells<sup>8.</sup> Thus NSAIDs do not predispose the patients to infection.

THERAPEUTIC EFFECTS OF NSAIDS: NSAIDs have Analgesic, antipyretic and anti inflammatory therapeutic effects. There are important differences in the magnitude of the various therapeutic activities of the individual groups of NSAIDs. The reason for this variation is not clear, though differences in the sensitivity of the target tissues may be responsible. Some of them have weak antipyretic effects e.g. Piroxicam.

NSAIDs are effective against mild to moderate pains, especially those associated with inflammation. Post operative pains are therefore quite susceptible while those arising from hollow organs respond poorly.

They provide symptomatic relief from pain by suppressing the inflammation associated with the disease process, as occurs in Rheumatoid arthritis, Ankylosing spondylitis, etc. NSAIDs do not necessarily arrest the progression of the pathological process/injury to the tissues. These drugs also do not change the perception of sensory modalities other than pain. They do not cause dependence and are therefore free from the CNS side effects of opioids.

SIDE EFFECTS: These are other unwanted effects of NSAIDs. Because they share many therapeutic effects, Aspirin-like drugs also share many side effects.

GASTRIC IRRITATION: This seems to be the most common side effect of NSAIDs. There is considerable variation in their tendency to cause this side effect. The gastric erosion effect is through both direct mucosal irritation and indirectly through the inhibition of  $PGI_2$  and  $PGE_3$  synthesis. These gastric prostaglandins promote the secretion of cytoprotective mucus in the intestines while inhibiting the acid secretion by the stomach. Analogs of these PGs can prevent mucosal damage; including that induced by anti-inflammatory drugs<sup>9</sup>.

Renal Dysfunction: NSAIDs have variable tendency to produce renal papillary necrosis and thus renal failure in certain predisposed patients. They however have little effect on renal function in normal subjects. They decrease renal blood flow and glomerular filtration rate in hypovolaemic patients, and those with congestive cardiac failure, renal insufficiency, chronic renal disease and liver cirrhosis. These effects appear to be as a result of the loss of the vaso-dilation effect of the renal prostaglandins which ordinarily mitigate the vaso-constrictive effects of nor-epinephrine and angiotensin II, thus allowing the pressor mechanisms to overplay. Thus the syndrome of analgesic nephropathy is also seen even with the newer generations of NSAIDs<sup>10</sup>.

FLUID RETENTION: NSAIDs promote salt and water retention by reducing the prostaglandininduced inhibition of the chloride resorption and inhibition action of the antidiuretic hormones. Significant edema may therefore develop in some patients on prolonged usage of NSAIDs; especially in those with low cardiac reserve who may show signs of overt cardiac failure. The abuse of analgesic mixtures is much more commonly associated with this problem and the development of chronic interstitial nephritis and papillary necrosis<sup>11</sup>. The injury is expectedly insidious in onset and initially manifest as reduced concentrating ability which may progress to irreversible renal insufficiency and outright chronic renal failure if misuse continues. Females are involved more often and there is usually a history of recurrent urinary tract infection with emotional disturbances.

CNS Side Effects: Headache, dizziness, confusion and occasionally, loss of consciousness have all been observed in patients taking NSAIDs especially among the elderly.

Coagulation: NSAIDs cause disturbances in platelet function by inhibiting the formation of thromboxane  $A_2$  (a potent platelet aggregator) through the cyclooxygenase pathway. Aspirin causes the most of such inhibition of all the drugs in the class. The inhibition lasts the life time of the individual platelet. This inhibition of platelet aggregation accounts for the increase in bleeding time in patients taking NSAIDs. Thus, their use prior to surgery or trauma might cause coagulation problems and lead to significant increase in blood loss. Thus NSAIDs should be stopped at least a week to any elective surgery.

Precipitation/Aggregation of Allergies: About 20-25% of adults with Asthma and other allergies will experience this syndrome on ingestion of NSAIDs. It is however rare in children.

The underlying mechanism is unclear and does not appear to be immunologic. It appears that the inhibition of the Cox enzymes and the diversion of the arachidonic acid metabolism towards the formation of increased amounts of leukotrienes and other products of the pathway may be responsible.

A variety of manifestations are observed, ranging from bronchial Asthma, vasomotor rhinitis, Bronchoconstriction, laryngeal edema, angionuerotic edema to complete cardiovascular collapse.

The above view however does not explain why only a minority of the patients with allergies display the reaction while taking Aspirin-like drugs.

Prolongation of Gestation and Labor: PGE and PGF are potent uterotropic agents that play major roles in the initiation and progression of labor. Thus, inhibition of PG can postpone Labor as well as prolong its course.

# INDICATION FOR NSAIDS IN ORTHOPAEDIC PRACTICE

- i. Treatment of acute pain associated with inflammation as occurs in acute trauma and gouty arthritis.
- ii. Treatment of chronic pains associated with inflammation e.g. Rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.
- iii. Suppression of inflammation and inflammatory edema following acute infections.
- iv. Treatment of febrile illness to reduce body temperature and as adjuncts in the treatment of acute infections.
- v. Prevention, control and treatment of myositis ossificans (hetertropic calcification). Indomethacin seems to be the drug of choice.

- vi. Metastatic disease of bone
- vii. Management of Post operative pains.
- viii. Other Malignancies. Indomethiacin has proven usefulness as an antipyretic in Hogkins disease when the fever has been refractory to other agents.
- ix. Treatment of soft tissue rheumatism.
- x. Prevention of thromboembolic phenomenon on the arterial side of the vasculature.
- xi. Neuritis, lumbago and myalgias.

CONTRA-INDICATIONS TO THE USE OF NSAIDS: Hypersensitivity to Aspirin is a contra indication to therapy with the Aspirin-like drugs. Administration of any of these drugs could provoke a life threatening hypersensitivity reaction in the form of anaphylaxis.

CHOICE OF NSAIDS TO BE PRESCRIBED: The choice of an agent as a simple antipyretic or analgesic is seldom a problem. In the field of rheumatology however, this decision becomes complex and involves the consideration of a number of factors; and providing the patient with the most effective analgesic and precise dosing schedule for a specific pain problem is difficult and time consuming. These difficulties arise as a result of toxic side effects of these agents and the wide individual variations in the response to the therapeutic effects of the drugs; which seem to follow no specific pattern <sup>12</sup>. Thus several steps should be taken and several factors considered before analgesics are prescribed. To reach a therapeutic plan for the individual patient, detailed history and physical examination is necessary.

FACTORS TO CONSIDER: Age of the Patient: Elderly patients are more prone to toxic effects of NSAIDS, especially the CNS and GIT problems. Drugs with less GIT side effects (e.g. cox-2 selective NSAIDS or ibuprofen) are preferred with commensurate dosage adjustments.

Pregnancy and Lactation: In children and pregnant women, the choice of drugs is considerably restricted (see side effects). Only drugs that have been extensively tested in children (Ibuprofen, Naproxen and Aspirin) should be prescribed.

State of health of the Patient (co-morbid conditions): Common diseases that could be made worse by the use of NSAIDs include Asthma, Renal and heart diseases (CCF). Patients with nasal polyps and history of allergies could display severe intolerance including anaphylaxis.

Dominant needed effect of the NSAID: Different NSAIDs have variable analgesic, antipyretic and antiinflammatory properties; for instance, piroxicam does not have any significant antipyretic properties Drug Interactions: The common drugs with which NSAIDs Interact includes: Digoxin, Methotrexate, Diuretics, anticoagulants and oral hypo-glycaemics, Cyclosporin and quinolones, etc. Drugs that bind heavily to plasma proteins are potentiated as they are usually displaced by NSAIDs.

The quinolones are commonly prescribed antibiotics in Orthopedics/traumatology and their interaction with NSAIDs should be noted.

Cost of the drugs, especially in relation to affordability by the patient.

Nature of the disease producing the pain: NSAIDs are most useful in diseases associated with inflammation.

Physical and Nutritional Status of the patient: Seriously physically debilitated patients tolerate NSAIDs poorly and have greater tendency towards toxicity especially CNS side effects.

Renal and Hepatic functions: (see side effects). Hepato-toxicity is commoner with Cox-2 selective NSAIDs.

Mental status and compliance ability to follow medical directives.

Family Support: The family should be made aware of the planned treatment program; and the Common Side effect to expect.

The basic rule in the choice of these drugs is to use the most effective drug or combination of drugs for relief of a specific pain state that produces the least serious or distressful side effects. The choice of NSAIDs for the treatment of arthritis is largely empirical. A drug is usually chosen after the above considerations and given for 1 2 weeks; if the therapeutic effect is adequate, treatment should be continued unless toxicity supervenes. Even when the alternatives are closely related chemically, a patient may do well on one agent and not the other (e.g. ibuprofen and ketoprofen).

#### USES IN SPECIFIC CONDITONS:

Metastatic disease of bone: Aspirin and Indomethacin are the analgesic drugs of choice for the initial treatment of pain associated with metastases to the bones. However, because of the severity of the side effects of these drugs especially indomethacin, it is advocated that their use be limited to 2-3 weeks and less toxic drugs then substituted by this time when the inflammation and pain is under control.

Osteoarthritis: This is probably the commonest singular indication of NSAIDs in our environment. The choice of

drugs is empirical and the administration cyclical, depending on the state of exacerbation and remission of the disease. The lowest effective dose should be used at any given time; and monitoring the patient for the common complication is paramount. Similar therapeutic approach is applied in the management of rheumatoid arthritis and ankylosing spondylitis.

Treatment of gout and pseudo gout: NSAIDs in high doses are quite useful in treatment of these conditions. Indomethacin and phenylbutazone have added uricosuric effects.

Treatment of fractures: The Cox enzymes play important roles in fracture repairs. Thus inhibition of these enzymes may delay bone healing <sup>5.</sup> Gerstenfeld et al.<sup>13</sup> noted that Cox-2 specific anti-inflammatory drugs inhibit fracture healing more than non-specific traditional NSAIDs and that the magnitude of the effect is related to the duration of treatment. Thus cautious use of NSAIDs in patients with fractures is advocated. It is recommended that the duration be limited to a maximum of five days. Discontinuation of the NSAID results in the return of the level of the PGs (PGE<sub>2</sub>) in a few days and restoration of the healing potential/strength to levels similar to the control.

Soft tissue injuries: NSAIDs are very useful in the relief of pains arising from soft tissues, especially when used in combination with skeletal muscle relaxants; since muscle spasms contribute significantly to the severity of the pain. In severe injuries inject able NSAIDs are advocated.

Post operative Pain: NSAIDs can be superior to the opioids in some situations such as following chest surgeries because of the respiratory depressant effects of opioids. It has also been shown that clonixin and anilonicotinic acid derivatives NSAIDs at doses of 600 mg is as effective as 10 mg of morphine for the relief of post operative pain.

COMPLICATIONS OF USE OF NSAID: These arise from the side effects of NSAIDs. The safety of drugs used in pain management has become of utmost concern to clinicians world wide due to GIT ulceration caused by nonselective NSAIDs with rising incidents globally. These complications are commoner in the patients taking NSAIDs for prolonged period (> 6 weeks), but could also occur following ingestion of a few doses; especially the GIT complications.

Gastro-intestinal Complications are the commonest and occur in the form of dyspepsia, gastric erosion, upper gastro intestinal bleeding, obstruction and perforation <sup>14</sup>.

Peptic ulcer disease can develop from the gastric erosion. NSAIDs are also associated with lower GIT harm<sup>15</sup>.

In the urogenital system, papillary necrosis, chronic interstitial nephritis and chronic renal failure can occur following prolonged use of NSAIDs. They are also associated with acute renal failure <sup>16</sup>.

Congestive Cardiac failure and chronic edema are associated with prolonged consumption of NSAIDs<sup>17,18</sup>. Other complications include anaphylaxis / allergies, Blood dyscrasias of various types, auto immune haemolytic anaemias and toxicity. The fenamic acid and pyrazolon derivatives are more associated with blood dyscrasias than the other classes of NSAIDs.

ABUSES OF NSAIDS: This group of drugs is probably the most commonly abused in the West African Sub region. The causes of these abuses stem from:

Poor prescription habits by health professionals. It is common to see or hear a Doctor, Pharmacist and other Paramedics make prescriptions of analgesics over a telephone or casually during a discussion without attention to the due process as outline in the choice of NSAIDs. This malpractice gives the wrong impression to the public that NSAIDs are no serious drugs and can be taken randomly.

Indiscriminate ingestion of combinations of NSAIDs of same or different class/generics by self medicating patients and those being treated by quacks and charlatans. This predisposes to higher complication incidence.

The proliferation by the pharmaceutical companies of different brands and generics with little or no difference.

Over the Counter Purchase of NSAIDs

This is even encouraged by the Pharmacists/Companies in their adverts -- If symptoms persist after three days, consult the Doctor. In the USA and UK, some of the less toxic brands like ibuprofen can be purchased over the counter but people are more discrete.

Preventive Strategies to Reduce Complications of NSAIDs Despite the fact that the efficacy of the NSAIDs is well documented across multiple indications, it is also recognized that patients who use these agents are at increased risk of upper gastro intestinal toxicity. Some important risk factors which heighten the rate of the NSAID associated upper gastro- intestinal toxicity have also been identified. These have necessitated the formulation of some preventive strategies and guidelines to minimize these adverse systemic effects and improve upper gastro-intestinal outcomes in patients taking NSAIDs. This is important in Orthopedics/Trauma care since NSAIDs are the most commonly used drugs. The preventive strategies include:

Treatment of Helicobacter Pyloric Infection.

Helicobacter pyloric infection is strongly associated with Gastro intestinal diseases such as chronic active gastritis and peptic ulcer disease <sup>19</sup>, especially in patients who use NSAIDS <sup>20</sup> in whom it increases the risk of ulcer two to four folds<sup>21</sup>. The need for the eradication of the H. pylori infection before commencing a patient on NSAID <sup>22</sup> is thus obvious, especially in orthopedic patients most of whom are regular and chronic users of this class of very useful drugs.

Different treatment regimens for H. Pylori eradication exist but none of them has an optimal eradication rate. The combination of a proton pump inhibitor or Ranitidine bismuth citrate plus clarithromycin plus amoxicillin or metronidazole for 7-14 days had been proposed as first line therapy for this purpose<sup>23</sup>.

In the field of Orthopedics/Trammatology NSAIDs are commonly prescribed for acute pains and emergencies; and this make it impracticable to aim at the eradication of the H. pyloric infection before their use. Besides, the facilities for diagnosis of this infection can only be found in four centers in the West African sub region. The infection can be diagnosed using the Chair side 13c urea breath test and through histological examination of gastric endoscopic biopsy specimen<sup>24</sup>. Because of the above difficulties and peculiarities of Trauma/Orthopedic practice, we recommend that patients who are going to be placed on regular NSAIDs for prolonged period should be treated for Helicobacter Pylori at the same stage. Since there is no significant negative drug drug interaction between the NSAIDs and Maastrict 2-2000 recommended first line drugs (Proton Pump Inhibitor, Ranitidine, Clarithromycin, Amoxicillin)<sup>23</sup>, these could be administered alongside with the NSAIDs. However, in patients who need other prescriptions that may lead to increased chances of side effects and complications, the treatment of H. Pylori infection can be suspended until the acute pain abates when NSAIDs can be discontinued temporarily and the anti H pylori agents administered before recommencing the drugs. During this period Acetaminophen and tramadol can be used for pain control.

H Pylori are normal commensals of the oral cavity, especially in dental plague. It has been shown that there is a direct relationship between the number/quantity in

dental plaque and severity of peptic ulcer diseases<sup>25,26</sup>. Hence, it might be possible that direct inoculation of gastric mucosa by H. pylori occurs from the oral cavity, especially in patients with poor oral hygiene<sup>24</sup>.

### Gastro Protective Agents:

The use of gastro protective agents (GPA) had consistently been recommended in the preventive strategies and guidelines for Patients receiving NSAIDs. The gastro protective agents include Misoprostol, proton pump inhibitors (PPI) and Histamine receptor antagonists<sup>27</sup>. These agents reduce the well recognized upper gastro-intestinal symptoms and ulcer complications associated with non-specific (traditional) NSAIDs, especially in high risk patients<sup>24</sup>. The problem with the use of the GPAs in our environment where most patients are poor is additional cost and the possible reduction in compliance by the Patients. However adequate Patient education and motivation can readily obviate it. It appears however that a lot of the prescribers of NSAIDs do not appreciate the benefits of the GPAs and therefore under utilize them; a problem that is not peculiar to developing countries like Nigeria<sup>28</sup>.

Cox-2 Selective Inhibitors (Coxibs):

The use of Cox-2 specific inhibitors (Coxibs) has been known and recommended as part of the preventive strategies to improve gastro-intestinal outcome in NSAID users<sup>28</sup>. They reduce the gastro-intestinal symptoms and ulcers in patients using NSAIDs especially in high risk patients. The evidence in reducing upper gastro-intestinal bleeding is considerable for Coxibs compared to gastro-protective agents prescribed with NSAIDs<sup>24</sup>. The major problem associated with Coxibs in our environment is the prohibitive cost and the risk of cardiovascular adverse events than with traditional NSAIDs. Thus the prescription of these agents in orthopedic patients who use NSAIDS for prolonged periods should be done with caution especially in those with cardiovascular complaints<sup>29.</sup>

Regular Dental Check-up and Treatment of Dental Caries:

The treatment of dental caries to eliminate the plaque and reduce the population of H. pyloric has been proposed as a preventive strategy, especially in those with poor oral hygiene<sup>24</sup>. Improvement in dental hygiene and health is readily achievable through simple patient education at first contact. The use of chlorhexidine mouth rinse in Patients with poor oral hygiene as a chemical means of reducing plaque and microbial population of the buccal cavity can be of immense help in trauma/orthopedic Patients with acute pain; in whom there may be urgent need to commence the NSAIDs before a Dentist's consult. Regular dental check-up is advocated in the chronic users of NSAIDs as seen in orthopedic practice.

- Finally, the cyclical use of NSAIDS in some Orthopedic conditions Like Osteo-arthritis and Rheumatoid Arthritis; that require prolonged use of NSAIDs may be helpful in reducing the complications. The use of drugs combinations that contain NSAID and gastroprotective agents is advocated in these chronic users.
- Generally, when skeletal muscle relaxants are prescribed together with NSAIDs for diseases associated with spasm of the muscles, lower doses of NSAIDs are often usually needed. Higher doses of NSAIDs predispose the patient to greater complication rate. The use of topical agents also generally reduces the effective systemic dosage of NSAIDs with possible reduction in the incidence of complications.
- It is important to note that complications of NSAID usage are more common when taken with other drugs than when taken alone. Thus the fewer the number of other drugs prescribed with NSAIDs the safer for the patient.
- Most Patients who experience severe chronic pains require strong Psychological support. This is often accomplished by the attitude of the Physician which should be reassuring, cheerful, sympathetic and understanding; as most patients are quick to sense an attitude of hopelessness or lack of interest on the part of the physician and other health workers. Thus the physician and the members of his team should do every thing possible to provide a sense of security and assure the patients that attempts will be made to

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relieve their suffering by all available means since GIT complications of NSAIDs appear to be commoner in depressed patients.

#### CONCLUSIONS

NSAIDs are the most commonly prescribed group of drugs in Orthopedics and Trauma practice. They constitute a great asset to the Doctors and Paramedics who deal with pains caused by inflammation. They are quite effective in the relief of pains of this nature, but their usage is froth with significant life threatening complications; mainly resulting from their mechanism of action. The newer cox-2 selective inhibitors therefore appear safer than the traditional non-selective inhibitors, in terms of complication profile.

The more toxic NSAIDs like fenamic acid and pyrazolon derivatives should only be prescribed when the patient does not respond well to safer drugs, and this must be with circumspection and for short periods.

A high index of suspicion of the possibility of development of the complications and adequate monitoring of the patient on the drugs is paramount. The assessment of the renal function should be done twice yearly.

Health workers are responsible for a greater percentage of the abuses of these drugs as a result of their attitude towards them.

A good knowledge of the preventive strategies is sine quanon in the use of NSAIDs in Orthopedics and Trauma practice.

#### RECOMMENDATIONS

We suggest better education for Orthopedic and Trauma Surgeons, Trainees Surgeons, Doctors, Paramedics and patients on the risks associated with NSAID use. The development of preventive strategies for our environment (the West African sub region) is overdue to determine appropriate guidelines toward the goal of preventing NSAID associated complications.

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