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The Pattern of NSAIDs Drugs Use by Libyans Patients for Acute Tissue Injury

Samia A Hassan[1,2*], Mahammed M Jibreel[1], Hanan M Mady[1] and Lamis A BenSaad[2]

[1]*Alghad University Department of Pharmacy*

[2]*Tripoli university, Medical school, Pharmacology Department*

[*]Corresponding Author
Samia A Hassan, Alghad University Department of Pharmacy.

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Abstract

Introduction: *NSAIDs are a family of drugs that have achieved widespread use in sports medicine in both prescription and over-the counter (OTC) forms. NSAIDs are often administered after acute soft tissue injury in an effort to reduce pain and inflammation and thus speed an injured athlete's return to competition. However, recent evidence suggests that the short term benefits of NSAID therapy may adversely affect the long-term healing of injured soft tissues.*

Method: *The study was performed to test pattern of NSAIDs use by Libyan patients. Patients were asked to complete a self-report questionnaires while attending orthopedic clinic at Al-Haraysh hospital at Darna City (Libya) during the period from March to May 2022.*

Result: *Panadol (acetaminophen) consumption was reported by 6 (40%). Equivalent data for ketoprofen (Fastum gel) were 6 (40%) for topical preparation. Tewinty percent (3) of the participants consumed Muscadol (Paracetamol 450mg + Orphenadrine citrate 35mg)-based drugs. These were ibuprofen (ketoprofen)-based drugs used by 3 (20%) of respondent . The 2 (13%) consumed Naproxen (Nopain) and only the 1 (6.6%) used Aspirin for their injuries.*

Conclusion: *NSAIDs are commonly used in the treatment of acute soft tissue injuries in athletes. Because of the diverse of adverse effects associated with NSAIDs, athletic trainers must be aware of the potential benefits and liabilities of NSAIDs use by injured.*

1. Introduction

Aspirin (acetylsalicylic acid), originally derived from the bark of the willow tree, was the first non-steroidal anti-inflammatory drugs (NSAID) and has been used in several forms to treat human disorder for centuries. Although aspirin was used for centuries, its mechanism of action was not established until 1971, when Vane determined it inhibited production of all prostaglandins, work which simultaneously garnered him and his colleagues the Nobel Prize for Medicine in 1982 [1,2]. when Vane reported that prostaglandin production was inhibited by aspirin. Examining side effects of aspirin such as stomach bleeding. These side effects aroused the search for chemically similar drugs with similar analgesic and anti-inflammatory properties but without associated side effects [3]. In contrast to newer generation NSAIDs whose COX inhibition is reversible, aspirin-induced COX inhibition is irreversible due to the fact platelets have no DNA and are thus unable to synthesize new COX enzymes [4].

NSAIDs are a family of drugs that have performed widespread use in sports medicine in both prescription and over-the counter (OTC) forms. NSAIDs are often managed for acute soft tissue injury in an effort to reduce pain and inflammation and thus speed an injured athlete's return to competition. However, recent evidence suggests that the short term benefits of NSAID therapy may adversely affect the long-term healing of injured soft tissues [5].

Therefore, Non-steroidal anti-inflammatory drugs are used for their analgesic, antipyretic, anti-inflammatory, and anticoagulant effects [5]. According to National Health And Nutrition Examination Survey (NHANES) the number of Americans using NSAIDs on a frequent monthly basis doubled between 1994 and 2000 [6].

OTC NSAIDs are available in doses that primarily producing analgesic and antipyretic effects, but not anti-inflammatory effects. The dosage to achieve anti-inflammatory effects generally is twice of analgesic effects. Clinically, it is very difficult to differentiate between the anti-inflammatory and analgesic effects of NSAIDs [5].

The effects of COX–inhibiting drugs are tissue-specific. Ibuprofen, for instance, has a major effect on COX in the peripheral tissues, while acetaminophen performs its COX–inhibition in the

central nervous system. The effects of COX-inhibiting drugs are also dose-dependent, and analgesic doses tend to be 50-75% of anti-inflammatory doses, both in terms of dosage and duration of treatment [2,7,8]. Over-the-counter, or nonprescription NSAIDs are accessible in doses that primarily produce analgesic and antipyretic, but not anti-inflammatory effects [9].

The most NSAIDs inhibit COX by transacetylation of the active center of the enzyme, competing with the cell membrane substrate arachidonic acid for the enzyme's active site. Definitely, drugs such as aspirin and indomethacin, acetylate prostaglandin endoperoxide synthetase (PGG and PGH), resulting in loss of COX activity, which subsequently inhibits prostaglandin production. COX lies in two distinct isoforms- COX-1 and COX-2. COX-3 is a third isoform recently identified as a variant of the COX-1 gene, and it appears to regulate fever within the central nervous system [2,10,11]. Despite a high sequence of homology between the two isoforms, differences in the active sites of the enzymes have been pharmaceutically exploited to develop inhibitors selective for COX-2 [12].

Therefore, COX-1 functions as a physiologic servant and induces prostaglandin synthesis for normal healthy body functions, for instance, producing cytoprotective mucus in the digestive tract. Prostaglandins are required for normal physiologic processes to occur in the gastrointestinal tract, kidneys, liver, and other organs. When COX-1 is inhibited by NSAIDs, prostaglandin synthesis does not occur in the gastrointestinal tract, kidneys, and other organs, and, thus, the normal physiologic functions carried out by prostaglandins cannot occur. Inhibition of COX-1 causes many of the visceral side effects associated with NSAIDs (Lipsky, 1999; Adelizzi, 1999).

COX-2 is present in most tissues in little amounts, but levels are enhanced considerably at sites of inflammation. Furthermore, COX-2 is involved in prostaglandin synthesis associated with the inflammatory process. NSAIDs blocking COX-2 thus inhibit prostaglandin synthesis associated with inflammation. Hence, the ultimate anti-inflammatory drug would theoretically inhibits prostaglandin synthesis mediated by COX-2 while having no effect on COX-1 [13,14]. COX-2 is found in the kidneys and central nervous system. Novak et al., (2009) also revealed its expression in the skeletal muscle fiber periphery, in addition to, near nuclei of myogenic precursor cells (satellite cells) [15].

NSAIDs deviate from their anti-inflammatory effectiveness as well as their ability to inhibit COX-1 and COX-2. Several commonly known NSAIDs for instance piroxicam, indomethacin, and Aspirin preferentially inhibit COX-1 and are associated with a greater risk of gastrointestinal and renal complication. Non-selective NSAIDs inhibit both COX isoforms, but it is their advantageous inhibition of COX-2 that is their primary analgesic mechanism. This selective COX-2 inhibition also have tendency to fewer GI complications [10].

In additional, NSAIDs have anti-inflammatory effects unrelated to arachidonic acid. NSAIDs are noticed to inhibit neutrophil aggregation and migration to sites of inflammation. Other amendments of neutrophil function are also affected, including the slowing of lysosomal enzyme release, decreased oxidative phosphorylation, and decreased production of substances that are chemotactic for other leukocytes. Oxygen free-radical production by neutrophils and phagocytes is also decreased in the presence of NSAIDs [15-17].

2. Aims of the Study

To investigate the most frequent NSAIDs used by Libyan patients for acute tissue injury.

3. Method

The study was performed to test pattern of NSAIDs use by Libyan patients. Ethical approved was obtained from the head of hospital. Patients were asked to complete a self-report questionnaires while attending orthopedic clinic at Al-Haraysh hospital at Darna City (Libya) during the period from March to May 2022.

The complete a self-report questionnaires was designed to elicit information on the type of NSAIDs drugs, time of use before or after injury and adverse effects. And specific indication for medication consumption were also obtained. Details of age and gender were recorded. Data were coded for each participant's questionnaire.

Frequency of medication use in the study was calculated. Proportions were compared by Chi-square tests to examine the comparability of exposure in population as a whole using Graphic Pad (Prism)5 . statistical significance were taken at $P \leq 0.05$ level (significant $P=0.034$).

4. Results

A total of 20 participants were interviewed. Only 15 participant's questionnaire respondents (75%). Their mean age was 26 year (range 18-35). NSAIDs products were used most commonly by male patients (100%) which had sport or exercise-related injuries.

Panadol (acetaminophen) consumption was reported by 6 (40%). Equivalent data for ketoprofen (Fastum gel) were 6 (40%) for topical preparation (Figure 1).

Tewinty percent (3) of the participants consumed Muscadol (Paracetamol 450mg + Orphenadrine citrate 35mg)-based drugs.

These were ibuprofen (ketoprofen)-based drugs used by 3 (20%) of respondent. The 2 (13%) consumed Naproxen (Nopain) and only the 1 (6.6%) used Aspirin for their injuries.

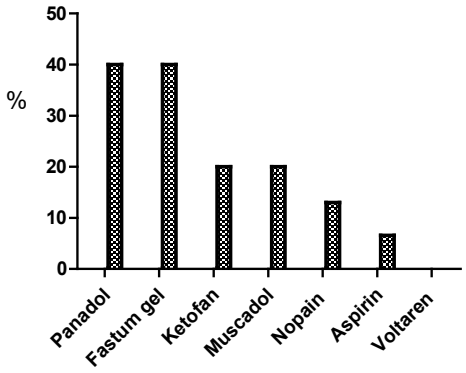

Figure 1: Types of NSAIDs were taken

Eighty-seven percent used non-prescription NSAIDs on as a daily-needed for short time, while 13% used as a daily basis for long time.

Eighty percent consumed the recommended drugs for acute injuries, while 20% used the exact drugs for chronic disease.

The most frequent reported reasons for non-prescription NSAID use included muscular ache (29.4%), arthritis (17.6%), back pain (5.9%), joint pain (17.6%). and joint pain (17.6%).

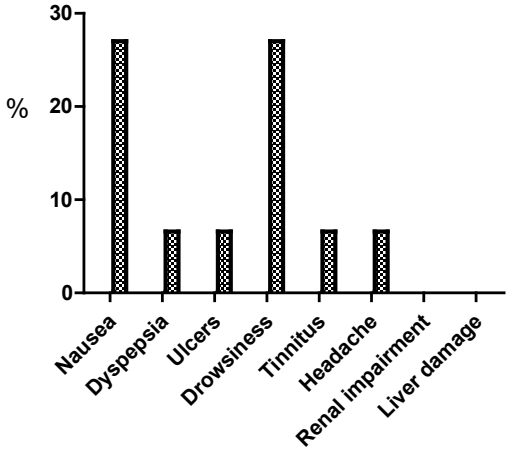

Figure 2: Side effects of drugs

There are 27% reported nausea as adverse effects on oral therapy, where as 6.6% have dyspepsia and 6.6% ulcers. As well as 27% have drowsiness, 6.6% headache and 6.6% have tinnitus (Figure 2).

However, in this study that particular other side effects for instance, liver damage or renal impairment no patient suffering from them.

5. Discussion

NSAIDs are commonly prescribed for patients who have an acute injury, with the primary reason for relief of pain. Analgesics are used frequently in sport to treat pain and inflammation associated with injury [18]. The average age of participants in the current study was 26 years where used NSAIDs for sport and work injuries. Such as injuries are excessively common among athletes, military personnel, and civilians of all ages [19]. There is documentation that NSAID administration 47 hrs post-injury significantly increase of the circulating group A streptococcus to the injured site [20]. Other report suggested that that NSAID use early post injury lead to down-regulates several anti-apoptosis proteins that inhibit the extrinsic pathway of programmed cell death [21].

Paracetamol, ketoprofen gel, ketoprofen, muscadol (Paracetamol 450mg + Orphenadrine citrate 35mg) and Naproxen were used by athletes Within the 14 days after exercise or injury. On other hand, few patients were used NSAIDs frequently (≥3 months). Previous research support this study, Ibuprofen was the most commonly chosen analgesic, selected by 80% of football players, confirming the analgesic's popularity as reported in other surveys of the general adult population [6,22,23] .

Moreover, the most NSAIDs drugs were applied for acute injuries rather than chronic disease. For instance, The most often reported reasons for non-prescription NSAID use muscular ache, arthritis, joint pain , and back pain were the most injuries found in this study, all of participating patient used NSAIDs only after injury. However, there is growing evidence that some athletes might be taking these substances prophylactically, in an attempt to enhance performance [24].

Although NSAID use before injury is not a typical practice in the general population, these results clearly indicate that prophylactic use of NSAIDs, as is common among professional and athletes [25].

The effects of NSAIDs on human muscle inflammation have been studied using the induction of delayed-onset muscle soreness (DOMS) after repetitive eccentric contractions as a model of muscle injury in humans. Bouts of eccentric exercise generate small amounts of muscle fiber damage and result in significant pain in the days after eccentric exercise [23].

Furthermore, Researchers using animal models to study the histological effects of NSAIDs on muscle and ligament injury have shown that NSAIDs result short-term improvements in muscle healing and function, but either no long-term benefits or potentially deleterious long-term effects on muscle structure and function [26].

In additional, previous studies demonstrate that the effects of piroxicam on the healing and function of anterior tibialis muscle strains in rabbits, the piroxicam-treated group was able to generate more contractile force than the placebo group on the day after injury. No significant differences were found in maximum tetanic contraction between the groups through 1 week post-injury. However, the piroxicam-treated group subjectively appeared to have delayed inflammation and healing compared with the placebo group throughout the first week after injury .

However, In the case of muscle injury, the evidence suggests that NSAID use can significantly delay muscle regeneration and decrease muscle strength and size after repair. This seems to be an inevitable consequence of the fact that the inflammatory response to injury is a necessary phase of soft tissue healing [23].

Finding documents that the most common side effect regarding gastrointestinal tract such as nausea, dyspepsia, gastric ulcers. And other adverse effect drowsiness, headache and tinnitus.

This report consist with previous studies the most common side effects associated with NSAIDs are gastrointestinal tract such as dyspepsia, nausea, gastrointestinal bleeding, and ulcers. These effects stem primarily from the inhibition of prostaglandins in the gastric mucosa (Bindu et al., 2020). Prostaglandins normally decrease gastric acid secretion and increase bicarbonate and mucus secretion. However, in the presence of prostaglandin-inhibiting drugs, these protective mechanisms cannot occur. Gastrointestinal symptoms are most often related to chronic NSAID use but may also be seen with short-term use [28].

on other hand, a less frequent side effect involves renal dysfunction after use of NSAIDs (Lucas G.N.C et al., 2019). This adverse effect is the most common reported in the elderly and those with previous kidney damage. Prostaglandins are involved in the regulation of normal renal homeostasis, therefore, normal renal function can be inhibited by NSAIDs [27]. However, NSAID administration to individuals who are dehydrated may cause depletion in renal plasma flow and glomerular filtration rate within hours. This acute hemodynamic effect is the most common renal syndrome caused by NSAIDs [29].

Certain of NSAIDs, especially Aspirin (the salicylates), are shown that to impair normal coagulation by inhibiting platelet aggregation. This effect is potentially danger during periods of acute inflammation because it may lead to hugely accelerates of hematoma after injury. The adverse effects on clotting mechanisms associated with NSAIDs are of particular importance in patients who have a coagulopathy or a closed head injury. Aspirin permanently inhibits cyclooxygenase for the length of an erythrocyte's life and can thus impair clotting for up to a week after injury [3].

Moreover, Aspirin has an allergic reaction resulting in urticaria, angioedema, and asthma [30]. Of more concern to otherwise healthy athletes however is that NSAID use has also been linked to poor wound healing and to increased risk of complications following surgery [31]. The limited human data available are not prevent the use of NSAIDs postoperatively, in specific, for short-term less than 2 weeks [32].

In addition, other side effects less frequent associated with NSAIDs use include hepatic damage and central nervous system dysfunction. Liver damage typically occurs only in individuals who have suffered previous from liver damage [33]. The most common central nervous system effects include headache, tinnitus, and drowsiness. Auriel et al., (2014) support this finding the most or all drugs used for the treatment of headache, including NSAIDs, may cause a condition known as medication overuse headache a refractory

chronic daily headache that tends to improve following discontinuation of the analgesics [34]. However, Several studies have demonstrated that various NSAIDs may play a role in the prevention of neurodegenerative diseases including Parkinson's disease (PD) and dementia [35].

6. Conclusion

NSAIDs are commonly used in the treatment of acute soft tissue injuries in athletes, yet their efficacy is not substantiated in the scientific literature. While NSAIDs are often prescribed for their anti-inflammatory, analgesic, and antipyretic effects after acute injury, there is little evidence to support the claim that NSAIDs accelerate the return of injured athletes to competition. In addition, separating the anti-inflammatory effects from the analgesic effects is not easy. Recent evidence from studies using animal models suggests that the short-term benefits of NSAIDs may be outweighed by long-term compromise of the structure and function of the injured tissue.

Because of the diverse of adverse effects associated with NSAIDs, athletic trainers must be aware of the potential benefits and liabilities of NSAIDs use by injured athletes. Further research must address the effectiveness of NSAIDs in clinical trials involving injured athletes.

A reasonable use of these substances seems to be necessary. However, the prescription of NSAIDs is justified in certain cases, it should always be the minimal effective dose and the short-

est possible length of administration.

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