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Efficacy of non-steroidal anti-inflammatory inhibitors as an anticonvulsant drug

فعالية مثبطات مضادات الالتهاب غير الستيرويدية كدواء مضاد للاختلاج

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Abstract

NSAIDs are mostly used as analgesics for mild to severe pain. NSAIDs are provided to people who have infections to reduce their pain. They are also employed for anti-inflammatory, anti-pyretic, anti-rheumatic, anti-thrombotic, and spasmolytic effects. This study aims to look into the most important characteristics, clinical uses and side effects of NSAIDs. When taken as analgesics, NSAIDs are often helpful against mild to moderate pain, such as toothache. Even though their effectiveness is often significantly lower than that of opioids, NSAIDs are preferred because they have less adverse effects on the central nervous system (CNS), such as respiratory depression and the possibility for physical dependence. NSAIDs have a number of risk factors that can affect several systems in the body such as cardiovascular system, gastrointestinal system and brain side effects. Therefore, it is therefore recommended to administer NSAIDs and other analgesics, and doctors need to undergo training through educational sessions such certification courses on pharmacotherapy (in particular pain drugs. The government should also amend the relevant laws to clarify the obligations placed on physiotherapists in terms of prescribing medications.

Keywords: *Anti-Inflammatory Drugs, Anticonvulsant, NSAIDs, side effects.*

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ملخص

تستخدم مضادات الالتهاب غير الستيرويدية في الغالب كمسكنات للألم الخفيف إلى الشديد، حيث يتم تقديم مضادات الالتهاب غير الستيرويدية للأشخاص المصابين بعدوى لتقليل آلامهم. كما أنها تستخدم كمضادات للالتهابات، ومضادة للحمى، ومضادة للروماتيزم، ومضادة للتخثر، ومضادة للتشنج. تهدف هذه الدراسة إلى النظر في أهم الخصائص والاستخدامات السريرية والآثار الجانبية لمضادات الالتهاب غير الستيرويدية. فعند تناولها كمسكنات، غالبًا ما تكون مضادات الالتهاب غير الستيرويدية مفيدة في علاج الألم الخفيف إلى المتوسط ، مثل ألم الأسنان. وعلى الرغم من أن فعاليتها غالبًا ما تكون أقل بكثير من فعالية المواد الأفيونية، إلا أن مضادات الالتهاب غير الستيرويدية مفضلة لدى الكثير لان لها ضرر أقل نسبياً على الجهاز العصبي المركزي (CNS)، مثل تثبيط الجهاز التنفسي وإمكانية الاعتماد الجسدي. تحتوي مضادات الالتهاب غير الستيرويدية على عدد من عوامل الخطر التي يمكن أن تؤثر على العديد من أجهزة الجسم مثل الجهاز القلبي الوعائي والجهاز الهضمي والعديد من الآثار الجانبية التي تؤثر على الدماغ. لذلك، يوصى بإعطاء مضادات الالتهاب غير الستيرويدية والمسكنات الأخرى، يحتاج اختصاصيو الأدوية إلى الخضوع للتدريب من خلال الدورات التعليمية مثل دورات الشهادات في العلاج الدوائي، خاصة أدوية مسكنات الألم. كما ويجب على الدول أيضًا تعديل القوانين ذات الصلة لتوضيح الالتزامات المفروضة على عمليات وصف الأدوية.

الكلمات المفتاحية: الأدوية المضادة للالتهابات، مضادات الاختلاج، مضادات الالتهاب غير الستيرويدية، آثار جانبية.

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1- Introduction:

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used medications, supporting their inclusion on the WHO's Model List of Essential Medicines worldwide. This is due to their effectiveness in lowering pain and inflammation. NSAID use is obviously unavoidable, given the rising incidence of musculoskeletal problems, as shown by the 2016 Global Burden of Disease data. In addition to their analgesic, anti-inflammatory, and antipyretic effects, NSAIDs have also been shown to provide protection against a number of serious diseases, such as cancer and heart attacks (Bindu et al., 2020).

NSAIDs were traditionally grouped according to their chemical properties, with the majority of the well-known NSAIDs being classified as significant derivatives of salicylic acid, acetic acid, enolic acid, anthranilic acid, or propionic acid. However, as scientific understanding has increased, the classification of NSAIDs has also changed (Abdu et al., 2020).

Due to the significantly lower drug-substance concentrations in the systemic blood pool, the clinical trial data provided in Matyushkin & Lvanova (2021) showed that NSAIDs in topical dose forms are more effective and secure than peroral medications. The most frequent side effects of topical NSAIDs are skin rashes at the treatment site.

Additionally, in clinical practice, no steroidal anti-inflammatory medicines (NSAIDs) are frequently used as anti-inflammatory, analgesic, and antipyretic medications. Therefore, this study is conducted to review

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the efficacy of non-steroidal anti-inflammatory inhibitors as an anticonvulsant drug, through viewing their characteristics, uses and different side effects.

2- Research Problem & Questions:

Different types of pain can be treated with a variety of pharmacological groups, including non-steroidal anti-inflammatory medicines (NSAIDs), opioids, corticosteroids, antidepressants, and anticonvulsants. A significant clinical issue in the management of pain is the interindividual diversity in medication response. Additionally, these medications are linked to a number of pertinent side effects, particularly when used long-term, which may have the potential to raise morbidity and mortality. Moreover, long-term opioid medication raises the possibility of being diagnosed with opioid misuse or dependence (Grunze et al., 2022).

Based on the forgoing, this study aims to look into the most important characteristics, clinical uses and side effects of NSAIDs. Therefore, the problem addressed in this research study can be posed through the following main question:

"How effective are non-steroidal anti-inflammatory drugs as anticonvulsants?"

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Through which we pose the following **sub-divided question**:

1- What are the main characteristics of NSAIDs?
2- What are the most important uses of NSAIDs including anticonvulsant drugs?
3- What are the common side effects of using NSAIDs?

3- Characteristics of NSAIDs:

Non-steroidal anti-inflammatory medications (NSAIDs) have had a blockbuster reputation in the pharmaceutical industry ever since Salicyclate was isolated from willow bark in the 1830s, followed by the discovery of aspirin (acetyl salicyclate) by Felix Hoffman of Bayer Industry in 1897 (Bindu et al., 2020).

The most popular class of medications used to treat pain is the non-steroidal anti-inflammatory drug (NSAID) class. However, systemic NSAID use frequently results in negative side effects. In order to achieve effective blood concentrations of the drug substances in target tissues that are significantly lower than those for systemic administration of NSAIDs are, anti-inflammatory and analgesic medications in dosage forms for external application can be used to treat musculoskeletal pain by applying them to the skin in close proximity to the affected area. Due to lower blood concentrations of the drug compounds than those from systemic administration of NSAIDs, usage of NSAIDs in topical dosage forms is

associated with a decreased risk of side effects and the metabolism of the active chemicals in the liver (Abdu et al., 2020).

Five primary signs of inflammation include swelling, redness, heat, discomfort, and loss of function (reported by Cornelius Celsus in the first century). With annual sales of more than US $6 billion, non-steroidal anti-inflammatory medicines (NSAIDs) are the most widely used medications for the management of pain and inflammation, including the treatment of chronic conditions such rheumatoid arthritis and osteoarthritis.

NSAIDs are well absorbed when taken orally and reach their maximal blood levels in 2 to 3 hours. However, the presence of food and antacids slows their absorption via the GI tract. Some NSAIDs, like nabumetone and diclofenac, are subject to the first pass effect and are removed prior to absorption. As parenteral formulations, diclofenac, ibuprofen, ketorolac, and paracetamol are given. These treatments can lessen the GI tract's immediate local side effects (Zhang et al., 2021).

On the other hand, many NSAIDs are used as topical preparations to lessen their systemic adverse effects, for example, diclofenac is added to topical solutions or transdermal patches and gel formulations for absorption through the skin, where it is then transferred to the joints and muscles where it acts.

Since the majority of NSAIDs are very mildly acidic, after absorption and transit into the bloodstream, they are highly linked to plasma proteins, particularly albumin (>90percentage). Furthermore, when the NSAID concentration exceeds the albumin concentration, the plasma may

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become saturated. NSAIDs compete with other medications that have a high affinity for proteins for binding sites. The plasma concentration of the active NSAID molecules will rise if other medications have already taken up the binding sites, at least briefly. A number of pathophysiological circumstances, such as secondary hypoalbuminemia linked to active rheumatoid arthritis, can cause an NSAID's free plasma percentage to rise (Zobdeh et al., 2022).

4- Uses of NSAIDs:

Non-steroidal anti-inflammatory drug (NSAID) use has been reported as common among older people with chronic pain. Although NSAIDs are essential to preserving their quality of life, the risk of polypharmacy, drug interactions, and side effects is of utmost relevance because older people typically need many drugs for their co-morbidities. Prescriptions that are not properly monitored and managed may expose patients to dangerous drug interactions and possibly deadly negative consequences (Abdu et al., 2020).

NSAIDs are typically effective against low to moderate levels of pain, such as toothache, when used as analgesics. NSAIDs are chosen because they have less negative effects on the central nervous system (CNS), such as respiratory depression and the potential for physical dependence, even if their effectiveness is typically much lower than that of opioids. NSAIDs, in particular, provide pain relief for chronic pain brought on by inflammation (such as somatic discomfort) and post-operative pain.

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NSAIDs are widely prescribed by doctors to treat rheumatoid arthritis and osteoarthritis. Over 65-year-old, adults who have osteoarthritis account for almost 60% of the population. It is characterized by osteophytes at the joint borders, articular inflammation, and subchondral bone degradation. Pain reduction and the return of joint function are the goals of osteoarthritis treatment. In the early stages of osteoarthritis treatment, paracetamol is used to relieve pain. If the pain is ongoing and paracetamol is not providing enough relief, other oral NSAIDs are advised for treatment (Bindu et al., 2020).

Not to forget, migraine is a severely crippling disorder that affects 12 to 15% of women and 8% of men. It is characterized by recurring attacks of unilateral, pulsatile headaches that are frequently accompanied by nausea and vomiting as well as phonophobia and photophobia. The medications that are most frequently used to lessen the impact of migraine attacks are NSAIDs. This is primarily due to over-the-counter sales, which are widely available, inexpensive, and, most significantly, offer a favorable "efficacy to adverse effect" profile for at least mild to moderate attacks. Ibuprofen and paracetamol were noted as two of the most and least effective therapies, respectively, in an evaluation of migraine treatment procedures (Msadrakis & Baldwin, 2021).

In patients with discomfort from renal colic, NSAIDs may be taken alone or in conjunction with opioids. They are delivered intravenously or orally, and they help lessen oedema, inflammation, and hyperactivity of the ureteric muscles. To get a quick reaction in an emergency, the latter path should be taken. Among the medications that can be used for this are

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piroxicam, diclofenac, ibuprofen, ketorolac, naproxen, and paracetamol (Kaplan, 2021).

5- Side effects of NSAIDs:

NSAIDs have a number of risk factors that can affect the cardiovascular system, central nervous system (CNS), and gastrointestinal tract. Myocardial infarction (MI) and ischemia are two cardiovascular problems that NSAIDs have been linked to NSAIDs (both selective and non-selective) and harmful cardiovascular events have been linked in recent research (Shaikh et al., 2021).

Regarding Gastrointestinal system, the phospholipids that preserve GI integrity are held together by the mucus layer of the GI tract. NSAIDs engage in interactions with both the mucus layer and the phospholipid bilayer of cells. Because of the interaction between NSAIDs and phospholipids, the hydrophobic lining is put at risk, which exposes the mucosa to substances that break down luminal barriers, such as pepsin and hydrochloric acid in the stomach and bacteria and bile in the small intestine. The presence of substances that cause mucosal breakdown and the reduction in mucosal PG synthesis may have a significant negative impact on microcirculation, resulting in severe inflammatory and ulcerative damage (Kaplan, 2021).

To reduce their negative systemic effects, opical NSAIDs have been created. For administering diclofenac, for instance, there are topical preparations in solution, gel, and patches. Recent studies have

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demonstrated that topical formulations are superior to oral formulations in their ability to reduce GI side effects and relieve pain. Patients over 75 years of age with osteoarthritis of the knee are advised to use topical formulations rather than oral NSAIDs, but not with osteoarthritis of the hip (Kaplan, 2021).

The most frequent Brain side effect in children on long-term NSAID therapy is headache. There may also be additional CNS symptoms such hyperactivity, sleep issues, and exhaustion. Ibuprofen can cause aseptic meningitis when an NSAID is involved, especially in those with systemic lupus erythematosus (Zhang et al., 2021).

Additionally, diclofenac prevents neuronal growth and differentiation. Following prenatal exposure to diclofenac, male rats' Purkinje cells, sciatic nerve, granular, and hippocampal pyramidal cells have been shown to have negative impacts. In a different study, diclofenac similarly decreased the quantity of hippocampus pyramidal cells in rat brain (Shaikh et al., 2021).

6- Conclusion:

In conclusion, despite having a limited awareness of the health hazards, side effects, and pharmacological interactions of NSAIDs, the majority of physiotherapists still advise them to their patients.

On long-term NSAID therapy, headache is the most common Brain side effect. Additionally, there could be CNS symptoms such hyperactivity, difficulty sleeping, and tiredness. Ibuprofen, especially in people with

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systemic lupus erythematosus, can result in aseptic meningitis when an NSAID is involved.

It is therefore recommended to administer NSAIDs and other analgesics, physiotherapists need undergo training through educational sessions such certification courses on pharmacotherapy (in particular pain drugs). The government should also amend the relevant laws to clarify the obligations placed on physiotherapists in terms of prescribing medications. These initiatives will be beneficial for pharmacy doctors who use painkillers in a method that is supported by evidence and secure for the patients.

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