

“A Review on Drug Induced Pruritus”

Viresh .K. Chandur¹, K. Anjali^{2*}, Ramakrishna Shabaraya A³

¹Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangalore, Karnataka, INDIA.

²Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangalore, Karnataka, INDIA.

³Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangalore, Karnataka, INDIA.

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ABSTRACT:

Drug-induced pruritus, also known as medication-induced itching, is a common side effect of various medications. It can range from mild irritation to severe discomfort and can occur with both over-the-counter and prescription drugs. This condition is a result of the body's reaction to certain drugs, and its underlying mechanisms can vary depending on the specific medication involved. The itching sensation associated with drug-induced pruritus can occur on the skin's surface or in more localized areas, such as the hands, feet, or genitalia. It may present as a temporary nuisance or persist for an extended period, sometimes leading to scratching, skin damage, and discomfort. The types of drugs that commonly cause pruritus include opioids, certain antibiotics, antifungals, chemotherapy drugs, and some medications used to treat psychiatric disorders. Early identification of the causative drug, discontinuation when appropriate, and targeted symptom management are key to alleviating itching and improving the patient's quality of life. In some cases, dosage adjustments or alternative medications may be considered under the supervision of a healthcare professional. Additionally, treatments to relieve the itching and discomfort, such as antihistamines, topical creams, or other medications, may be prescribed. Close collaboration between healthcare providers and patients is essential for successful management.

Keywords: Drug, Pruritus, Skin damage.

I. INTRODUCTION:

Drug-induced pruritus refers to itching or an extreme sense of skin irritation that is caused by the use of certain medications or drugs. Pruritus is a common side effect of many drugs and can range from mild discomfort to severe and distressing symptoms. ¹It is important to note that drug-induced pruritus can affect people differently, and the intensity varies depending on the drug, the individual's sensitivity, and the dosage. It may appear as a short-term discomfort or last for a long

time, and in certain cases, it can cause discomfort, skin damage, and scratching.²

The exact mechanism by which drugs induce pruritus can vary depending on the medication. Some drugs may directly irritate the skin or activate specific receptors in the nervous system, while others may lead to allergic reactions or systemic changes that result in itching. The types of drugs that commonly cause pruritus include opioids, certain antibiotics, antifungals, chemotherapy drugs, and some medications used to treat psychiatric disorders.^{3,4}

Early detection of the causative drug, discontinuation when appropriate, and targeted symptom management are key to alleviating itching and enhancing the patient's quality of life. Close collaboration between healthcare providers and patients is essential for successful management. Understanding drug-induced pruritus is essential, as it can significantly impact a patient's quality of life and adherence to prescribed treatments. This introduction provides an overview of the mechanism, management strategies associated with various types of drug-induced pruritus. Monitoring and managing this side effect can help improve a person's quality of life and ensure that their medical treatment remains effective and safe.⁵

Mechanism of drug induced pruritus:

Allergic Reactions:

Drug-induced pruritus resulting from allergic reactions to drug can vary in severity and presentation. These reactions are typically immunologically mediated, involving the immune system's response to the drug or its metabolites. In an allergic reaction to a medication, the patient is often sensitized to the drug, meaning their immune system has been exposed to the drug before, usually during a prior administration. During this initial exposure, the immune system recognizes the drug as foreign or harmful.⁶ Drug-induced allergic reactions involve immunoglobulin E (IgE), a type

of antibody. During sensitization, the body produces IgE antibodies specific to that drug. These antibodies attach to mast cells and basophils in the body.⁷When the patient is exposed to the drug again, the drug binds to the IgE antibodies on mast cells and basophils.⁸Binding of the drug to IgE antibodies triggers mast cell and basophil activation. This activation leads to the release of various substances, including histamine, which is a potent mediator of allergic responses.^{8,9}Histamine is released from mast cells and basophils into the bloodstream and surrounding tissues. Histamine's effects on histamine receptors (particularly H1 receptors) on sensory nerve endings in the skin lead to itching and the sensation of pruritus. In addition to histamine, other inflammatory mediators, such as leukotrienes and cytokines, may be released during the allergic reaction. These substances can contribute to the inflammatory response in the skin, further intensifying itching. The allergic reaction may manifest as localized pruritus at the site of drug administration or can lead to more widespread itching and other symptoms, such as hives, skin rash, facial swelling, shortness of breath, or anaphylaxis.^{8,9,10,11,12,13}

Direct skin irritants:

Direct skin irritants causing drug-induced pruritus refer to medications or substances that can directly irritate the skin upon contact, leading to itching and other skin reactions.

Drug-induced pruritus cases result from the use of topical medications, such as creams, ointments, and patches. These medications are applied directly to the skin or mucous membranes, and they can cause irritation, which may manifest as itching. Some medications contain chemical compounds that are known skin irritants. For example, certain antimicrobial agents, such as benzalkonium chloride or iodine-based preparations, can cause skin irritation and itching when applied topically. Excipients are inactive ingredients used in medications to enhance their stability or delivery. Some excipients may be irritants to the skin. For example, alcohol-based gels or creams can cause skin dryness and irritation, leading to pruritus.^{14,15}

Psychological factors:

Psychological stress, anxiety, and negative emotions can lead to the release of stress hormones like cortisol. Elevated cortisol levels have been associated with skin reactions, including itching. Stress and anxiety may also contribute to the

perception of itching, even if there is no direct physiological cause. In some cases, people with pre-existing skin conditions, such as eczema or psoriasis, may experience heightened psychological distress due to the visible nature of their skin issues. This distress can trigger or exacerbate itching, which may be misattributed to the drug they are taking.^{16,17}

Toxic metabolites:

In some cases, the metabolism of a drug can result in the formation of metabolites that have irritating or toxic properties. These metabolites can be chemically reactive or have the ability to interact with skin cells in a way that triggers an inflammatory response.

Individual susceptibility:

Genetic variations can influence an individual's susceptibility to drug-induced pruritus. Some people may have genetic predispositions that make them more or less sensitive to certain medications or the development of hypersensitivity reactions, which can lead to itching. The immune system's response to a medication can vary among individuals. Some people may mount a more robust immune response to certain drugs, resulting in an increased risk of hypersensitivity reactions and pruritus. A person's history of allergies, especially to drugs, can influence their susceptibility to drug-induced pruritus. If someone has a history of drug allergies, they may be at a higher risk of experiencing itching as a side effect when exposed to similar medications. The use of other medications in combination with the drug in question can influence susceptibility to drug-induced pruritus. Drug interactions can lead to unexpected side effects or exacerbate existing ones.¹⁸

Types of drugs associated with pruritus:

Opioid-induced pruritus:

Opioid-induced pruritus (OIP) is a condition characterized by itching that occurs as a side effect of taking opioid medications. Opioids are powerful pain-relieving medications commonly used to manage severe pain, but they can also have various side effects, including itching.

Mechanism: Opioids bind to specific receptors in the brain and spinal cord, which can lead to the release of histamines and other substances that trigger itching. Histamine is a key mediator of itching produced by orally administered opioids. Some opioids, such as morphine or codeine, may directly release histamine from mast cells in a

nonimmunological manner. More than one mechanism may be involved in producing opioid-induced pruritus. The dorsal region of spinal cord and the trigeminal nerve nucleus are areas that have a high density of both mu-opioid and serotonin-type 3 (5-HT₃) receptors, there is raised the interaction between opioids and 5-HT₃ receptors may play a role in the development of pruritus. Prostaglandins, dopamine type 2 receptors, and antagonism of gamma-aminobutyric acid and glycine receptors in the central nervous system have also been suggested as possible mechanisms of opioid-induced pruritus. Also, systemic administration of opioids morphine, codeine, and meperidine can induce mast cell activation and histamine release.^{8,19,20,21,22,23}

OIP can occur shortly after taking an opioid medication or may develop after prolonged use. It can be acute or chronic. Acute OIP usually resolves quickly after discontinuation of the opioid, while chronic OIP may persist as long as the opioid therapy continues.

Management and Treatment:

In some cases, reducing the opioid dose may alleviate or reduce itching. However, this needs to be carefully managed by a healthcare professional to ensure effective pain control. Switching to a different opioid medication with a different receptor profile may help in managing OIP. Antihistamine medications can be used to reduce itching associated with OIP. They work by blocking the effects of histamine, which is one of the substances involved in the itching response. In some cases, naloxone, an opioid receptor antagonist, may be administered to reverse the effects of opioids and relieve itching. Topical creams or ointments containing soothing ingredients like hydrocortisone may be used to relieve localized itching.^{21,22,23,24}

Antibiotic induced pruritus:

Antibiotic-induced pruritus can arise for various reasons, and it may manifest differently depending on the individual and the specific antibiotic being used. Certain classes of antibiotics are more commonly associated with itching as a side effect which includes Penicillins such as amoxicillin and ampicillin, Sulfonamides antibiotics like sulfamethoxazole and trimethoprim, Tetracycline antibiotics, including doxycycline and minocycline, Macrolide antibiotics like erythromycin and azithromycin.

Mechanisms:

Antibiotics can sometimes trigger allergic reactions in certain individuals. Pruritus is one of the possible symptoms of an allergic reaction. This itching may be accompanied by other symptoms like hives, rash, swelling, or difficulty breathing. Allergic reactions can range from mild to severe, with severe cases constituting a medical emergency. Antibiotics, especially when administered intravenously, can irritate the skin and blood vessels at the injection site, leading to localized itching.

Management and Treatment:

If antibiotic-induced pruritus is suspected, healthcare provider may consider discontinuing the antibiotic and replacing it with an alternative that the patient can tolerate. Over-the-counter or prescription antihistamines can help alleviate itching caused by allergic reactions or drug rashes. These medications work by blocking the effects of histamine, a chemical involved in the itching response. Topical creams or ointments containing corticosteroids can be applied to the itchy areas to reduce inflammation and provide relief. Using moisturizers can help soothe dry and irritated skin, reducing itching.^{25,26,27}

Psychiatric medication induced pruritus:

While pruritus can potentially occur with any psychiatric medication, some medications are more commonly associated with itching. Antipsychotic medications, such as chlorpromazine, quetiapine, and risperidone, antidepressants particularly tricyclic antidepressants like amitriptyline and nortriptyline, have been associated with pruritus in some cases.

Mechanisms:

Some individuals may be hypersensitive or allergic to specific psychiatric drugs, which can lead to itching as one of the allergic symptoms. This itching may be accompanied by skin rash, hives, swelling, or difficulty breathing. Some psychiatric drugs can affect the nervous system and neurotransmitters, potentially leading to changes in sensory perception, including itchiness. These mechanisms are not entirely understood and may vary depending on the specific medication. Certain psychiatric medications, particularly antipsychotics and antidepressants, can cause dry skin as a side effect. Dry skin is more prone to itching. In some cases, psychiatric medications may exacerbate or

trigger pre-existing skin conditions, such as eczema or psoriasis, leading to pruritus.

Management and Treatment:

If pruritus occurs as a side effect of a psychiatric drug, clinician evaluate the situation and may recommend discontinuing the medication, switching to an alternative psychiatric drug or adjusting the dosage of the psychiatric medication to minimize side effects. Antihistamines can help alleviate itching associated with allergic reactions or drug-induced pruritus. For localized itching, using a moisturizing cream or ointment can help soothe and hydrate dry skin.^{22,28,29}

Anti-malarial induced pruritus:

Different anti-malarial drugs may have varying rates of pruritus as a side effect. Chloroquine and Hydroxychloroquine, Mefloquine, Quinidine also cause itching as a side effect.

Mechanisms:

Pruritus can occur as part of an allergic reaction to anti-malarial medications. Some individuals may be hypersensitive to specific anti-malarials, leading to itching along with other allergic symptoms such as skin rash, hives, swelling, or difficulty breathing. Some anti-malarial drugs, particularly those administered topically, can cause skin irritation or contact dermatitis, leading to itching as a side effect. This is more common with drugs like chloroquine and hydroxychloroquine.^{8,22}

Management and Treatment:

Healthcare provider may recommend dosage adjustments, switching to a different anti-malarial medication, discontinuing the medication or dosage adjustments. Over-the-counter or prescription antihistamines can help relieve itching associated with allergic reactions or drug-induced pruritus.

Using a soothing and moisturizing cream or ointment can help alleviate discomfort and dryness of the skin.^{8,30,31,32}

Chemotherapy drug induced pruritus:

Common Chemotherapy Drugs Associated with Pruritus includes Paclitaxel and Docetaxel, Cetuximab and Panitumumab, Bortezomib,

Pruritus, or itching, can be a side effect of chemotherapy, which is a common treatment for various types of cancer. Itching can be distressing

for cancer patients, and its severity can vary depending on the type of chemotherapy drug used and the individual's sensitivity to the medication. Here's some information on chemotherapy drug-induced pruritus:

Mechanisms:

Chemotherapy drugs can cause skin reactions, including itching. These reactions can range from mild to severe and may include dryness, rash, redness, or peeling of the skin. The specific mechanisms behind chemotherapy-induced pruritus are not fully understood but may involve inflammation, changes in skin hydration, or interactions with nerve fibers in the skin. In some cases, individuals may develop an allergic reaction to certain chemotherapy drugs, leading to itching as one of the allergic symptoms. This type of itching is typically accompanied by other allergic manifestations such as hives, swelling, or difficulty breathing. Chemotherapy drugs can affect the entire body, including the nervous system. Some individuals may experience itching as a result of these systemic effects.^{8,22}

Management and Treatment:

Discontinuation is not the choice for itch caused by anticancer drugs. One should continue with anticancer therapy with the aid of symptomatic antipruritic treatment in order to avoid dose reduction and discontinuance of anticancer drugs. A short-term systemic cortisone application should also be considered as a symptomatic treatment. If itching is not sufficiently reduced after discontinuation of the suspected drug, symptomatic treatment should be applied. First-line symptomatic treatment includes topical moisturizers, systemic H₁ -antihistamines, and topical corticosteroids in case secondary eczematous lesions exist. In some cases, oral or topical steroids can be prescribed to reduce inflammation and itching.^{8,22,33,34}

II. CONCLUSION:

Managing drug-induced pruritus involves addressing the underlying cause, alleviating the symptoms, and discontinuing or changing the medication responsible for the condition. Managing drug-induced itching involves identifying and stopping the medication responsible. Symptomatic relief can be achieved through measures like topical treatments, antihistamines, and cool compresses. In severe cases, oral corticosteroids or immunosuppressive agents may be considered. It's important to address underlying causes and

consider preventive measures. Patients should communicate any unusual symptoms to their healthcare provider for proper evaluation and guidance. Overall, a tailored approach with medical supervision is key for effective treatment of drug-induced pruritus.^{35,36,37,38}

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