



Phototoxicity of Drugs

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Abstract:

The awareness about the adverse effect of the drugs prescribed by the doctors is very less. Phototoxicity being one such adverse effect there has to be a potential awareness among people. Few such drugs which causes that kind of toxicity is being discussed here.

INTRODUCTION:

The drugs which we use besides its therapeutical property has some side effects. Few if these side effects would have an adverse effect on d human body. One such adverse effect of the drug is known as phototoxicity. Not all the drugs has this property. There are few drugs that elicit this property. Some of those drugs which fall into this category are discussed here.

PHOTOTOXICITY :

Phototoxicity, also called photoirritation, is a chemically induced skin irritation requiring light that does not involve the immune system. It is a type of photosensitivity.[1][2] The skin response resembles an exaggerated sunburn. The involved chemical may enter into the skin by topical administration or it may reach the skin via systemic circulation following ingestion or parenteral administration.

The chemical needs to be "photoactive", which means that when it absorbs photons, the absorbed energy produces molecular changes that cause toxicity. Many synthetic compounds, including drug substances like tetracyclines or fluoroquinolones, are known to cause these effects.

DRUGS THAT PRODUCE PHOTOTOXICITY :

There are various drugs that produces phototoxicity . These drugs falls under the categories of Antibiotics, Non-steroidal anti-inflammatory drugs, Diuretics, Retinoid, Para amino benzoic acid, Epidermal growth factor inhibitor, Anti fungal ,Neuroleptic drugs and few other drugs.

MECHANISM:

Phototoxic reactions occur because of the damaging effects of photoactivated compound on cellular structures such as cell membranes or DNA. Many compounds have the potential to cause phototoxicity. Most have at least one resonating double bond or an aromatic ring that can absorb radiant energy. In most instances, photoactivation of a compound results in the

excitation of electrons from the stable singlet state to an excited triplet state. As excited-state electrons return to a more stable configuration, they transfer their energy to oxygen, leading to the formation of reactive oxygen intermediates. Reactive oxygen intermediates such as an oxygen singlet, superoxide anion, and hydrogen peroxide damage cell membranes and DNA. Signal transduction pathways that lead to the production of proinflammatory cytokines and arachidonic acid metabolites are also activated. The result is an inflammatory response that has the clinical appearance of an exaggerated sunburn reaction. (3)

ANTIBIOTICS:

Few antibiotics produce phototoxicity. Few such drugs are tetracyclines ,fluoroquinolones, sulfonamides. Tetracycline phototoxicity in vitro was partially oxygen-dependent and possibly singlet oxygen is involved. The contribution of photoproducts to the phototoxic process may be the basis for the reported differences between the in vivo action spectrum and the absorption spectrum of demethylchlorotetracycline. A mechanistic model for in vivo phototoxicity is proposed where the absorption of UVA radiation by TC leads to at least two main processes: (i) photosensitization by the drug of biologic molecules to cause phototoxicity; (ii) production of one or more photoproducts which photosensitize by absorption of visible radiation.(4) Sulfonamide derived drugs and diuretics are seen to show phototoxicity in culture cells. It's component Bendroflumothiazide was found to be phototoxic and higher concentration of few other components like Hydroflumethizide was also found to be phototoxic. On electron microscopy these drugs are found to produce swelling of mitochondria and endoplasmic reticulum.(5)

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS:

Phototoxicity is a well known side effect of the NON-STEROIDAL ANTI-INFLAMMATORY DRUGS, which is aggravated by UV rays. Phototoxic effect induced by visible light is important regarding the clinical

photosensitization.(6) Ketoprofen has often implicated photosensitive reaction. It increases the photolysis of erythrocytes suspensions. It may also induce DNA damage in vitro on irradiation. It is the main drug involved in photo allergic contact dermatitis.(7)

DIURETICS:

Several oral anti diabetics and diuretics are found to be phototoxic. Inhibiting effects of antioxidants point towards involvement of reactive oxygen species in phototoxic DNA damage. Excessive exposure of UV radiation on patients treated with these drugs may result deleterious to the patients (8).

Furosemide is an phototoxic diuretics. It is photolabile under aerobic and anaerobic condition. But on irradiation it produces singlet oxygen and photoproducts which are responsible for the phototoxic effect. (9)

RETINOIDS:

The side effect, phototoxicity, of these retinoids are not fully experimented. But still these drugs are found to produce side effects. Because they are exposed to the environment, the skin and eyes are more vulnerable to phototoxic damage than other organ systems. Retinoids are naturally abundant in both of these tissues and participate in specific phototoxic mechanisms. Photoirradiation of retinoids may generate acute and chronic toxicity through the formation of photoreaction products that are toxic, or photoexcitation of retinoids forming the excited retinoid species that exert toxicity directly or indirectly. Retinoids absorb light in the UVA range. For instance, RP has a maximum UV-visible absorption at 326 nm and thus, may be able to absorb UVA light and act as a photosensitizer. Thus, photoactivation of RP could generate short-lived ROS that have been shown to damage DNA and proteins and lead to tumors.(10)

HMG CoA REDUCTASE INHIBITOR:

HMG CoA reductase inhibitors are also seen to produce phototoxicity. Fluvastatin which is a HMG CoA reductase inhibitor is seen to undergo photo degradation on irradiation to UVA, which resulted in the formation of a polycyclic compound resembling a benzene ring. This product is seen to produce phototoxic effect. It was seen to reduce cell viability and increase necrosis. There also occurs increase in intracellular calcium level which leads to extensive cell lipid membrane peroxidation.(11)

NEUROLEPTIC DRUGS:

Most neuroleptics are phototoxic invitro indicating a potential risk of photo reactions. (12)

ANTI FUNGAL:

Even these drugs are found to produce phototoxic side effects. An important drug falling under that category variconazole. Variconazole is a highly selective inhibitor of fungal cytochrome P450 enzymes.(13)

CONCLUSION

Phototoxicity of various drugs have been discussed here. It is a common effect and patients should be potentially aware of this toxicity. Awareness of the causes may help to reduce the incidence of this problem. This kind of awareness is needed in both patients and the practioners.

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