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Unpredictable Systemic Risks to Topical Drugs

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An adverse drug reaction (ADR) is commonly defined as undesired reaction experienced as a result of parenteral or oral drug administration. Virtually, every drug is able to produce unwanted adverse effects which can be predictable from the drug's known pharmacology and are usually dose dependent with high morbidity rate or unpredictable on the basis of the drug's pharmacology. The latter reactions are generally unrelated to dosage and though comparatively rare, but they often cause serious illness and death. Topical drugs are often applied to lower such risks of systemic side effects, indeed; mishandling them can lead to unpredicted complications in patients or administrator of the drug [1].

Many topical drugs are applied directly to the skin, or may be inhaled such as in the treatment of asthma, or applied to tissue surfaces as eye or ear drops, all intended with local effects rather than systemic. Such drugs are applied in the form of cream, gel, lotion, ointment or powder and often available over-the-counter. Depending on the dose and the physico-chemical properties, e.g. lipophilic, topical (dermal, ocular, optical) drugs containing such as glucocorticoids, beta-blockers (e.g. timolol) and antibiotics (e.g. chloramphenicol) can be well absorbed through the skin and cause rather serious systemic side effects.

Among the adverse events associated with topical glucocorticoid dermal use, the most serious is the hypothalamic-pituitary adrenal (HPA) axis suppression which can be life threatening, resulting in decreased levels of ACTH, atrophy of cells of the adrenal cortex [2]. Also, topical ocular and otic medications were associated with similar serious adverse reactions [3,4]. Moreover, changes in liver metabolism have been also described as a result of local corticosteroid application [4]. Pediatric and elderly patients are particularly vulnerable to systemic effects of topically applied drugs. Thus, since it is currently intended to produce drugs on the basis of topical formulations, serious care should be taken when drugs that produce systemic side effects are applied locally to the skin, eye or ear, and physician should be aware of steps taken to minimize systemic adverse reactions. Furthermore, more insight has to be provided to which extent adverse reactions can occur particularly in adults, children or elderly patients in relation to local therapy.

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