Rational Use of Antihistamines in Allergic Dermatological Conditions

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Summary

For many years, the use of antihistamines in dermatological conditions has been closely linked to the treatment of urticarias and to the symptomatic relief of pruritus. H₁-receptor antagonists are the first-line drugs for urticarias. Those urticarias of type I immunological origin respond better than physical urticarias. H₂-receptor antagonists may be added for refractory patients but are rarely effective alone. Conventional H₁-blockers are frequently associated with somnolence and anticholinergic effects. Therefore, new antihistamines without depressive effects on the central nervous system have recently been introduced.

In other pruritic conditions such as atopic dermatitis the limited effects of these drugs suggest that histamine is not the only mediator involved in pruritus. In these cases, their...
For a long time antihistamines have been considered very useful in the clinical management of certain cutaneous allergic disorders; their first indication remains urticarias, but they are also useful for relieving pruritus associated with various dermatoses such as eczema. Earlier antihistamines were poorly tolerated by many patients because of their sedative effects. The newer generation of histamine H₁-receptor antagonists which are devoid of central sedating effects, and the appearance of histamine H₂-blockers, has led us to question the value of conventional H₁-receptor antagonists. It is worth examining whether antihistamines are still of interest today, or if the new drugs provide a complete substitute for all indications. The use of H₂-receptor antagonists in dermatological disorders is also of interest.

This article attempts to answer these questions by examining the way in which histamine is involved in the various cutaneous pathologies, and the differences between antihistamines in addition to their central effects. Finally, how to choose and prescribe an antihistamine in dermatology is considered.

1. Histamine and the Skin

In normal skin, histamine is stored mainly in the granules of dermal mast cells (Eady et al. 1979), and to a lesser extent in vascular walls (El Ackad & Brody 1975). Under the influence of various exogenous or endogenous pharmacological or immunological stimuli, it may be released in situ. The mechanisms of degranulation in such cases are not specific to the skin. Under certain pathological conditions of the delayed hypersensitivity type, histamine may also be released from cutaneous infiltrates of basophils (Goldman et al. 1973).

1.1 Action of Histamine on the Skin

The action of histamine on the skin is manifested by the classical Lewis triple response (Lewis 1927): (a) an intradermal injection of histamine leads to oedema (weal) and erythema; (b) erythema is initially localised at the site of injection due to direct vasodilatation (redness), but spreads rapidly due to axon reflex (flare); and (c) the injection also induces pruritus or pain depending on whether it is intraepidermal or intradermal.

Direct vasodilatation is difficult to detect as it is quickly masked by the axon reflex; it only appears after this reflex has been blocked with lignocaine (lidocaine). The axon reflex is conveyed by myelinic nociceptive fibres and seems to be mediated by various substances, including substance P; it is blocked by capsaicin (Foreman & Jordan 1983). The mechanism of formation of the oedematous papule has not yet been clearly determined and in its last phase, it may involve other mediators such as prostaglandins (PGs) or endogenous peptides. Its development is impaired by noradrenaline (norepinephrine) [an α-adrenoceptor agonist] and by salbutamol (albuterol) [a β₂-adrenoceptor agonist] (Basran et al. 1982). The reaction is greatest about 10 minutes after the injection and almost totally subsides within 1 hour. The intensity of skin reactions to histamine diminishes with age; it follows a circadian rhythm and is maximal at night (Reinberg et al. 1964). Repeated injections result in tachyphylaxis.

1.2 Skin H₁- and H₂-Histamine Receptors

The partial failure of conventional antihistamines in the treatment of urticaria has led researchers to postulate that other mediators beside histamine (e.g. bradykinins and prostaglandins) may be involved in the vascular changes observed, and that the skin may contain several types of hist-